

Efficacy and safety of acellular dermal matrix versus connective tissue graft for root coverage of Miller's Class I and II gingival recession: a systematic review and meta-analysis

Min Zhang¹, Mengxi Wang², Chunli Zhang³

¹Department of Prosthodontics, Suqian Stomatological Hospital, Suqian, China; ²Department of Periodontology, Suqian Stomatological Hospital, Suqian, China; ³Department of Orthodontics, Suqian Stomatological Hospital, Suqian, China

Contributions: (I) Conception and design: M Zhang, M Wang; (II) Administrative support: M Wang; (III) Provision of study materials or patients: M Wang; (IV) Collection and assembly of data: M Zhang, M Wang; (V) Data analysis and interpretation: M Zhang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Chunli Zhang. Department of Orthodontics, Suqian Stomatological Hospital, 308 Shifu East Road, Sucheng District, Suqian 223800, China. Email: CLzhang_doctor@163.com.

Background: The efficacy and safety between connective tissue graft (CTG) and acellular dermal matrix (ADM) remain inconsistent. Meta-analysis is a valuable approach to resolve inconsistencies across studies and provide a high level of evidence to comprehensively evaluate the effect and safety of ADM versus CTG for root coverage of Miller's Class I and II gingival recession. Our study was conducted to comprehensively analyze the efficacy and safety of ADM versus CTG for root coverage in patients with gingival recession.

Methods: Articles on randomized controlled trials (RCTs) that compared the ADM with CTG for adult patients with the gingival recession in terms of percent root coverage (PRC), clinical attachment level (CAL), keratinized tissue (KT), probing depth (PD), recession width (RW), and recession depth (RD) were identified in PubMed, Embase, Cochrane Library, and Web of Science databases until 15 May 2020. Weighted mean difference (WMD) was used as the statistic for measurement data and the effect sizes were expressed as 95% confidence intervals (CIs).

Results: A total of 24 RCTs were eligible for the final analysis. A total of 587 patients with 1,315 gingival recession sites were involved in the study. There were 724 loci in the ADM group and 591 loci in the CTG group. The patients who underwent ADM had a higher gain in CAL (WMD: 0.25, 95% CI: 0.03 to 0.47, P=0.026) but a smaller gain in KT width (WMD: -0.44, 95% CI: -0.63 to -0.25, P<0.001) than those who underwent CTG. No significant differences were found between the patients who underwent ADM and those who received CTG in PRC (WMD: -1.61, 95% CI: -3.49 to 0.28, P=0.094), PD (WMD: 0.07, 95% CI: -0.01 to 0.14, P=0.067), RW (WMD: 0.07, 95% CI: -0.10 to 0.23, P=0.437), and RD (WMD: 0.11, 95% CI: -0.10 to 0.31, P=0.294).

Discussion: The ADM treatment for patients with gingival recession may be superior to CTG in gaining CAL, but CTG has a significant advantage over ADM for gaining KT width. ADM can be considered in the future as a treatment for root coverage in patients with gingival recession.

Keywords: Acellular dermal matrix (ADM); connective tissue graft (CTG); gingival recession; root coverage; meta-analysis

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Introduction

Gingival recession is defined as the exposure of the root surface following an apical shift in the position of the gingiva beyond the cementoenamel junction (CEJ) (1). It can locally or generally affect one or more tooth surfaces, and is more common in adults (2,3). As a highly prevalent condition worldwide, gingival recession can increase the risk of root caries and affect patient comfort and esthetics (4). In addition, progressive gingival recession has also been found to be associated with an increased risk of tooth loss secondary to clinical attachment loss (CAL) (5). It is universally recognized that anatomical abnormalities, inflammation, trauma, and iatrogenic factors including placement of orthodontic appliances and improper denture design can lead to gingival recession (6). Although reducing these causes is conducive to decreasing its incidence and severity, it is very important to implement practical management and preventative strategies in clinic.

In recent years, numerous techniques have been developed to treat gingival recessions. The subepithelial connective tissue graft (CTG) is considered the gold standard for localized recession defects because of its predictability in increasing the width of keratinized gingiva and in achieving root coverage (7). This technique requires tissue to be harvested from the palate and then placed over an appropriate recession defect with coronal advancement of the flap over the donor graft (8). However, harvest tissue from the palatal area is time consuming and increases the postoperative morbidity of patients, such as pain, bleeding, and hyposensitivity (9,10). In case of a lack of sufficient donor material, an increased number of staged surgeries may be needed for patients with multiple recessions. Acellular dermal matrix (ADM) was developed as a substitute for autogenous CTG and has presented a potential alternative to thicken soft tissues and cover multiple gingival recessions (11). Al-Hamdan et al. found that the use of ADM with the coronally advanced flap resulted in a significant increase in keratinized tissue (KT) and percent root coverage (PRC) (12). Nevertheless, CTG may be slightly superior to ADM if the gain of keratinized mucosal width is taken as a main goal (13). Another study (14) evaluating the 9-year assessment of treated isolated gingival recessions and their adjacent untreated sites reported that ADMtreated sites displayed recession relapse from 1 to 9 years. However, Maluta et al. demonstrated that both treatments were effective for treating multiple gingival recessions (15). Barros et al. also reported that ADM presents consistent

levels of root coverage when compared with CTG (16). This may be due to inconsistent differences in study design, such as search sources, results measurements, and sample sizes. Meta-analysis is a statistical analysis method based on evidence-based medicine. The purpose of meta-analysis is to comprehensively analyze the research results of multiple small samples of the same subject, so as to increase the sample size, improve the research efficiency of the original results, and make the conclusions more representative. A meta-analysis based on the randomized controlled trials (RCTs) that comprehensively analyze the efficacy and safety of ADM versus CTG for root coverage in patients with gingival recession is needed.

The current meta-analysis was conducted to comprehensively analyze the efficacy and safety of these two procedures for root coverage among patients presenting with gingival recession. We present the following article in accordance with the PRISMA reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-656/rc).

Methods

Search strategy

This procedure of search was conducted by two of the researchers (Min Zhang and Mengxi Wang). Databases including PubMed, Embase, Cochrane Library, and Web of Science were searched for articles until 15 May 2020. Terms used for search in various combinations included 'acellular dermis', 'connective tissue graft', 'root coverage', and 'gingival recession'.

Inclusion and exclusion criteria

Study inclusion and exclusion criteria was conducted by Min Zhang. The inclusion criteria in a patient/population, intervention, comparison, and outcomes (PICOS) format were as follows: (I) population (P): adults with gingival recession; (II) intervention (I): ADM; (III) comparison (C): CTG; (IV) outcome (O): PRC as the primary outcome, clinical attachment level (CAL), KT, probing depth (PD), recession width (RW), and recession depth (RD) as secondary outcomes; and (V) study design (S): RCTs with the study length of 3 months or above. Studies from which we were unable to extract the valid data, those not published in English, as well as meta-analyses, reviews, case reports, and animal experiments were all excluded.



Figure 1 Flow diagram of the screening and selection process of studies.

Literature bias risk and quality evaluation

The risk of bias and quality of in RCTs were assessed by the Cochrane Risk of Bias 2.0 Tool according to the Cochrane Handbook for Systematic Reviews of Interventions (17). The literature quality evaluation was completed by two reviewers (Min Zhang and Mengxi Wang) independently. In case of any disagreement, the third reviewer (Chunli Zhang) would be invited to resolve the disagreement by arbitration.

Data extraction

A list of articles was compiled by two researchers (Min Zhang and Mengxi Wang). After filtering out duplicate articles, initial screening by reading article titles and abstracts was performed. Further screening by reading the full text to screen articles based on inclusion and exclusion criteria. If two researchers disagreed during the extraction process, a third person was consulted for arbitration. The extracted data contained the first author, year of publication, country, study length, participants, Miller classification, surgical methods, postoperative intervention, number of sites and patients, gender, age, and quality assessment.

Statistical analysis

All studies were statistically analyzed using Stata 15.1 software (Stata Corporation, College Station, TX, USA). Weighted mean difference (WMD) was used as the statistics for measurement data and the effect sizes were expressed as 95% confidence intervals (CI). Heterogeneity tests were performed for each effect size, and random effects models were adopted when $I^2 \ge 50\%$, otherwise the fixed effects model was applied. A difference was considered statistically significant at P<0.05. When $I^2 \ge 50\%$ and P<0.05, subgroup analysis was performed according to the study length and quality of literature. Publication bias was tested by Begg's test.

Results

Baseline information of included studies

According to the search strategy, 24 RCTs (13,16,18-39) were finally included in this meta-analysis (*Figure 1*). A total of 587 patients with 1,315 gingival recession sites were involved in the study. There were 724 loci in the ADM group and 591 loci in the CTG group. *Table 1* shows the baseline information of included studies.

Table 1 Base	line inform	nation of included studi	SS						
Study	Study length	Participants/Miller classification	Surgical methods	Postoperative intervention	Groups	No. of sites	No. of patients	Male/ female	Age (years)
Harris (21), 2000 America	3 months	50 participants; Miller Class I or II recessions	ADM vs. CTG (CT side toward flap); releasing incisions; no root	Routine postoperative instructions; dressing; suture removal at 14 days	ADM CTG	25 25	25 25	12/13 10/15	40.8±12.2 39.6±11.7
			condition						
Aichelmann- Reidy (18), 2001 America	6 months	22 participants; Miller Class I or II recessions of at least 2 mm	ADM vs. CTG (CT side toward tooth); releasing incisions; no root conditioning	NSAID and amoxicillin (dose and duration not provided); dressing; suture removal at 10 days; no CHX	ADM CTG	22 22	22 22	7/15 7/15	47.2 [24–67]* 47.2 [24–67]*
Henderson	12 months	10 participants; Miller Class I or II recessions	ADM vs. CTG (CT side toward flao): releasing incisions: no root	Systemic doxycycline hyclate 50mg once a day for 14 days. Dexamethasone taking 3 mg for 3 days. 2 mg for	ADM	10	10	5/5	42.2±16.7
America		of at least 3 mm	conditioning	3 days, then 1 mg for 3 days, one dose daily; Naproxen 375 mg every 12 hours for 7 days;0.12% CHX	CTG	10	10	5/5	42.2±16.7
Novaes (27),	6 months	9 participants; Miller	ADM vs. CTG (CT side toward flap);	Amoxicillin (500 mg tid for 7 days); dressing; suture	ADM	15	6	2/7	42±9.42
		Class I of II	releasing incisions, root condutoring with tetracycline	removariat 15 days, U. 1270 CFIX	CTG	15	6	2/7	42±9.42
Paolantonio	12 months	30 participants; Miller	ADM vs. CTG (CT side toward	Analgesics; no dressing; suture removal at 15 days;	ADM	15	15	11/19	34.5±5.2
(zø), zuuz, Italy		of at least 3 mm	tooth); releasing incisions when needed; no root conditioning	U.12% CHX	CTG	15	15		34.5±5.2
Hirsch (23), 2005 Israel	24 months	166 participants; Miller Class I or II	ADM vs. CTG (CT side toward tooth); releasing incisions; no root	Amoxicillin (500 mg tid) and ibuprofen (400 mg x2) were prescribed. Chlorhexidine gluconate mouth rinses (0.2%)	ADM	262	101	37/64	24.0±0.5
			conditioning	bid) were also prescribed. Sutures were removed after 10 days in most cases	CTG	169	65	22/43	25.4±2.3
Rahmani (29),	6 months	14 participants; Miller	ADM vs. CTG (CT side toward	No prescriptions mentioned; dressing; suture removal	ADM	10	14	8/6	41.7 [23–62]*
2006, Iran		Class I or II recessions	tooth); releasing incisions; no root conditioning	not specified; 0.2% CHX (starting 2 days prior; the duration of use not specified)	CTG	10	14	8/6	41.7 [23–62]*
Joly (25), 2007	6 months	10 participants; Miller	ADM vs. CTG (orientation not	NSAID and acetaminophen; no dressing; suture removal	ADM	10	10	6/4	[27–51]*
Brazil		Class I or II recessions of at least 3 mm	provided); no releasing incisions; conditioned with tetracycline	at 14 days, 0.12% CHX	CTG	10	10	6/4	[27–51]*
Haghighati	6 months	16 participants; Miller	ADM vs. CTG (CT side toward	NSAID; dressing; suture removal at 10 days; 0.2% CHX	ADM	16	16	8/8	NA
(20), 2009 Irar	-	Class I or II recessions of at least 2 mm	ttap); releasing incisions; no root conditioning		CTG	16	16	8/8	NA
Sadat	6 months	5 participants; Miller	ADM vs. CTG (CT side toward	NSAID and amoxicillin; dressing; suture removal at 15	ADM	0	£	2/3	37.6±8.26
2010 Iran	_	Class I or II recessions of at least 2 mm	itap); releasing incisions; no root conditioning	days; U.2% CHX	CTG	6	Q	2/3	37.6±8.26
Moslemi (26),	5 years	15 participants; Miller	ADM vs. CTG (CT side toward	NSAID; dressing; suture removal at 10 days; 0.2% CHX	ADM	15	15	7/8	39.4±5.2
2011 Iran		Class I or II recessions of at least 2 mm	tooth); releasing incisions; no root conditioning		CTG	15	15	7/8	39.4±5.2
Table 1 (contin	(pən								

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	Childry	Dottininate // Aillor				Jo P			
Study	length	classification	Surgical methods	Postoperative intervention	Groups	sites	patients	female	Age (years)
Koudale (39),	6 months	10 participants; Miller	ADM vs. CTG (CT side toward	NSAID, acetaminophen, and amoxicillin (500 mg tid for	ADM	Ð	Ð	AN	22.5±8.23
2012 India		Class I or II recessions of at least 2 mm	flap); releasing incisions; no root conditioning	7 days); dressing; suture removal at 14 days; 0.12% CHX	CTG	2ı	2	٩N	22.5±8.23
Gholami (38),	6 months	16 participants;	ADM vs. CTG (CT side toward	Acetaminophen and amoxicillin (500 mg tid for 7 days);	ADM	16	16	ΑN	NA
2013 India		Miller Class I or II recessions	tlap); double papillary tlap; root conditioning with tetracycline	dressing; suture removal at 10 days;0.12% CHX	CTG	16	16	٩N	AN
Shori (37),	6 months	20 participants; Miller	ADM vs. CTG (CT side toward	NSAID, acetaminophen, and amoxicillin (500 mg tid for	ADM	10	10	AN	29.7±4.35
2013 India		Class I or II recessions of at least 3 mm	tooth); releasing incisions; no root conditioning	7 days); dressing; suture removal not specified; 0.2% CHX	CTG	10	10	٩N	29.7±4.35
Thomas (33),	6 months	10 participants; Miller	ADM vs. CTG (CT side toward	NSAID and amoxicillin (500 mg tid for 5 days); dressing;	ADM	10	10	AN	34 [18–50]*
2013 India		Class I of II recessions	tootn); releasing incisions; no root conditioning	suture removal at 14 days; U.2% CHX	CTG	10	10	AN	34 [18–50]*
Goyal (36),	6 months	30 participants; Miller	ADM vs. CTG (orientation not	NSAID and doxycycline hyclate (200 mg on 1st day and	ADM	15	15	AN	NA
2014 India		Class II recessions of at least 4 mm	provided); releasing incisions; no root conditioning	iou mg/day ror / days); no dressing; suture removal at 10 days; 0.2% CHX	CTG	15	15	AN	AN
Barros (16), 2015 Brazil	12 months	15 participants; Miller Class I or II recessions	ADM vs. CTG (CT side toward tooth); releasing incisions and	NSAID and amoxicillin (500 mg tid for 7 days); no dressing; suture removal at 15 days; 0.12% CHX	ADM	15	15	5/10	[23–54]*
		of at least 3 mm	extended flap technique; root conditioning with EDTA		CTG	15	15	5/10	[23–54]*
Taiyeb Ali (32)), 6 months	6 participants; Miller	ADM vs. CTG (CT side toward	0.12% CHX; No other postoperative details	ADM	4	ю	3/3	37.8 [23–58]*
2015 Malaysi	Ø	Class I or II recessions of at least 3 mm	tooth); releasing incisions; root conditioning with tetracycline		CTG	4	ო		37.8 [23–58]
Thakare (35),	6 months	20 participants; Miller	ADM vs. CTG (CT side toward	NSAID and acetaminophen; dressing; suture removal at	ADM	21	10	ΝA	[18–50]*
		Class I or II recessions of at least 2 mm	itap); releasing incisions; no root conditioning	14 days; 0.2% CHX	CTG	23	10	NA	[18–50]*
Hutton (24), 2018 America	4 months	20 participants; Miller Class I or II recessions	ADM vs. CTG (CT side toward flap); releasing incisions; no root	Amoxicillin 500 mg for 7 days, Clindamycin 300 mg for 7 days. An NSAID (Ibuprofen 600 mg every 6-8 hours for	ADM	10	10	6/4	59.7±10.9
			conditioning	3 to 5 days) and a narcotic pain reliever (hydrocodone/ APAP 5/325 mg every 6-8 hours as needed for pain, up to 4 days)	СТG	10	10	5/5	51.2±11.0
Vreeburg (34), 2018 America	, 6 months	24 participants; Miller Class I. II. or III	ADM vs. CTG (CT side toward flao): releasing incisions: no root	500 mg amoxicillin, 3 times daily for 7 days, or 300 mg cilindamycin. 3 times daily for 7 days if the patient was	ADM	.	÷	9/15	50.5 [26–78]*
		recessions of at least	conditioning	allergic to penicillin. 50 mg Tramadol was prescribed for					
		2 mm		post-operative analgesia. Ice pack application was used immediately after surgery on an intermittent basis for the	CTG	13	13		50.5 [26–78]*
				first 3 to 4 hours at the surgical sites. 0.2% CHX for 2 weeks					

Table 1 (continued)

Table 1 (continued)

Table 1 (conti-	nned)								
Study	Study length	Participants/Miller classification	Surgical methods	Postoperative intervention	Groups	No. of sites p	No. of oatients	Male/ female	Age (years)
Gürlek (19), 2020 Turkey	18 months	12 participants; Miller Class I or II recessions	ADM vs. CTG (CT side toward flap); releasing incisions; no root conditioning	The patient was prescribed a nonsteroidal anti- inflammatory medication postoperatively and instructed not to brush the teeth in the operation areas	ADM CTG	41 41	12 12	4/8 4/8	31.41±13.32 31.41±13.32
Kroiss (13), 2019 Germany	5 years	39 participants; Miller Class I or II recessions	ADM vs. CTG (CT side toward flap); releasing incisions; no root conditioning	All patients were placed on 0.12% CHX twice a day for 1 min for 2 weeks, and NSAID and analgesic medication (ibuprofen 400 mg) was prescribed	ADM CTG	141 97	20 19	5/15 2/17	46.6 [25–69]* 43.6 [24–64]*
Suzuki (31), 2020 Brazil	6 months	18 participants; Miller Class I or II recessions	ADM vs. CTG (CT side toward flap); releasing incisions; no root	0.12% CHX twice a day for the first 15 days. Amoxicillin (500 mg) three times daily for 7 days-starting 24 h before	ADM	16	18	6/6	34.5±7.5
			conditioning	surgery-ibuprofen (600 mg) three times daily for 5 days, and dipyrone sodium (500 mg) four times daily for 3 days-both beginning before surgery	СТG	16	18	6/6	34.5±7.5
					C			ТС. 1 0,	

*, the extreme value. Data are shown as median, range, and interquartile range or mean ± SD. ADM, acellular dermal matrix; CTG, connective tissue graft; CT, connective tissue; NSAID, nonsteroidal anti-inflammatory drug; CHX, chlorhexidine; EDTA, ethylene diamine tetraacetic acid; NA, data deficient.

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Table 2 Results of overall meta-analysis

Characteristics	WMD (95% CI)	P value	l² (%)
PRC (%)			
Overall	-1.61 (-3.49, 0.28)	0.094	86.0
Publication bias	Z=0.55	0.583	
Study length			
<6 months	-0.19 (-1.38, 4.01)	0.931	0.0
6–12 months	-0.52 (-5.78, 4.74)	0.845	44.5
>12 months	0.84 (-8.26, 9.95)	0.856	20.2
CAL (mm)			
Overall	0.25 (0.03, 0.47)	0.026	54.8
Publication bias	Z=-0.20	0.843	
Study length			
<6 months	0.31 (0.04, 0.58)	0.027	0.0
6–12 months	0.29 (0.18, 0.39)	<0.001	59.5
>12 months	0.39 (0.16, 0.63)	0.001	0.0
KT (mm)			
Overall	-0.44 (-0.63, -0.25)	<0.001	56.8
Publication bias	Z=-0.02	0.986	
Study length			
<6 months	-0.29 (-0.50, -0.07)	0.009	18.9
6–12 months	-0.36 (-0.53, -0.19)	<0.001	40.2
>12 months	-0.78 (-1.07, -0.48)	<0.001	32.7
Quality assessment			
High quality	-0.35 (-0.50, -0.20)	<0.001	51.2
Low quality	-0.77 (-1.23, -0.30)	0.001	42.8
PD (mm)			
Overall	0.07 (-0.01, 0.14)	0.067	39.9
Publication bias	Z=-0.26	0.795	
Study length			
<6 months	0.11 (-0.01, 0.23)	0.078	71.1
6–12 months	-0.00 (-0.07, 0.07)	0.978	0.0
>12 months	0.04 (-0.08, 0.17)	0.495	68.9
RW (mm)			
Overall	0.07 (-0.10, 0.23)	0.437	32.5
Publication bias	Z=-0.09	0.928	
Study length			

Table 2 (continued)

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Table 2 (continued)			
Characteristics	WMD (95% CI)	P value	l ² (%)
<6 months	-0.08 (-0.49, 0.33)	0.716	6.3
6–12 months	0.07 (-0.10, 0.23)	0.434	23.7
>12 months	0.43(-0.02, 0.87)	0.059	79.9
RD (mm)			
Overall	0.11(-0.10, 0.31)	0.294	52.1
Publication bias	Z=0.41	0.680	
Study length			
<6 months	-0.20 (-0.66, 0.26)	0.385	72.7
6–12 months	0.06 (-0.24, 0.36)	0.686	66.4
>12 months	-0.089 (-0.81, 0.63)	0.809	72.9

PRC, percent root coverage; CAL, clinical attachment level; KT, keratinized tissue; PD, probing depth; RW, recession width; RD, recession depth.

Bias risk evaluation of included literature

Firstly, the bias risk assessment tool recommended by the Cochrane systematic review manual was used to evaluate the bias of the included literature. The results are shown in Table S1. The five included studies showed the largest percentage of "low risk", indicating that the included studies met the requirements of the analysis.

PRC

A total of 10 RCTs reported the PRC, and the pooled results showed that there was no difference in PRC between the ADM group and the CTG group (WMD: -1.61, 95% CI: -3.49 to 0.28, P=0.094; I²=86.0%) (*Table 2*, *Figure 2*).

Gain in CAL

The CAL was mentioned in 17 RCTs. The pooled analysis demonstrated that patients who underwent ADM treatment had a higher gain in CAL than those who underwent CTG (WMD: 0.25, 95% CI: 0.03 to 0.47, P=0.026; I²=54.8%) (*Table 2, Figure 3*). Subgroup analysis also showed a higher gain in CAL of the ADM group than that of the CTG group regarding the study length (<6 months, WMD: 0.31, 95% CI: 0.04 to 0.58, P=0.027; 6–12 months, WMD: 0.29, 95% CI: 0.18 to 0.39, P<0.001; >12 months, WMD: 0.39,

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Figure 2 Forest plot of the percent root coverage between the ADM group and the CTG group. ADM, acellular dermal matrix; CTG, connective tissue graft.



Figure 3 Forest plot of the gain in clinical attachment level between the ADM group and the CTG group. ADM, acellular dermal matrix; CTG, connective tissue graft.

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Study				%
ID	ADM	CTG	WMD (95% CI)	Weight
Harris (2000)	-+	-	-0.60 (-0.99, -0.21)	7.04
Alchelmann-Reldy (2001)	•		-0.60 (-1.31, 0.11)	4.16
Henderson (2001)			-0.50 (-1.42, 0.42)	5.52
Novaes (2001)	•		0.20 (-0.34, 0.74)	2.96
Paolantonio (2002)	•		-1.40 (-2.19, -0.61)	3.65
Rahmani (2006)		•	0.40 (-0.26, 1.06)	4.53
Joly (2007)	٠		-0.80 (-1.94, 0.34)	2.15
Sadat Mansouri (2010)	-	•	0.11 (-0.46, 0.68)	5.25
Moslemi (2011)	• 1	_	-0.83 (-1.69, 0.03)	3.24
Koudale (2012)		•	-0.20 (-1.10, 0.70)	3.04
Gholami (2013)	+ ¹	-	-0.60 (-1.09, -0.11)	6.01
Thomas (2013)	+	<u> </u>	-0.50 (-0.94, -0.06)	6.54
Goyal (2014)			-0.53 (-1.11, 0.05)	5.17
Barros (2015)	-		0.00 (-0.64, 0.64)	4.64
Talyeb Ali (2015)		<u> </u>	-1.25 (-2.80, 0.30)	1.29
Thakare (2015)	- + · ·	-	-0.74 (-1.24, -0.24)	5.93
Hutton (2018)		•	0.05 (-0.87, 0.97)	2.98
Vreeburg (2018)			-0.05 (-1.33, 1.23)	1.77
Gürlek (2020)	•	<u> </u>	-0.50 (-0.91, -0.09)	6.80
Kreiss (2019)			-0.92 (-1.16, -0.68)	8.71
Suzuki (2020)	+	•	-0.26 (-0.51, -0.01)	8.61
Overall (I-squared =56.8%)	\$	>	-0.44 (-0.63, -0.25)	100.00
NOTE: Weights are from random effects	analysis			
-2.8		0	2.8	

Figure 4 Forest plot of the width of keratinized tissues between the ADM group and the CTG group. ADM, acellular dermal matrix; CTG, connective tissue graft.

95% CI: 0.16 to 0.63, P=0.001) (Table 2).

Gain in KT width

A total of 21 studies referenced the KT width. Patients who received the ADM treatment showed a smaller gain in KT width than those that underwent CTG (WMD: -0.44, 95% CI: -0.63 to -0.25, P<0.001; I^2 =56.8%) (*Table 2, Figure 4*). Subgroup analysis exhibited the same results in both the study length (<6 months, WMD: -0.29, 95% CI: -0.50 to -0.07, P=0.009; 6-12 months, WMD: -0.36, 95% CI: -0.53 to -0.19, P<0.001; >12 months, WMD: -0.78, 95% CI: -1.07 to -0.48, P<0.001) and quality assessment (high quality, WMD: -0.35, 95% CI: -0.50 to -0.20, P<0.001; low quality, WMD: -0.77, 95% CI: -1.23 to -0.30, P=0.001) (*Table 2*).

PD

The post-treatment PD was reported in 18 RCTs. No difference in PD was found between the ADM group and the CTG group (WMD: 0.07, 95% CI: -0.01 to 0.14, P=0.067; I^2 =39.9%) (*Table 2, Figure 5*).

RW

A total of 11 RCTs mentioned the post-treatment RW. There was no difference in RW between the two groups (WMD: 0.07, 95% CI: -0.10 to 0.23, P=0.437; I²=32.5%) (*Table 2, Figure 6*).

RD

The outcome of RD was reported in 11 RCTs. The pooled

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Figure 5 Forest plot of the probing depth between the ADM group and the CTG group. ADM, acellular dermal matrix; CTG, connective tissue graft.



Figure 6 Forest plot of the recession width between the ADM group and the CTG group. ADM, acellular dermal matrix; CTG, connective tissue graft.



Figure 7 Forest plot of the recession depth between the ADM group and the CTG group. ADM, acellular dermal matrix; CTG, connective tissue graft.

analysis did not detect a difference in RD between patients who underwent ADM and those receiving CTG (WMD: 0.11, 95% CI: -0.10 to 0.31, P=0.294; I^2 =52.1%) (*Table 2, Figure 7*).

Publication bias

No publication bias was found in PRC (Z=0.55, P=0.583), gain in CAL (Z=-0.20, P=0.843), gain in KT width (Z=-0.02, P=0.986), PD (Z=-0.26, P=0.795), RW (Z=-0.09, P=0.928), and RD (Z=0.41, P=0.680) (*Table 2*).

Discussion

The prevalence of gingival recession is high worldwide. The objective of the present meta-analysis was to make a comparison between ADM and the gold standard, CTG, for root coverage in patients with gingival resection. A total of 24 RCTs including 587 participants were included, and the results showed that patients who accepted ADM had a higher gain in CAL but a smaller gain in KT width than those receiving CTG; no differences were found between these two techniques in PRC, PD, RW, and RD. These findings suggest that patients with gingival recession may experience a benefit from the ADM treatment that is comparable to the CTG as the gold standard, especially in gaining CAL, but CTG may have a significant advantage over ADM in gaining KT width.

Both ADM and CTG have good efficacy in gaining CAL during root coverage procedures (13,38). In contrast to the previous studies that showed no significant differences in gaining CAL between different treatment modalities (7,40), our study exhibited that patients who underwent ADM treatment had a higher gain in CAL than those who receiving CTG, as supported by the Kroiss *et al.* study results at the time of 6-month examination (13).

Cieślik-Wegemund *et al.* found a similar gain in KT width between ADM and CTG after the tunnel technique (41). Joly *et al.* also obtained similar results (25). The results of the meta-analysis performed by Gallagher *et al.* were in favor of ADM regarding gain of KT width (42). They speculated that the reason for keratinizing effects might primarily result from the dermal origin of the graft or, more probably, from the migration of host cells, which were likely to trigger the keratinization of the overlying epithelium (36,37). On the contrary, our study found that patients who received the ADM treatment had a smaller gain in KT width than those who received CTG treatment, which was in line with the results reported by Shori *et al.* and by Harris that CTG had an advantage in gaining KT width (37,43). An RCT also demonstrated that the KT showed a significant increase after 3 and 6 months in both groups (31). It can be hypothesized from the results above that the gain in KT width after root coverage treatments may be influenced by several factors such as source of graft materials and the flap design.

The development of keratinized epithelium can only be induced by the cells from periodontal ligament and gingival connective tissue (44). The induction characteristic of ADM grafts will rely on the percentage of colonization of nonvital graft by the host cell deriving from these tissues which can induce keratinization. In contrast, CTGs are entirely composed of the tissues capable of inducing the epithelial keratinization. A significantly higher PRC after CTG treatment was reported by Cieślik-Wegemund *et al.* (41) and Pietruska *et al.* (45). However, no significant difference was found in PRC between the ADM group and the CTG group, and neither in PD, RW, or RD, which were in accordance with the previous studies (16,19,40).

The major superiority of our meta-analysis was that more studies and outcomes (KT width, PD, RW, and RD) were included compared with the previous metaanalysis (42), which made our results more reliable and convincing. However, there were several limitations that should be interpreted cautiously. First, the description of the randomization method was inadequate in some studies, which may have influenced the accuracy of the results. Second, only a small number of included studies involved long-term follow-up, leading to the limited applicability to clinical situations. Third, other data sources, which are not considered in this study, may increase the quantity and quality of RCTs retrieved. Due to the small number of studies included, the results should be interpreted with caution. In the future, more well-designed studies with long-term follow-up need to be conducted to further verify our findings.

Conclusions

Our results suggested that the ADM treatment for patients with gingival recession might be superior to CTG in gaining CAL, but CTG might have a significant advantage over ADM in gaining KT width.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-656/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm. amegroups.com/article/view/10.21037/apm-22-656/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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(English Language Editor: J. Jones)

Table S1 Bias risk assessment of literature included in the study

	Risk of bias arising from the randomization process						ias arising from the randomization process Risk of bias due to deviations from the intended interventions								isk of bias du	e to missing	g outcome o	data		Risk of bia	s in meas	urement of th	ne outcome		Risk of bi	ias in selectio	on of the repr	orted result
Author	Year	Sequence random	Allocation concealed	Imbalance suggest problem	Risk-of-bias judgement	Participants aware	Personnel aware	Any deviations	Affecting outcomes	Balanced deviations	Appropriate analysis	Potential impact on result due to switching groups in analysis	Risk-of-bias judgement	Complete data	Evidence of N bias	Could depend on true	Likely depend on true	Risk-of-bias judgement	Inappropriate	Differed between groups	Aware	Could be influenced	Likely to be influenced	Risk-of-bias judgement	In accordance with plan	Selected from multiple outcomes	Selected from multiple analyses	Risk-of-bias judgement
Harris	2000	Y	Y	Ν	Low	Y	Y	PN	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Aichelmann- Reidy	2001	Y	Y	PN	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Henderson	2001	Y	Y	Ν	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	PY	Ν	Ν	Low
Nvaes	2001	Y	Y	Ν	Low	Y	Y	PN	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	NI	Ν	Ν	Some concerns
Paolantonio	2002	Υ	PY	PN	Low	Y	Y	Ν	NA	NA	PY	NA	Low	PY	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	PY	Ν	Ν	Low
Hirsch	2005	Y	Y	Ν	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	PY	Ν	Ν	Low
Rahmani	2006	Y	Y	Ν	Low	Y	Y	PN	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Joly	2007	Y	Y	Ν	Low	Y	Y	Ν	NA	NA	Y	NA	Low	PY	NA	NA	NA	Low	PN	Ν	Y	Ν	NA	Low	NI	Ν	Ν	Some concerns
Haghighati	2009	Υ	Y	PN	Low	Y	Y	Ν	NA	NA	Y	NA	Low	PY	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Sadat Mansouri	2010	Y	PY	Ν	Low	Y	Y	Ν	NA	NA	PY	NA	Low	Y	NA	NA	NA	Low	PN	Ν	Y	Ν	NA	Low	NI	Ν	Ν	Some concerns
Moslemi	2011	Υ	Y	Ν	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Koudale	2012	Y	Y	PN	Low	Y	Y	NI	NI	NI	Y	NA	Some concerns	PY	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Gholami	2013	Y	Ν	PN	Some concerns	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Shori	2013	Υ	Y	PN	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	PN	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Thomas	2013	Y	Y	PN	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	NI	Ν	Ν	Some concerns
Goyal	2014	Y	Ν	PN	Some concerns	Y	Y	NI	NI	NI	Y	NA	Some concerns	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Barros	2015	Y	Y	Ν	Low	Y	Y	PN	NA	NA	Y	NA	Low	PY	NA	NA	NA	Low	PN	Ν	Y	Ν	NA	Low	PY	Ν	Ν	Low
Taiyeb Ali	2015	Y	Y	PN	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Thakare	2015	Y	Y	Ν	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	PN	Ν	Y	Ν	NA	Low	NI	Ν	Ν	Some concerns
Hutton	2018	Y	PY	Ν	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Vreeburg	2018	Y	Y	Ν	Low	Y	Y	NI	NI	NI	Y	NA	Some concerns	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Gürlek	2020	Y	Y	Ν	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	PN	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Kroiss	2019	Y	Y	Ν	Low	Y	Y	PN	NA	NA	Y	NA	Low	PY	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low
Suzuki	2020	Υ	PY	Ν	Low	Y	Y	Ν	NA	NA	Y	NA	Low	Y	NA	NA	NA	Low	Ν	Ν	Y	Ν	NA	Low	Y	Ν	Ν	Low

Y/PY, 'Yes' or 'Probably yes'; N/PN, 'N' or 'Probably N'; NI, 'N information'; NA, not applicable.

Risk of bias in selection of the reported res	รน
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