Review Article

Efficacy of platelet-rich fibrin in papilla reconstruction: A systematic review and meta-analysis

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ABSTRACT

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Address for correspondence: Dr. Mahsa Ahmadishadmehri, No. 59, 5th Sadaf St., Vakilabad Blv., Mashhad, Iran. E-mail: mhs.ahmadishad mehri@gmail.com This systematic review and meta-analysis aimed to compare the efficacy of using platelet-rich fibrin (PRF) or connective tissue graft (CTG) for papilla reconstruction in the treatment of black triangles. A comprehensive electronic search across PubMed, Cochrane, Web of Science, ProQuest, and Scopus was conducted to identify the relevant randomized-controlled trials (RCTs), cohort studies, and case series. Quality assessment and meta-analysis were performed using R Statistical Software, focusing on the parameters such as papilla height, gingival index, plaque index (PI), clinical attachment level (CAL), and pocket probing depth. Registration number: CRD42022322934. From 191 initial studies, 7 were eligible for full-text review, with 4 RCTs and one retrospective study included in the meta-analysis. The analysis favored CTG over PRF in terms of black triangle height at 3–6 months postsurgery and in PI improvement at 3 months. No significant differences were found in CAL and probing pocket depth. While PRF can yield satisfactory results in papilla augmentation, CTG demonstrates superior clinical outcomes in specific parameters. Further research with more extensive clinical data is warranted.

Key Words: Connective tissue, interdental papilla, platelet-rich fibrin, systematic review

INTRODUCTION

Various factors such as gingival inflammation, attachment loss, and interproximal bone resorption contribute to the creation of black triangles in the interdental areas, which is associated with many problems such as food entrapment, speech disorders, and esthetic problems, especially in patients with high lip line.^[1,2] Although modifications in teeth morphology and adjustments in interdental contact points through prosthetic and orthodontic treatments provide partial solutions, they frequently do not completely address

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Website: www.drj.ir www.drjjournal.net www.ncbi.nlm.nih.gov/pmc/journals/1480 these esthetic complications. Consequently, surgical intervention becomes a necessity.^[3,4] However, surgical approaches for interdental papilla augmentation often face limitations due to the minimal blood supply in the targeted area. To overcome these challenges, various techniques have been proposed, including conservative mucoperiosteal flap designs, pedicle or free gingival grafts, with or without guided bone regeneration or guided tissue regeneration, and the utilization of biologic matrices.^[5,6]

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In this context, platelet-rich fibrin (PRF) emerges as a promising matrix aiding in the differentiation of precursor cells for the regeneration of interdental papilla. Its role as a carrier of cells involved in tissue regeneration, coupled with its potential for gradual growth factor release, positions it as a significant tool in dental surgery.^[7] Notably, PRF's involvement in neo-angiogenesis could potentially reduce necrosis and shrinkage of the surgical flap.^[3,8]

Despite PRF's potential in reducing complications associated with papilla reconstruction and soft tissue donor site morbidities, literature exploring its use in papilla regeneration remains sparse. This systematic review, therefore, seeks to address a crucial question: Does the application of PRF in the treatment of deficient papilla result in enhanced papilla fill and improvements in probing pocket depth (PPD), clinical attachment level (CAL), gingival index (GI), and plaque index (PI) when compared to connective tissue graft (CTG)?

MATERIALS AND METHODS

This study was registered in the International Prospective Register of Systematic Reviews (PROSPERO), under registration number CRD42022322934 and is prepared in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-analyses^[9] and Cochrane collaboration guidelines.^[9,10]

The null hypothesis was no difference in the clinical parameters after using CTG or PRF for interdental papilla augmentation. The focused question was: "Is PRF more effective for the treatment of deficient interdental papilla than CTG?" the PICO was: Deficiency or absence of interdental papilla (problem), PRF (intervention), CTG (comparison), and papilla fill (primary outcome) [Supplementary Table 1].

Search strategy

An electronic search was conducted in databases including PubMed, Cochrane, Web of Science, ProQuest, and Scopus, limited to English articles published until March 2022. The search employed a model using Boolean operators: (Interdental papilla OR papilla*) AND (PRF OR L-PRF OR PRP) in TITLE/SUBJECT/ABSTRACT, tailored to each database's specific search strategy [Supplementary Table 2]. In addition, the reference sections of included studies were scrutinized for further relevant studies.

Selection criteria

The search aimed to identify randomized-controlled clinical trials, prospective or retrospective clinical studies, cohort studies, and case series. Excluded were animal studies, *in vitro* studies, case reports, finite element analysis studies, and reviews. Eligible studies provided data on PRF usage in baseline assessments and had a minimum follow-up period of 3 months.

Screening and selection of papers

Duplicate studies were removed both automatically and manually. Titles and abstracts were initially screened by two independent authors (Z.A. and M.A.). For papers with insufficient information on papilla fill, corresponding authors were contacted for clarification or additional data.

Characteristics of outcome measures

Primary outcome measures

Changes in contact point to the tip of papillae (CPTP) which is the distance from the apically portion of contact point to the tip of papilla. Also reported as contact point to interdental papilla distance or black triangle height in different studies.

Secondary outcome measures

- PI
- GI
- PPD
- CAL.

Quality assessment

Quality assessment of the controlled clinical trials was performed by the Cochrane risk of bias tool. When the study met all criteria, the degree of bias was considered as low risk; if one or some components were unclear, the degree of bias was considered as moderate risk; and if at least one component was at high risk, the degree of bias was considered as high. Quality assessment of the observational studies was performed using the Joanna Briggs Institute (JBI) checklist which includes 9 items. For the answer "yes," the item is scored 1 point and scored 0 point for a "no," "not clear," or "not applicable" answer. Studies scoring seven points or more were considered to be of high quality.

Meta-analysis and synthesis of results

Meta-analysis of mean differences (MDs) was performed using R Statistical Software (Version 4.1.1, R Core Team, Vienna, Austria) according to the published procedures.^[11,12] The analyses were performed in the following categories: CPTP, CI, PI, CAL and PPD. Data wrangling and manipulation were performed using the statistical packages "tidyverse,"^[13] "dplyr"^[14] and "ggplot2"^[15] in Rstudio (Rstudio Inc., Boston, MA, USA).^[16] Meta-analytic syntheses and further investigations were done by "meta" and "dmetar" in RStudio (Rstudio Inc., Boston, MA, USA).^[17,18] Raw effect size data in the form of means and standard deviations of two groups can be pooled using metacont function provided by "meta." Heterogeneity was assessed using Cochran's Q and I²-statistics. A random effects model was retained to pool effect sizes to better account for the differences in design among the included studies. The restricted maximum likelihood estimator was used to calculate the heterogeneity variance $\tau^{2,[19]}$ Knapp-Hartung adjustments were used to calculate the confidence interval (CI) around the pooled effect.^[20] Funnel plots for investigating publication bias were made using the functionalities of the "meta" package. In addition, drapery plots were produced based on P value functions.

RESULTS

Characteristics of included studies

Altogether, the search strategy yielded 191 papers in the first selection step. One hundred and twenty-eight articles remained after the elimination of duplicate records. Of them, 121 were omitted on the assessment of titles and abstracts. Full text assessment was performed on 8 remaining articles. Finally, 7 publications were included in the systematic review and 5 of them were includable for the meta-analysis [Supplementary Figure 1].^[1,5,21-23] Detailed characteristics of the 8 included studies are described in Table 1.

A total of 84 sites were treated with PRF and 83 other sites were treated with CTGs, and 112 patients were enrolled in these studies.^[1,5,21-23] Moreover, two prospective studies^[6,24] evaluated 50 sites treated with PRF in 38 patients. All the sites were located in the maxillary esthetic area, and the papillary classification was class I and class II according to Nordland and Tarnow classification.^[25] Four studies^[1,6,21,23] used the surgical technique introduced by Han and Takei,^[26] while one study^[22] performed microsurgical Azzi technique.^[27] and another one^[24] used pouch technique. Other study prepared a minimal labial and palatal tunneling across the interdental gingiva.^[5] The PRF was made in regard to the first Choukroun Protocol

which centrifuged the blood sample at 3000 rpm for 10 min^[1,5,21] or 12 min.^[22] All studies used one PRF membrane for the test group. Original data from included studies for meta-analysis are provided in Table 2.

Risk of bias

All four studies^[1,5,21,22] were deemed low risk due to clear randomization methods. Except one study, the other three did not describe the allocation concealment and thus were judged to be at unclear risk of bias in this regard.^[1,5,21] As the interventions were completely different by nature, double-blinding to include operators or patients was not possible. Nevertheless, three of the studies^[1,5,22] reported blinding of the assessors and were grouped as low risk of bias and one study had no information regarding blinding of participants. For attrition and reporting biases, all the studies were rated as low risk and two studies^[1,21] had unclear risk for "other bias" due to some issues with the reported mean and SD in their results [Supplementary Figure 2]. According to JBI checklist, both prospective studies and the retrospective study were scored high quality^[6,24] [Supplementary Table 3].

Effect of intervention

Four studies^[1,21-23] compared the changes in CPTP after 3 month of papilla augmentation with CTG or PRF with the baseline [Figure 1a] and three studies^[1,5,23] compared the parameter after 6 month with the baseline [Figure 1b]. They all reported significant differences in this regard (weighted MD [WMD]: -0.39; 95% CI: -0.57 to -0.21; P < 0.01) and (WMD: -0.74; 95% CI: -1.30 to -0.17; P = 0.03).

Four studies^[1,21-23] evaluated changes in GI after 3 month from the surgery [Figure 2a] and two studies compared the parameter after 6 months [Figure 2b], and the results showed no significant difference (P = 0.50) and (P = 0.59).

Plaque index was evaluated in three studies^[1,22,23] after 3 month of papilla augmentation [Figure 2c] and significant difference was identified (WMD: 0.10; 95% CI: 0.08–0.12; P < 0.01) and two studies compared the parameter after 6 months [Figure 2d]. Moreover, the results showed no significant difference (P = 0.28).

When comparing PPD between groups, four studies^[1,21-23] compared the parameter after 3 months [Figure 2e] and three other studies after

Author/year	Country	Number of male/ female age	Study design	Number of treated sites Number of participants	Type of defects*	Type of Surgical defects* site	Surgical technique	Follow up period	Parameters recorded
Goyal/2021 ^[1]	India	Test: 10/6 Control: 11/5 Test: 18–48 Control: 22–55	RCT	32 patients 32 sites (16 test/16 control)	Class I and Class II	Maxillary anterior	Han and Takei	6 months	CPTP, PI, GI, WKG, PBI, PPD
Sharma/2020 ^[21] India	India	NM: 18–50	RCT	20 sites (10 test/10 control)	Class I and Class II	Maxillary anterior	Han and Takei	3 months	CPTP, PI, GI, PH, PPI, PPD, relative CAL, and distance from contact point to alveolar crest (CP-BC)
Abirami/2019 ^[5]	India	Test: 6 male/4 female Control: 7 male/3 female Test: 37.10±8.79 Control: 39.30±5.75	RCT	20 sites (10 test/10 control)	Class I and Class II	Maxillary anterior	A minimal accessed labial and palatal tunneling across the interdental gingiva	6 months	CPTP, PPD and CAL at the surgical site, plaque score (FMPS), bleeding scores (FMBS), PH, along with VAS by dentist and by patient
Singh/2019 ^[22]	India	Both group: 4 male/3 female 18–40	RCT	40 sites (20 test/20 control) 14 patients	Class I and Class II	Maxillary anterior	Azzi (by microscope)	3 months	CPTP, PI, GI, PPD, CAL, height of IDP, PIS and PES
Raval/2021 ^[24]	India	13 male/12 female 19–33	Prospective	25 patients	MN	ΣN	Pouch technique	12 weeks	CPTP, TW, PPI, percentage fill
Ahila/2018 ^[6]	India	NM: 18–55	Prospective	25 sites 13 patients	Class I and Class II	Maxillary anterior	Han and Takei (by loop)	6 months	CPTP, WKG, Jemt index, healing index (1 st , 2 nd and 3 rd week postoperatively), VAS (esthetics)
Ozcan Bulut/2022 ^[23]	Turkey	Test: 2/10 Control: 3/5 Test: 44.6±13.8 Control: 46.3±5.6	Retrospective	20 patients (12 test/8 control) 55 sites (28 test/27 control)	MZ	Maxillary anterior	Han and Takei	6 months	CPTP, distance from contact point to alveolar crest (AC-IC), distance from AC-PT, Jemt index, PPI, GI, PI, PBI, PD, WKG, buccal GR, VAS
*According to Norc Analog Scale; PPI point-bone crest; F crest-papilla tip; G	lland and Tarr : Papilla Prest :MPS: Full mc R: Gingival rei	According to Nordland and Tarmow classification. NM: Not mentioned: RCT: Randc Analog Scale; PPI: Papilla Presence Index; CPTP: Contact point to the tip of papilla point-bone crest; FMPS: Full mouth plaque score; FMBS: full mouth bleeding score; crest-papilla tip; GR: Gingival recession; PD: Probing depth; IDP: Interdental papilla	ientioned; RCT: Ra oint to the tip of par mouth bleeding so DP: Interdental par	ndomized control trial; PPD: Pr billae; PH: Papillary height; TH: ore; PIS: Papilla index score; P billa	obing pocke Triangle hei ES: Patient	t depth; GI: (ght; WKG: V esthetic scor	äingival index; CAL: Clini /idth of keratinized gingiv e; TW: Triangle width; AC	cal attachme a; PBI: Papil ≻IC: Alveola	*According to Nordland and Tarmow classification. NM: Not mentioned; RCT: Randomized control trial; PPD: Probing pocket depth; GI: Gingival index; CAL: Clinical attachment level; PI: Plaque index; VAS: Visual Analog Scale; PPI: Papilla Presence Index; CPTP: Contact point to the tip of papillae; PH: Papillary height; TH: Triangle height; WKG: Width of keratinized gingiva; PBI: Papillary bleeding index; CP-BC: Contact point-bone crest; FMPS: Full mouth plaque score; PIS: Papilla index score; PES: Patient esthetic score; TW: Triangle width; AC-IC: Alveolar crest-interdental contact; AC-PT: Alveolar crest; PRPS: Full mouth plaque score; PIS: Papilla index score; PES: Patient esthetic score; TW: Triangle width; AC-IC: Alveolar crest-interdental contact; AC-PT: Alveolar crest-papilla tip; GR: Gingival recession; PD: Probing depth; IDP: Interdental papilla

Table 1: Detailed characteristics of the included studies

Afshari, et al.: PRF for papilla reconstruction

Afshari, et al.: PRF for papilla reconstruction

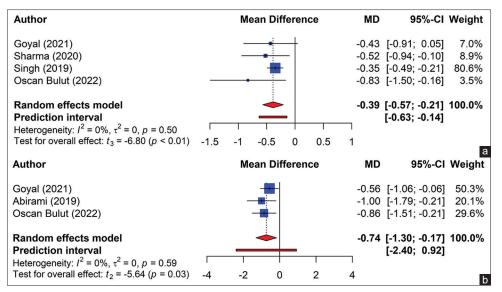


Figure 1: Comparison of changes in contact point to the tip of papillae (a) after 3 months (b) after 6 months. MD: Mean difference, CI: Confidence interval.

6 months with the baseline^[1,5,23] [Figure 2f]. The results showed no significant differences for both time periods (P = 0.38) and (P = 0.54).

In regard to CAL, two studies^[21,22] compared the parameter after 3 month and significant difference was reported (WMD: 0.05; 95% CI: 0.00–0.10; P = 0.05) [Figure 2g].

Heterogeneity

The results of Cochran's Q and *P*-statistics, and the corresponding *P* values indicated that between-study heterogeneity existed in GI and PPD categories and that the use of a random-effects model was appropriate. The heterogeneity among other categories was low; nevertheless, caution should be applied when interpreting these results, due to small sample sizes and statistical power [Supplementary Figure 3a-h].

Drapery plots

The resulting drapery plots are documented in the supplemental content [Supplementary Figure 4a-i]. Each plot contains a P value curve, in the shape of an upside down V, for each effect size under the normality assumption. The peak of the P value functions represents the exact value of the effect size in our meta-analysis. Gray curves correspond to primary studies, while the thick red line represents the average effect according to the random-effects model (studies in dark gray shows higher precision and those in light gray shows low precision). Y-axis shows the P values and while it gets smaller, the CI gets bigger, until we reach conventional significance thresholds, indicated by the dashed horizontal lines.

DISCUSSION

Interpretation and implication of main findings Our meta-analysis delineates a clear advantage for CTG over PRF in papilla reconstruction, particularly evident in the dimensional changes of CPTP at 3 and 6 months postsurgery. This advantage extends to PI improvements favoring CTG after 3 months. However, for CAL, GI, and PPD, our findings reveal no significant disparities between the groups.

The survival rate and efficacy of CTG in papilla reconstruction were posited by earlier studies.[1,21,22,28] Correlate with the graft's vascular supply and its intrinsic biological properties. The composition of CTG, inclusive of nerve structures, adipose tissues, and glands, contrasts with the simpler structure of PRF membranes, potentially contributing to CTG's resilience against postsurgical shrinkage.^[22] Beagle suggested the roll technique primarily, which is a combination of a pedicle flap with papilla preservation.^[29] Subsequently, Han and Takei introduced a technique with a semilunar incision and a subepithelial CTG beneath the papilla.^[26] Later, in a case report by Azzi et al., split-thickness buccal and palatal flaps were used in the company of CTG.^[27] In a case report in 2012, PRF was placed in a pouch in the interdental area, created with a semilunar incision.[3]

Studies by Ahila *et al.*^[6] and Raval *et al.*^[24] highlight the efficacy of PRF in achieving substantial papillary fill, with noted rapid healing and significant

Afshari, et al.: PRF for papilla reconstruction

-0.5 0 0.5 1 1. Mean Difference	-0.07 [-0.39; 0.11 [0.10; -0.09 [-0.18; 0.06 [-0.19; [-0.63;	0.41] 24.1% 0.25] 13.7% 0.12] 32.6% 0.00] 29.5% 0.31] 100.0% 0.75]
	-0.07 [-0.39; 0.11 [0.10; -0.09 [-0.18; 0.06 [-0.19; [-0.63;	0.25] 13.7% 0.12] 32.6% 0.00] 29.5% 0.31] 100.0%
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	-0.09 [-0.18; 0.06 [-0.19; [-0.63; 5	0.00] 29.5% 0.31] 100.0%
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	[-0.63 ;	
	5	0.75]
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Mean Difference	MD	
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	-0.03 [-0.11, 0.05] 52.5
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Mean Difference		5%-Ci weight
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		-0.02; 0.20] 51.5
	0.09 [-0.02, 0.20] 51.5
	0.17 [-	0.85; 1.18] 100.0
	1	
-2 -1 0 1 2	3	
Mean Difference	MD S	95%-CI Weight
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		; 0.19] 24.3%
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	0.09 [-0.13	; 0.31] 25.1%
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Mean Difference	MD	95%-CI Weigl
_		
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		3.34; 3.13]
		0.04, 0.10]
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 	•); 0.10] 100.0%
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Figure 2: Comparison of changes in parameters (a) 3 months gingival index (GI) (b) 6 months GI (c) 3 months plaque index (PI) (d) 6 months PI (e) 3 months probing pocket depth (PPD) (f) 6 months PPD (g) 3 months clinical attachment level. MD: Mean difference, CI: Confidence interval.

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Table 2: Original data from included studies for meta-analysis

Parameter						Author	hor					
	Ozo	Ozcan Bulut, 2022 ^[23]	.2 23		Goyal, 2021 ^[1]		Sharma, 2020 ^[21]	$2020^{[21]}$	Abirami, 2019 ^[5]	, 2019 ^[5]	Singh, 2019 ^[22]	2019 22
	Baseline	3 months	6 months	Baseline	3 months	6 months	Baseline	3 months	Baseline	6 months	Baseline	3 months
CPTP-PRF	3.04±0.79	1.54±1.55	1.64±1.50	1.69±0.7	1.5±0.73	1.44±0.81	1.51±0.44	1.16±0.54	3.4±1.17	2.5±1.08	3.55±0.27	0.45±0.28
CPTP-CTG	3.48±1.22	1.15±1.35	1.22±1.31	2.06±0.57	1.44±0.73	1.25±0.78	1.5±0.46	0.63±0.47	3.3±0.48	1.4±0.7	3.6±0.17	0.15±0.15
PI-PRF	0.34±0.31	0.01±0.023	0.08±0.03	0.27±0.21	0.21±0.25	0.13±0.12	1.45±0.44	ı	ı	·	1.34±0.02	1.02±0.03
PI-CTG	0.17±0.28	0.00±0.00	0.00±0.00	0.17±0.18	0.23 ± 0.32	0.28±0.19	1.55 ± 0.5	·			1.31±0.02	1.09±0.03
GI-PRF	0.11±0.21	0.07±0.14	0.00±0.02	0.22±0.26	0.17±0.25	0.06±0.12	1.08±0.26	0.35±0.4	ı		1.28±0.01	1.01±0.01
GI-CTG	0.14±0.22	0.01±0.05	0.00±0.00	0.12±0.17	0.32±0.25	0.24±0.31	1.15 ± 0.38	0.35±0.41	ı	·	1.27±0.02	1.11±0.02
PPD-PRF	1.57±0.54	1.61±0.40	1.59±0.46	2.15±0.31	2.09±0.29	2.17±0.31	2.2±0.42	1.2±0.4	1.22±0.23	1.44±0.22	1.7±0.11	0.95 ± 0.05
PPD-CTG	1.61±0.40	1.74±0.25	1.74±0.29	2.22±0.27	0.32 ± 0.25	2.17±0.24	2.4±0.52	1.2±0.42	1.46±0.55	1.28±0.25	1.65±0.11	0.95 ± 0.05
CAL-PRF				ı	·		10.5±0.71	9.5±0.71	1.14±0.77	0.51 ± 0.65	1.7±0.11	0.95 ± 0.05
CAL-CTG	ı	ı	ı	I	ı	ı	10.7±0.82	9.7±0.82	1.14±0.63	0.62±0.66	1.65±0.11	0.95±0.05
CPTP: Contact	point to the tip or	CPTP: Contact point to the tip of papillae; PI: Plaque index; PPD: Probing-pocket depth; GI: Gingival index; CAL: Clinical attachment level; PRF: Platelet rich fibrin; CTG: Connective tissue graft	que index; PPD: F	Probing-pocket de	epth; GI: Gingival	index; CAL: Clini	ical attachment le	vel; PRF: Platelet	rich fibrin; CTG:	Connective tissu	ue graft	

reductions in black triangle dimensions. This rapid tissue regeneration is likely attributed to the unique properties of PRF, particularly its high affinity for growth factors such as fibroblast growth factor-b, vascular endothelial growth factor, angiopoietin, and PDGF, and their subsequent role in enhancing angiogenesis.^[8] The ability of PRF to promote fibroblast proliferation and migration, vital for wound healing, underscores its potential in periodontal regeneration.^[6,8]

Despite these advantages, PRF is not without limitations. Its rapid degradation and consequent diminished release of biomolecules may impede the initial stabilization of periodontal tissues.^[30] However, its ease of preparation, cost-effectiveness, and reduced morbidity make it an attractive option in specific clinical scenarios.^[31] Advancements in PRF technology, particularly the potential increase in its layers, could significantly enhance its efficacy, possibly even surpassing that of CTG. This prospect opens up new avenues for research and clinical application.

Esthetic outcomes, a critical aspect of periodontal treatments, have shown encouraging results with PRF, as indicated by improvements in Visual Analog Scale scores.^[5,6] However, studies have demonstrated marginally superior esthetic outcomes with CTG,^[22,23] highlighting the need for a balanced approach when considering patient-specific parameters and treatment objectives. Given that this is the first systematic review and meta-analysis evaluating PRF's efficacy in papilla augmentation, and considering the limited number of randomized-controlled trials available, a definitive conclusion on its success remains elusive. Our findings suggest that exploring alternative surgical approaches or newer generations of PRF might be beneficial.

Limitation

This meta-analysis faces limitations due to the heterogeneity of study designs, follow-up durations, and variability in PRF production methods. The influence of site-specific factors such as tissue phenotype and tooth shape, as well as the nuances of CTG harvesting methods, need clearer reporting in future studies. Furthermore, the short-term nature of follow-up in these studies limits the long-term applicability of our findings. Future research should focus on addressing these gaps, possibly exploring newer generations of PRF or alternative surgical approaches.

CONCLUSION

This systematic review and meta-analysis reveal that while PRF offers beneficial short-term outcomes in papilla reconstruction, CTG demonstrates superior results in papilla height and periodontal indices. Nevertheless, the role of PRF in minimizing patient morbidity and its predictable clinical outcomes render it a feasible alternative in specific scenarios. The findings suggest a need for tailored approaches in periodontal surgery, balancing efficacy with patient-specific considerations.

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Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.

REFERENCES

- Goyal I, Tanwar N, Tewari S, Sharma R, Narula S. Comparative clinical evaluation of platelet rich fibrin and subepithelial connective tissue graft in interdental papilla reconstruction: A randomized controlled clinical trial. Eur J Dent Oral Health 2021;2:7-12.
- Prato GP, Rotundo R, Cortellini P, Tinti C, Azzi R. Interdental papilla management: A review and classification of the therapeutic approaches. Int J Periodontics Restorative Dent 2004;24:246-55.
- Arunachalam LT, Merugu S, Sudhakar U. A novel surgical procedure for papilla reconstruction using platelet rich fibrin. Contemp Clin Dent 2012;3:467-70.
- Zetu L, Wang HL. Management of inter-dental/inter-implant papilla. J Clin Periodontol 2005;32:831-9.
- Abirami T, Subramanian S, Prakash PS, Victor DJ, Devapriya AM. Comparison of connective tissue graft and platelet rich fibrin as matrices in a novel papillary augmentation access: A randomized controlled clinical trial. Eur J Dent 2019;13:607-12.
- 6. Ahila E, Saravana Kumar R, Reddy VK, Pratebha B, Jananni M, Priyadharshini V. Augmentation of interdental papilla with platelet-rich fibrin. Contemp Clin Dent 2018;9:213-7.
- Sanghani N, Apine A, Shivaprasad BM, Ritesh K, Nalini MS. Conquering the "dreaded" black triangles: A case series. J Evol Med Dent Sci JEMDS 2014;3:4636-42.
- Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, *et al.* Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part IV: Clinical effects on tissue healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:e56-60.
- 9. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews

and meta-analyses: The PRISMA statement. Open Med 2009;3:e123-30.9.

- Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, *et al.* Cochrane Handbook for Systematic Reviews of Interventions. 2nd Edition. Chichester (UK): John Wiley and Sons; 2019.
- Harrer M, Cuijpers P, Furukawa TA, Ebert DD. Doing Meta-analysis with R: A Hands-on Guide. Boca Raton, FL and London: Chapman and Hall/CRC; 2021.
- 12. Team R. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria; 2013.
- Wickham H. Welcome to the tidyverse. J Open Source Softw 2019;4:1686.
- Wickham H, François R, Henry L, Müller K. Dplyr: A Grammar of Data Manipulation. 2020. R Package Version 08; 2021. p. 4.
- 15. Wickham H. Ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New Y0rk; 2016.
- Team R. RStudio: Integrated Development Environment for R. URLRStudio, PBC, Boston, MA; 2021.
- 17. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: A practical tutorial. Evid Based Ment Health 2019;22:153-60.
- Harrer M, Cuijpers P, Furukawa T, Ebert DD. dmetar: Companion R Package for the Guide 'Doing Meta-Analysis in R'. R Package Version 0.0.9000; 2019.
- Veroniki AA, Jackson D, Viechtbauer W, Bender R, Bowden J, Knapp G, *et al.* Methods to estimate the between-study variance and its uncertainty in meta-analysis. Res Synth Methods 2016;7:55-79.
- 20. Knapp G, Hartung J. Improved tests for a random effects meta-regression with a single covariate. Stat Med 2003;22:2693-710.
- 21. Sharma P, Vaish S, Sharma N, Sekhar V, Achom M, Khan F. Comparative evaluation of efficacy of subepithelial connective tissue graft versus platelet-rich fibrin membrane in surgical reconstruction of interdental papillae using Han and Takie technique: A randomized controlled clinical trial. J Indian Soc Periodontol 2020;24:547-53.
- Singh D, Jhingran R, Bains VK, Madan R, Srivastava R. Efficacy of platelet-rich fibrin in interdental papilla reconstruction as compared to connective tissue using microsurgical approach. Contemp Clin Dent 2019;10:643-51.
- Ozcan Bulut S, Ilhan D, Karabulut E, Caglayan F, Keceli HG. Efficacy of platelet-rich fibrin and connective tissue graft in papilla reconstruction. J Esthet Restor Dent 2022;34:1096-104.
- Raval YH, Shah MA, Dave RD, Debnath AV. Evaluation of efficacy of platelet-rich fibrin for papilla reconstruction. Adv Hum Biol 2021;11:106-10.
- Nordland WP, Tarnow DP. A classification system for loss of papillary height. J Periodontol 1998;69:1124-6.
- Han TJ, Takei HH. Progress in gingival papilla reconstruction. Periodontol 2000 1996;11:65-8.
- Azzi R, Etienne D, Carranza F. Surgical reconstruction of the interdental papilla. Int J Periodontics Restorative Dent 1998;18:466-73.

- Sharma E, Sharma A, Singh K. The role of subepithelial connective tissue graft for reconstruction of interdental papilla: Clinical study. Singapore Dent J 2017;38:27-38.
- 29. Beagle JR. Surgical reconstruction of the interdental papilla: Case report. Int J Periodontics Restorative Dent 1992;12:145-51.
- 30. Dohan Ehrenfest DM, de Peppo GM, Doglioli P, Sammartino G. Slow release of growth factors and thrombospondin-1 in Choukroun's platelet-rich fibrin (PRF): A gold standard to achieve for all surgical platelet concentrates technologies. Growth Factors 2009;27:63-9.
- Aspalli S, Nagappa G, Jain A. Platelet rich fibrin: A panacea for lost interdental papilla. J Dent Spec 2016;3:217.

Supplementary Table 1: Problem, intervention, comparison, outcome, eligibility criteria, and research question formulation

Pico component	Description	Eligibility criteria
P (problem)	Deficiency or absence of interdental papilla	Studies investigating interdental papilla reconstruction
I (intervention)	Platelet-rich fibrin	Studies investigating interdental papilla reconstruction using PRF
C (comparison)	Connective tissue graft	Studies investigating interdental papilla reconstruction using CTG
O (outcome)	Mean papilla fill, PPD, CAL, PI, and GI	At least one of the measurements was reported
S (study design)	-	Randomized-controlled clinical trials, prospective or retrospective clinical studies, cohort studies and case series
Research question	Does treatment of the deficient papilla with PR and PI than CTG?	F results in better papilla fill and an improvement in PPD, CAL, GI,

PI: Plaque index; PPD: Probing pocket depth; GI: Gingival index; CAL: Clinical attachment level; PRF: Platelet-rich fibrin; CTG: Connective tissue graft

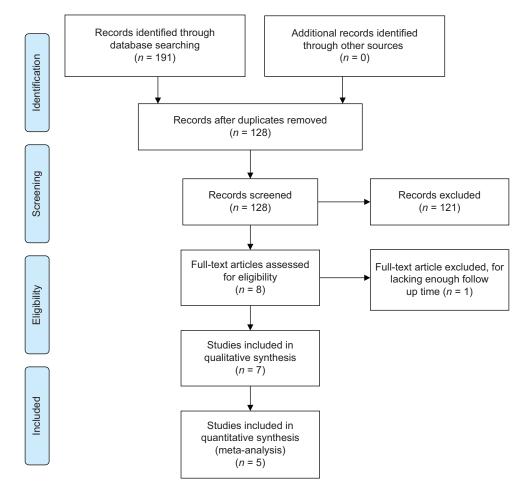
Supplementary Table 2: Search strategies: An electronic search was performed, with no time restrictions, in the following electronic bibliographic databases: PubMed, Cochrane, Web of Science, Scopus, and ProQuest up to March 25, 2022

Database	Search line	Number of retrieval record
General	(interdental papilla OR papilla*) AND (platelet-rich fibrin OR L-PRF OR PRP) in TITLE/ SUBJECT/ABSTRACT	191
WOS	(TS (interdental papilla OR papilla*) AND (platelet-rich fibrin OR L-PRF OR PRP)) Timespan: All years. Indexes: SCI-EXPANDED, SSCI, A&HCI, ESCI. AND LANGUAGE: (English)	75
Scopus	TITLE-ABS-KEY (((interdental papilla OR papilla*) AND (platelet-rich fibrin OR L-PRF OR PRP)) AND (LIMIT-TO (LANGUAGE, "English"))	10
PubMed	((interdental papilla[Title/Abstract] OR papilla*[Title/Abstract]) AND (platelet-rich fibrin[Title/ Abstract] OR L-PRF[Title/Abstract] OR PRP[Title/Abstract]))	59
Cochrane	((interdental papilla OR papilla*) AND (platelet-rich fibrin OR L-PRF OR PRP)) in Title Abstract Keyword - in Trials	32
ProQuest	ab((interdental papilla OR papilla*) AND (platelet-rich fibrin OR L-PRF OR PRP)) Databases: 1 databases searched (Publicly Available Content Database) , Limited by: Language: English	15

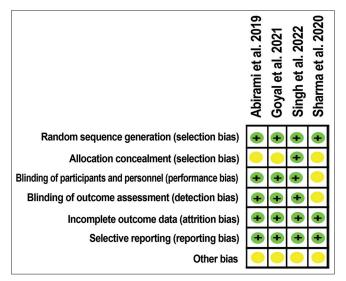
WOS: Web of Science

Supplementary Table 3: The summary of the risk of bias in the included prospective studies on the basis of Joanna Briggs Institute checklist

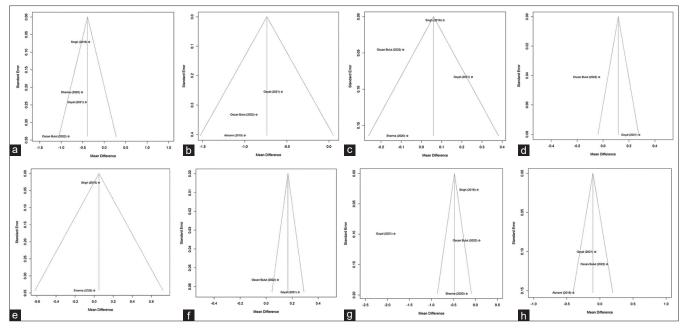
Question	A	uthor	
	Ozcan Bulut ^[23]	Ahila ^[6]	Raval ^[24]
1. Is it clear in the study what is the "cause" and what is the "effect"?	Yes	Yes	Yes
2. Were the participants included in any comparisons similar?	Yes	Yes	Unclear
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Yes	Yes	Yes
4. Was there a control group?	Yes	No	No
5. Were there multiple measurements of the outcome both pre- and post-intervention?	Yes	Yes	Yes
6. Was follow up complete and if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes
7. Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes	Yes
8. Were outcomes measured in a reliable way?	Yes	Yes	Yes
9. Was appropriate statistical analysis used?	Yes	Yes	Yes



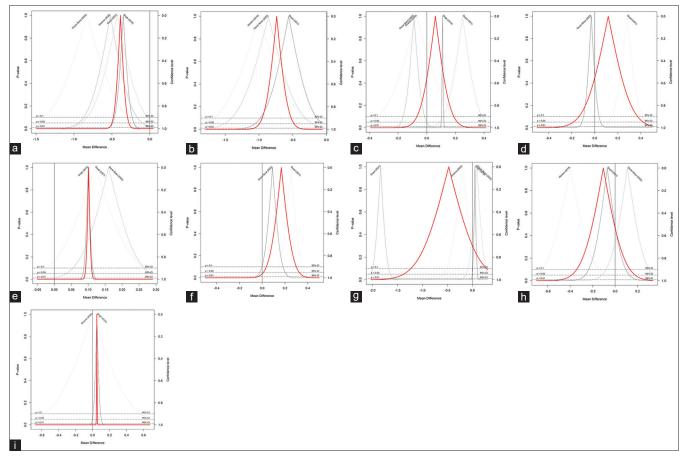
Supplementary Figure 1: Searching flowchart.



Supplementary Figure 2: Risk of bias summary: Review authors' judgments about each risk of bias item for each randomized-controlled trial.



Supplementary Figure 3: Funnel plot analysis for the changes in parameters: (a) Contact point to the tip of papillae (CPTP) in 3 months, (b) CPTP in 6 months, (c) gingival index (GI) in 3 months, (d) GI in 6 months, (e) CAL in 3 months, (f) plaque index in 3 months, (g) probing pocket depth (PPD) in 3 months, and (h) PPD in 6 months.



Supplementary Figure 4: Drapery plot showing *P* value curves (left) and its scaled version (right) for changes in parameters: (a) Contact point to the tip of papillae (CPTP) in 3 months, (b) CPTP in 6 months, (c) gingival index (GI) in 3 months, (d) GI in 6 months, (e and f) in plaque index in 3 months, (g) PPD in 3 months, (h) probing pocket depth (PPD) in 6 months, (i) CAL in 3 months. CI: Confidence interval.