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Review

Regenerative potential of connective tissue grafts vs. platelet-rich fibrin preparations in periodontal therapy: a comparative review

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Abstract: Connective tissue graft (CTG) is widely considered the gold standard due to its predictable and stable long-term results, particularly in cases requiring significant soft tissue augmentation. However, it necessitates a second surgical site, increasing patient discomfort. Platelet-rich fibrin (PRF), a minimally invasive alternative, promotes tissue regeneration through growth factor release, enhancing healing while reducing postoperative morbidity. A comprehensive analysis of scientific literature, including clinical studies and case reports, was conducted to compare the effectiveness of both techniques in achieving root coverage, increasing gingival thickness, and improving esthetic and patient-related outcomes. While CTG consistently demonstrates superior long-term stability, PRF offers promising regenerative potential with less postoperative discomfort. This review evaluates the efficacy, clinical outcomes, and patient satisfaction associated with CTG and PRF in the management of gingival recession. However, limitations such as variability in PRF preparation methods, lack of standardized protocols, and limited long-term clinical data hinder its widespread acceptance. Despite these challenges, PRF remains a viable option for patients seeking a less invasive approach with improved healing. Future research should focus on refining PRF protocols and establishing their long-term efficacy to broaden their application in periodontal therapy.

Keywords: connective tissue graft; growth factors; healing; periodontal regeneration; platelet-rich fibrin.

1. Introduction

In dentistry, symmetrical teeth arrangement and harmonious soft tissue morphology are prioritized for esthetic reasons. Marginal gingival recession results in esthetic difficulties and dental hypersensitivity because of root exposure. Periodontal plastic surgery attempts to regenerate the periodontal tissues that have been lost due to periodontitis [1]. Intraoral soft-tissue grafting is one of the dependable root-covering methods that has grown in popularity [2]. The choice of treatment depends on variables such as recession depth and post-operative esthetics [3]. Several techniques are employed, including the gold-standard method of using connective tissue grafts (CTGs) followed by envelope approach, lateral sliding flap, free gingival graft and coronally advanced flap, pouch and tunnel, vestibular incision supra-periosteal tunnel access (VISTA), and modified-VISTA [4]. However, conventional surgical techniques like CTGs and free gingival autografts have limitations, such as a second surgical site and lacking growth factors [5–7]. Growth factors are essential for faster healing and regeneration in periodontal treatment. Different preparation of platelet-rich fibrin (PRF) provides an alternative to CTG for the root coverage procedure. PRF has the advantage as it is less invasive, abundant with growth factors, and does not need require second surgical sites, but its outcomes are not always consistent [8,9]. To comprehensively evaluate the outcomes of root coverage procedures, it is essential to include not only clinical success parameters but also esthetic aspects. The root coverage esthetic score (RES) has been introduced as a standardized and quantitative tool to objectively assess esthetic outcomes, including gingival margin level, soft tissue contour, color match, and texture. Incorporating RES into studies that compare CTG and PRF enables a more detailed analysis of their esthetic performance, beyond the traditional measurement of root coverage alone. Two distinct approaches were recently put up to evaluate the esthetic results of root covering operations. In a previous study, a five-point ordinal improvement scale—poor, fair, good, very good, and excellent—was proposed following the panel scoring system. In order to assess the overall esthetic result following root coverage operations, the root coverage esthetic score (RES) system was also established. Five factors are evaluated to determine this score: gingival colour, soft tissue surface, marginal contour, gingival margin level, and MGJ position. Five factors are evaluated to determine this score: gingival colour, soft tissue surface, marginal contour, gingival margin level, and MGJ location. The range of RES values is 0 (i.e., final residual recession that is equal to or greater than the baseline recession) to 10 (i.e., CRC linked to the other four factors being fulfilled). In a study that contrasted the use of an acellular dermal matrix allograft seeded with autologous gingival fibroblasts with a subepithelial connective tissue transplant, RES was also utilized to assess the esthetic outcomes of localized recessions. To the best of our knowledge, the RES's interrater agreement has not been statistically evaluated, despite the fact that its preliminary proposal appears promising [10].

The electronic literature search was done for articles through PubMed, Scopus, and Google Scholar databases. Studies included in the review focused on periodontal regeneration using CTG and/or PRF. Clinical outcomes such as gingival thickness, probing depth reduction, clinical attachment level improvement, and keratinized tissue width were reported. Only studies involving human participants with no systemic health conditions affecting periodontal regeneration were included. Exclusion criteria included nonclinical studies, such as animal studies, in vitro experiments, or noncomparative studies and/or reviews. Studies involving patients with systemic conditions such as uncontrolled diabetes, active smoking, immunosuppressive disorders, or severe periodontal disease requiring unrelated treatments were excluded. Studies with poor oral hygiene compliance or untreated dental infections were excluded, along with editorials, opinion articles, or studies with insufficient data. Data extraction (Figure 1).

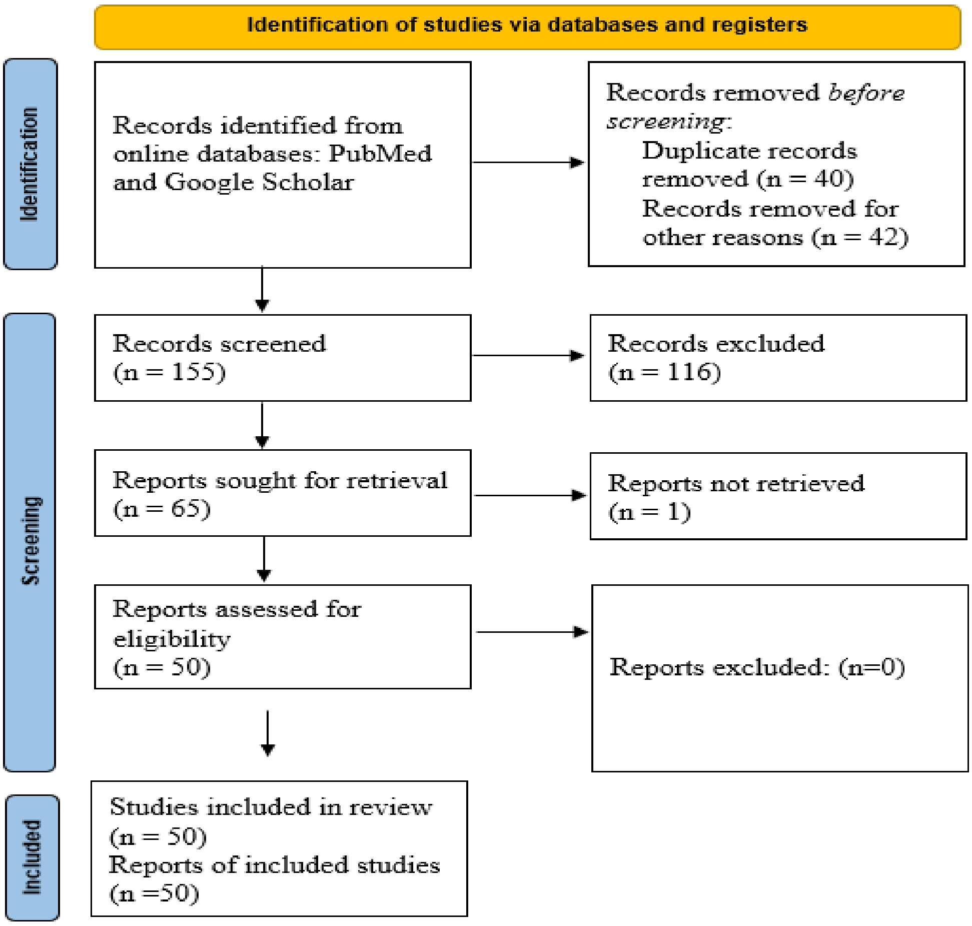

Figure 1. Data extraction from the electronic search databases.

1.1. CTG

CTG can be procured from the edentulous ridges, maxillary tuberosity, and palate, with the palate being the most frequently used donor site due to the large dimensions of graft that could be obtained and also the presence of histological similarity between the palatal mucosa and keratinized attached mucosa of the alveolar ridge [11]. The lateral palate, distal to the canine and mesial to the first molar's palatal ridge, has proven to be the best place to obtain connective tissue grafts. The majority of studies have demonstrated a satisfactory amount of vessels, cells, and fibers, especially found within the lamina propria, as well as an adequate tissue thickness for accomplishing good esthetic outcomes during root coverage methods, despite an observed variability in the histological composition of the tissues collected from this area [1]. The various locations and their structure are as follows:

1. Palatal mucosa: [2]

- Composition: Dense connective tissue rich in collagen fibers, fibroblasts, and a robust blood supply.
- Use: This is the most common donor site for connective tissue grafts. It provides thick, durable tissue ideal for root coverage, increasing keratinized tissue, and stabilizing gingival margins.
- Site characteristics: Tissue is typically harvested from the area between the first premolar and molar due to its optimal thickness and accessibility.

2. Maxillary tuberosity: [2]

- Composition: Soft connective tissue with higher elasticity and moderate collagen content.
- Use: Often used when thicker or more pliable tissue is needed, such as in esthetic zones or when palatal tissue is inadequate.
- Site characteristics: The tissue is softer and may have a better esthetic outcome in some cases, though it may be less stable under tension. An enhanced harvesting location for autografts with greater tissue thickness has been thought to be the tuberosity.

3. Edentulous ridge:

- Composition: Dense fibrous connective tissue with minimal glandular and fatty tissue.
- Use: Selected when additional tissue is needed for grafting, especially in patients with an edentulous site near the area of recession.
- Site characteristics: Offers stable and vascularized tissue for grafting in challenging cases.

4. Lateral pedicle graft (Adjacent tooth site): [3]

- Composition: Gingival tissue with intact vasculature from the adjacent tooth or site.
- Use: Used in single-tooth recession cases to mobilize tissue from a neighboring area without the need for a separate donor site.
- Site characteristics: Maintains blood supply, allowing rapid healing and effective root coverage.

1.2. PRF

PRF was initially created in France for use in oral and maxillofacial surgery. Since PRF is made as a natural concentrate without any anticoagulants added, it is categorized as a second-generation platelet concentrate [4]. Leukocytes; cytokines; structural glycoproteins; growth factors, including transforming growth factor B1, platelet-derived growth factor, vascular endothelial growth factor; and glycoproteins like thrombospondin-1 are all present in the thick fibrin matrix that is PRF [8]. Using a specialized centrifugation and collection kit, the patient's blood sample is extracted during the surgical operation and undergoes a single centrifugation without blood manipulation. Neither calcium chloride nor bovine thrombin were utilized for fibrin polymerization, nor was an anticoagulant used while blood collection. After centrifugation, three different portions are created: 1) red blood cells, which are concentrated at the bottom of the test tube and can be quickly disposed of; 2) the surface layer, which is a liquid serum of platelet-depleted plasma; and 3) the latter fraction, which is a dense PRF clot that is suitable for use as a membrane in clinical settings [12]. The primary PRF varieties utilized in periodontal procedures (Table 1)

1. Conventional PRF (Leukocyte-PRF [L-PRF]) [6]

- Preparation: Centrifugation of blood without anticoagulants, leading to a clot rich in fibrin, platelets, and leukocytes at 2700–3000 rpm for 12 minutes.
- Uses: Enhancing soft and hard tissue healing, promoting bone regeneration in guided bone regeneration (GBR), and supporting wound healing after flap surgeries.
- Advantages: L-PRF is a solid biomaterial that does not disperse soon after application. Solid-state L-PRF has been demonstrated to dramatically embed platelet and leukocyte growth factors into the fibrin matrix, resulting in an enhanced cytokine life span [13]. It is also easy to prepare, biodegradable, and biocompatible.
- Limitations: Requires rapid processing to prevent clotting.

2. Advanced PRF (A-PRF) [7]

- Preparation: Modified centrifugation (i.e., lower speed and longer time) to optimize cell and growth factor content at 1500 rpm for 14 minutes.
- Uses: Enhanced angiogenesis due to higher leukocyte and growth factor content that is effective in periodontal regeneration and defect healing.
- Advantages: Better release of growth factors over time compared to conventional PRF.
- Limitations: Requires precise centrifugation protocols, and the longer preparation time may not be ideal for immediate use.

3. Injectable PRF (i-PRF) [9]

- Preparation: Very low-speed centrifugation producing a liquid concentrate at 700–800 rpm for 3–4 minutes.
- Uses: Injectable form allows precise application in defect sites, mixed with bone grafts, or used as an injectable matrix for soft tissue healing.
- Advantages: The human liquid fibrinogen in i-PRF gradually transforms into a PRF clot rich in growth factors that release continuously for 10–14 days [14]. Nonclotting form is ideal for minimally invasive procedures.
- Limitations: Short working time before clot formation.

4. Titanium-PRF (T-PRF) [15]

- Preparation: Centrifugation in titanium tubes instead of glass (silica) tubes, which may reduce contamination and enhance biocompatibility at 2700 rpm for 12 minutes.
- Uses: Promoting osteogenesis and soft tissue healing.
- Advantages: Higher mechanical strength and growth factor release. Researchers discovered that co-aggregation brought on by titanium had been comparable to that, and that clots formed in titanium pipes were the same as those formed in glass vials. T-PRF has special advantages like improved biocompatibility since titanium particles, not silica particles, are employed to activate platelets.
- Limitations: Requires specialized equipment (i.e., titanium test tubes).

Table 1. Preparation features of different types of platelet-rich fibrin (PRF).

Sr. no.	Type of PRF	Centrifugation speed	Time	Tube type	Form	Features
1.	Conventional PRF (L-PRF)	2700–3000 rpm	12 minutes	Glass (no anticoagulant)	Solid clot	Quick processing required to avoid early clotting
2.	A-PRF	1500 rpm	14 minutes	Glass (modified protocol)	Solid clot	Lower speed and longer time optimize cell content
3.	i-PRF	700–800 rpm	3–4 minutes	Plastic (no anticoagulant)	Liquid form	Very short spin time yields nonclotting liquid form
4.	T-PRF	2700 rpm	12 minutes	Titanium tubes	Solid clot	Titanium enhances biocompatibility and mechanical strength

2. Discussion

The comparison between CTG and PRF in periodontal surgeries highlights their unique benefits and limitations, particularly in soft tissue augmentation and regenerative procedures. CTG, harvested from the patient's palate, is composed of a connective tissue matrix with fibroblasts and collagen, providing structural support and predictable outcomes for gingival recession treatment and tissue augmentation. Because it may thicken tissue and produce better functional and cosmetic outcomes, it is regarded as the gold standard for root covering [2]. However, CTG requires a second surgical site, leading to increased patient morbidity, prolonged healing time, and postoperative discomfort. In contrast, PRF, derived from autologous blood, contains a fibrin matrix rich in platelets; leukocytes;

and growth factors, such as PDGF, TGF-β, and VEGF. These factors promote angiogenesis, wound healing, and tissue regeneration. By doing away with the requirement for a donor site, PRF lowers discomfort following surgery and patient complications [4]. While PRF is effective in enhancing soft tissue healing and regeneration, its predictability for complete root coverage is lower compared to CTG (Table 2).

Table 2. Comparison of CTG and PRF in terms of patient morbidity, long-term stability, and outcomes.

Aspect	CTG	PRF
Root coverage success	90–97% (Consistently high)	70–80% (Moderate, less predictable)
Patient morbidity	Higher due to the second surgical site	Lower as no donor site is needed
Long-term stability	High tissue stability	Moderate; lacks structural support
Esthetic outcomes	Superior tissue thickness and color match	Improved vascularity but less tissue volume

Edel [16] and Broome and Taggart [17] introduced early trapdoor techniques, achieving approximately 85–88% root coverage by enhancing wound closure and healing. Langer and Calagna [18] refined the internal bevel flap technique, providing smoother tissue junctions with 90% coverage. Langer and Langer [19] established SCTG as a gold standard, demonstrating 90–100% success. Subsequent innovations, such as Harris' [20] parallel blade technique and Bouchard et al.'s SCTG for class I/II recessions, maintained high coverage rates (92%).

Minimally invasive approaches, like Hürzeler and Weng's [21] single incision and Zucchelli et al.'s [22] extraoral de-epithelialization, further optimized healing, achieving 88–90% coverage. Harris et al. [20] and Cairo et al. [23] reinforced CTG's effectiveness, reporting up to 94% root coverage. More recent studies, including Tadepalli et al. [24], compared tunnel and coronally advanced flap (CAF) techniques with CTG, reporting variable success rates (55–93%). Overall, CTG remains the most effective approach for root coverage, with consistent success in achieving optimal clinical outcomes (Table 3).

Table 3. Mean root coverage (%) in CTG group.

Author	Year	Technique	Material	Root Coverage (%)
Edel [16]	1974	Trapdoor technique	Complete wound closure	~85%
Broome and Taggart [17]	1976	Trapdoor using Brasher-Rees knife	Wider base, faster healing	~88%
Langer and Calagna [18]	1980	Internal bevel flap and parallel incision	Smoother junction, less shrinkage	~90%
Langer and Langer [19]	1985	SCTG for root coverage	Sub-epithelial CTG	90–100%
Harris [25]	1992	Parallel blade and ingraft knife technique	Uniformly thick CTG	~92%
Bouchard et al. [26]	1994	SCTG for class I and II recession	Sub-epithelial CTG	92%
Hürzeler and Weng [21]	1999	Single-incision	No vertical incisions	~88%
Lorenzana and Allen [27]	2000	Single-incision	Larger graft harvest	~90%
Del Pizzo et al. [28]	2002	Single-incision with periosteum preservation	Enhances healing	~89%
Zucchelli et al. [22]	2003	Extraoral de-epithelialization	Useful for thin palates	~90%
Bosco and Bosco [29]	2007	CTG from the thin palate	Minimizes vascular injury	~92%
Cairo et al. [23]	2008	CTG for Miller class I/II	CTG	>90%
McLeod et al. [30]	2009	Partial palatal de-epithelialization	Uniform, thin CTG	~91%
De Carvalho et al. [31]	2023	CTG with tunnel technique in gingival recession	CTG	55%
Tadepalli et al. [24]	2024	CAF + CTG in maxillary gingival recession	CTG	93%

Root coverage outcomes using PRF and related biomaterials in combination with CAF or other techniques. Early studies, such as Huang et al. [32] using PRP with CAF, showed moderate success (78.5%). Aroca et al. [33] and Jankovic et al. [34] introduced PRF membranes with CAF, achieving improved root coverage (85–87%).

Subsequent research, including Eren and Atilla [35], Agarwal et al. [36], and Oncu [37], reinforced PRF's efficacy, with coverage rates consistently around 85–89%. Alternative fibrin-based approaches, such as concentrated growth factors (CGF) used by Bozkurt Dogan et al. [38] and Xue et al. [39], reported higher success (~90–92.5%). Studies like Subbareddy et al. [40] applied PRF with the VISTA technique, achieving 91.3% coverage. Recent research by Tazegul et al. [41] demonstrated stable results (87–88%), supporting PRF's role in periodontal regeneration. Overall, PRF and CGF enhance root coverage outcomes, providing a viable alternative to traditional grafting techniques (Table 4).

Table 4. Mean root coverage (%) in PRF group.

Author	Year	Technique	Material	Root Coverage (%)
Aroca et al. [33]	2009	CAF + PRF	PRF membrane	85.2%
Huang et al. [32]	2005	CAF + PRP	Liquid PRP	78.5%
Jankovic et al. [34]	2010	CAF + PRF	PRF membrane	87.1%
Kumar et al. [42]	2013	CAF + PCG	Collagen sponge soaked with PCG	74.3%
Eren and Atilla. [35]	2014	CAF + PRF	PRF membrane	88.9%
Agarwal et al. [36]	2016	CAF + PRF	PRF membrane	86.5%
Bozkurt Dogan et al. [38]	2015	CAF + CGF	CGF membrane	90.3%
Gupta et al. [43]	2015	CAF + PRF	PRF membrane	83.7%
Oncu et al. [37]	2017	CAF + PRF	PRF membrane	89.2%
Jain et al. [44]	2017	CAF + PRF	PRF membrane	84.6%
Rehan et al. [45]	2018	CAF + PRF	PRF membrane	85.9%
Dholakia et al. [46]	2019	CAF + PRF	PRF membrane	87.4%
Subbareddy et al. [40]	2020	VISTA + PRF	PRF membrane	91.3%
Tazegul et al. [41]	2022	CAF + PRF	PRF membrane	88.1%
Xue et al. [39]	2022	TUN + CGF	CGF membrane	92.5%

Root coverage outcomes in CAF and tunnel techniques using either CTG or PRF. Collins et al. [47] and Eren and Atilla [35] demonstrated high root coverage with both CTG (~96–94%) and PRF (~93–92%). Hedge et al. [48] and Jankovic et al. [34] showed similar trends, with slightly lower percentages for PRF compared to CTG.

Joshi et al [49] reported a significant difference, with CTG achieving 93.33% root coverage compared to only 70.64% with PRF. Kumar et al. [42], however, observed better outcomes with PRF (74.4%) over CTG (58.9%), indicating potential variability in treatment response. Studies by Oncu [37], Tunali et al. [50], and Uraz et al. [50] consistently favored CTG over PRF, though differences remained moderate (96% vs. 75%).

Interestingly, Uzun et al. [4] found nearly identical results for CTG (93.22%) and PRF (93.29%) with the tunnel technique, suggesting PRF may be equally effective in certain surgical approaches. Overall, while CTG generally achieves higher root coverage, PRF remains a promising alternative, particularly in cases where autogenous grafting is less favorable (Table 5).

Table 5. Mean root coverage (%) in CTG + PRF group.

Author	Year	Technique	Material	Root Coverage (%)
Collins et al. [47]	2021	CAF + CTG vs. CAF + PRF	CTG, PRF membrane	96.97 / 93.33
Eren and Atilla [35]	2014	CAF + CTG vs. CAF + PRF	CTG, PRF membrane	94.2 / 92.7
Hedge et al. [48]	2021	VISTA + CTG vs. VISTA + PRF	CTG, PRF membrane	86.43 / 83.25
Jankovic et al. [34]	2012	CAF + CTG vs. CAF + PRF	CTG, PRF membrane	91.96 / 88.68
Joshi et al. [49]	2020	CAF + CTG vs. CAF + PRF	CTG, PRF membrane	93.33 / 70.64
Kumar et al. [42]	2017	CAF + CTG vs. CAF + PRF	CTG, PRF membrane	58.9 / 74.4
Oncu [37]	2017	CAF + CTG vs. CAF + PRF	CTG, PRF membrane	84 / 77.12
Tunali et al. [50]	2015	CAF + CTG vs. CAF + PRF	CTG, PRF membrane	77.36 / 76.63
Uraz et al. [50]	2015	CAF + CTG vs. CAF + PRF	CTG, PRF membrane	96.46 / 75.26
Uzun et al. [4]	2018	TUN + CTG vs. TUN + PRF	CTG, PRF membrane	93.22 / 93.29

CTG and PRF have potential applications beyond periodontology due to their regenerative properties. In oral and maxillofacial surgery, CTG is used for alveolar ridge augmentation and soft tissue reconstruction, while PRF enhances wound healing in sinus lifts, bone grafting, and cystic defect repairs. In implantology, CTG improves peri-implant soft tissue thickness, and PRF accelerates osseointegration and bone regeneration [51]. Dermatology and plastic surgery benefit from CTG for soft tissue augmentation and scar revision, whereas PRF is used in esthetic medicine for skin rejuvenation, chronic wound healing, and hair restoration [52]. PRF is also utilized in orthopedics and sports medicine for tendon, ligament, and joint injury healing, as well as in ophthalmology for corneal wound healing and ocular surface reconstruction [53]. These diverse applications highlight the broad regenerative potential of CTG and PRF across medical and dental fields.

3. Conclusion

CTG and PRF are effective in periodontal surgery, but their roles and outcomes differ. CTG is the gold standard for treating gingival recession, offering 90–97% root coverage, excellent tissue stability, and superior esthetics, making it ideal for severe or complex cases. However, it requires a secondary surgical site, leading to higher morbidity and longer recovery times.

PRF, a minimally invasive autologous biomaterial, accelerates healing and regeneration through its growth factors, achieving 70–80% root coverage. While less predictable than CTG, PRF is effective in enhancing angiogenesis and soft tissue healing, especially for mild-to-moderate cases or when combined with CTG.

On the other hand, PRF is easy to prepare, cost-effective, and associated with faster initial healing. It is more suitable for patients with mild to moderate recession or those who prefer less invasive treatment. While CTG achieves superior volume and thickness, PRF enhances soft tissue texture and vascularity but may not match CTG in volume augmentation. In some cases, combining CTG and PRF can yield synergistic benefits, leveraging the strengths of both approaches to optimize outcomes. Ultimately, the choice between CTG and PRF depends on patient preferences, defect characteristics, and clinical expertise.

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Conflict of interest

The authors declare no conflict of interest related to this study.

Authors contribution

Dr. Sanehi Punse was primarily responsible for the conception of the study, data collection, clinical procedures, analysis, and drafting of the manuscript. Dr. Prasad Dhadse provided overall supervision and expert guidance throughout the study, contributed to the study design, and critically reviewed the manuscript for important intellectual content. Dr. Anand Wankhede played a key role in the planning of the study, assisted with data interpretation, and provided valuable inputs during manuscript preparation. Dr. Ruchita Patil contributed to the literature review, clinical support, and compilation of data. Dr. Rutuja Karamore was involved in case documentation, clinical photography, and manuscript formatting. All authors have read and approved the final version of the manuscript.

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