Utilising blood-derived products for guided tissue regeneration in periradicular surgery: a systematic review and meta-analysis

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SYSTEMATIC REVIEW

REVISED Utilising blood-derived products for guided tissue regeneration in periradicular surgery: a systematic review and meta-analysis [version 2; peer review: 2 approved]

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Abstract

Background

Since 1982, guided tissue regeneration (GTR) has become increasingly popular. The recent progress in GTR research focuses on the application of blood-derived products. However, no comprehensive systematic review has been conducted to assess its effectiveness specifically in periradicular surgery. Therefore, the aim of this review was to analyse the outcomes of periradicular with GTR using blood-derived products compared to standard periradicular surgery.

Methods

This review was based on randomised controlled trials comparing periradicular surgery in conjunction with GTR with blood-derived products and the standard periapical surgery. The databases searched included Embase, MEDLINE, Cochrane CENTRAL, and Dentistry and Oral Sciences Source, with the most recent search conducted on December 16th, 2022. Additionally, reference lists of similar systematic reviews were examined, while international trials registries and repositories were consulted for unpublished studies. Two blinded independent reviewers carried out the screening and the included studies underwent critical appraisal. The findings are reported in accordance with the PRISMA guidelines.

Results

A total of 261 publications were initially reviewed based on their title

Open Peer Review

Approval Status ✓ ✓

	1	2
version 2 (revision) 08 Mar 2024		✓ view
version 1 14 Feb 2024	✓ view	

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Any reports and responses or comments on the article can be found at the end of the article.

and abstract, resulting in seventeen studies that underwent full-text screening. At this stage, 14 studies were excluded, leaving three randomised controlled trials to be included. These trials involved a total of 85 patients. A meta-analysis was conducted for the outcome of healing. The overall treatment effect was 0.78 (95% CI 0.18 to 3.34), indicating a preference towards the control group.

Conclusion

Based on a meta-analysis of three studies, there was no statistically significant distinction observed in terms of healing between the GTR involving blood-derived products and standard procedure groups. However, critical appraisal revealed indirectness and imprecision, resulting in a certainty rating of 'low'. Thus, additional robust evidence is necessary to support the utilisation of blood-derived products in GTR techniques to enhance periradicular surgery outcomes.

Systematic review registration number

PROSPERO CRD42020222663.

Keywords
Peri-radicular surgery; dental; blood-derived products, guided tissue regeneration

This article is included in the Biobased Materials for Additive Manufacturing collection.

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REVISED **Amendments from Version 1**

Some minor language edits have been made based on the reviewer feedback.

Any further responses from the reviewers can be found at the end of the article

Introduction

Guided tissue regeneration (GTR) has emerged as a valuable adjunct to surgical techniques in dentistry, aiming to enhance the restoration of periodontal tissues, collagen fibres, and alveolar bone regeneration. Extensive research on this topic has been conducted since 1982[1]. The primary objective of GTR is to prevent the downgrowth of epithelial cells, which can impede the regeneration process by inhibiting the presence of other healing cell types like osteoblasts[2]. By stabilising the blood clot, GTR safeguards the cavity and facilitates healing by primary intention[2]. In an ideal environment, GTR relies on three core principles: scaffolding generation, growth factors, and stem cells[3]. However, periapical surgery is mainly considered when a necrotic tooth is accompanied by a persistent periapical lesion, resulting in contamination of the periapical region, and complicating the healing process. Therefore, disinfection of the periapical area is paramount to eliminate bacterial load and enable the effective application of GTR principles.

Numerous studies have acknowledged the beneficial impact of GTR in the fields of implantology and periodontology. A systematic review and meta-analysis examined its effects in gingival and periodontal treatment and revealed enhanced outcomes that persisted for a minimum of ten years[4]. In the realm of implantology, GTR is frequently employed in conjunction with guided bone regeneration, demonstrating improved patient outcomes[5]. The utilisation of GTR in periradicular surgery has also been gaining increasing popularity[6]. Notable clinical advancements have been observed, particularly in cases of through-and-through lesions, leading to improved healing[7–11].

The latest progress in the field of GTR focuses on the use of blood-derived products (BDPs) such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), platelet-derived growth factor, and bone morphogenic proteins[12,13]. Each of these products plays a role in encouraging the healing of dental tissues through diverse mechanisms that mimic physiological healing and tissue repair processes[12,13]. Previous studies have suggested that the growth factors released from platelets accelerate the process of bone repair[14,15]. PRF offers certain advantages over PRP, including an easier preparation, potential to achieve haemostasis, absence of additives, and slower polymerisation, which enhances its repairing ability[16–21]. Leukocytes also play a significant role in tissue regeneration and have been combined with PRF and PRP to create leukocyte and platelet-rich plasma (L-PRP) and leukocyte and platelet-rich fibrin (L-PRF)[22,23]. The use of L-PRP and L-PRF has shown positive effects[24–27]. There are studies reporting that leukocytes within PRP may promote premature apoptosis and increase inflammation, potentially exerting a detrimental effect on healing[23,28–30]. However, others dispute this, stating that leukocytes do not participate in catabolic pathways or induce unfavourable effects[30,31].

Numerous recent RCTs have focused on examining the efficacy of GTR techniques utilising BDPs in periradicular surgery. However, no existing systematic reviews addressing this specific topic were found during the search. The aim of this systematic review and meta-analysis was to evaluate whether the use of GTR techniques involving BDPs during periradicular surgery leads to improved outcomes in comparison to employing standard surgery.

Methods

This study followed the systematic review methodology for assessing the effectiveness of evidence as outlined by the Joanna Briggs Institute (JBI) [https://synthesismanual.jbi.global] as explained below. Reporting of the findings followed guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA 2020) checklists[32] and summarised provided in Table 1 and Table 2, in supplementary data file.) The review has also been registered with PROSPERO (registration number CRD42020222663) to ensure transparency and prevent any inadvertent duplication of research efforts. The protocol for this review was published by JBI[33] to provide clarity and avoid unnecessary repetition.

Eligibility criteria

Table 1 presents the Population, Intervention, Comparator, and Outcome (PICO) criteria for the study.

Included in this review were randomised controlled trials involving adults undergoing periradicular surgery for endodontically treated teeth. Studies including patients who had periradicular surgery in the past or if surgery was performed on unrestorable teeth were excluded.

The interventions considered in this study encompassed GTR techniques involving BDPs, which were utilised to address the remaining bone cavity after removing periradicular infection during periradicular surgery. There were no specific restrictions regarding the type of BDPs or the use of a membrane following the procedure. Studies involving bone substitutes were not considered. The comparator group consisted of periapical surgery not involving the implementation of a GTR technique during the surgical procedure.

Table 1. PICO criteria.

Population	Adult patients undergoing periradicular surgery
Intervention	Guided tissue regeneration techniques utilising blood-derived products
Comparator	Standard surgical periapical treatment
Outcome	Success or failure to heal following the surgical periradicular procedure

The primary outcome considered was the success or failure of healing following the procedure, as assessed using Molven's criteria. This is explained further in the Data Items section.

Information sources

To identify published reports of relevant studies, a thorough search was conducted in several databases, including Embase (Ovid), MEDLINE (Ovid), Dentistry and Oral Sciences Source (EBSCOhost) and Cochrane CENTRAL. Furthermore, reference lists of relevant past systematic reviews were examined to recognise and include additional studies. Unpublished studies were pursued by exploring international trials registries like ClinicalTrials.gov and repositories such as the British Library EThOS database. The initial search was conducted on May 7, 2021, and an update search was performed on December 16, 2022, without any time restrictions.

Search strategy

To ensure comprehensive coverage, a systematic search strategy was devised. Initially, a limited search was conducted on the MEDLINE database to identify relevant published RCTs. The index terms and keywords present in the titles and abstracts of relevant articles were utilised to develop a comprehensive search strategy. The complete search strategy is provided in Table 3, supplementary data file[34] and was applied across all the databases searched. Furthermore, manual searches were conducted, and the reference lists of all included sources of evidence were inspected to identify additional studies. Language restrictions were not imposed; however, only studies published in English were considered, without any limitations on the publication dates.

Selection process

After conducting the comprehensive search, all studies were imported into EndNote v.X7 (Clarivate Analytics, PA, USA (https://endnote.com/). Duplicate records were eliminated by the software. The records were subsequently uploaded into JBI System for the Unified Management, Assessment, and Review of Information (JBI SUMARI; JBI, Adelaide, Australia)[35]. Two independent reviewers, who were blinded to each other's evaluations, screened the titles and abstracts. Relevant trials were obtained in full-text format and assessed by the same two independent blinded reviewers. Any studies that did not meet the inclusion criteria at the full-text stage were recorded and reported with the reasons for exclusion. In case of any disagreements, a discussion was held to reach a consensus, involving a third reviewer if necessary. The results of the search are presented in a PRISMA 2020 flow diagram (Figure 1)

Data collection process

To ensure comprehensive data collection, the JBI SUMARI tool was employed to extract information from the included studies[36]. Two independent blinded reviewers (G.B, L.B) conducted the data review process.

Data items

The extracted data encompassed various aspects, including participant characteristics, sample size and outcomes relevant to this review. This included details about the type of GTR used, presence of a comparator, and clinical and radiographic outcomes. The outcome was evaluated using Molven's criteria, which are widely accepted and defined as follows[35]:

Failure to heal clinically is noted in cases that resulted in pain, swelling, and tenderness to percussion or palpation, suppuration, presence of a sinus tract, and tooth mobility. Failure to heal radiographically is indicated if there is no reduction or if there is increase in lesion size. Success is defined as the absence of clinical and radiographic signs of failure.

The studies were examined for four possible outcomes: complete healing, incomplete healing, uncertain healing, and failure to heal. These outcomes were evaluated through clinical and radiographic assessments. Additionally, they were dichotomized into "success" or "failure." For this analysis, success was considered in cases of complete or incomplete healing.

Risk of bias and certainty assessment

Two independent reviewers conducted a risk of bias assessment for the three RCTs utilising the automated JBI SUMARI critical appraisal tool. The findings from this assessment are provided in extended data[34]. In the event of disagreements between the reviewers, consensus was reached through discussion.

To determine the certainty of the evidence, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used[37]. A Summary of Findings (SoF) was generated using GRADEPro GDT (McMaster University, ON, Canada). The SoF focused on the outcomes of success or failure to heal.

Effect measures

The studies were subjected to a statistical comparative meta-analysis using JBI SUMARI[35]. The effect sizes were represented as odds ratios, and their corresponding 95% confidence intervals were calculated for the analysis. The standard I2 test was utilised to assess statistical heterogeneity. A random-effects model was employed for the statistical analysis due to the presence of clinical and methodological heterogeneity[38].

Synthesis methods

Angerame *et al.* (2015) organised their results in graphical form, which were then converted into Molven's scores for interpretation[39]. In the case of Meschi *et al.* (2020), the trial reported percentages of teeth within each Molven's category, as determined by two observers[40]. Since this presentation format was not directly comparable to the other trials, the authors modified the results by converting the percentages to whole numbers for each observer. The average number and percentage values were calculated for each score, rounded to whole numbers, and repeated for each Molven's score. Furthermore, it was not possible to separate the results of the control group with no intervention, from the intervention group with no other additional intervention because of the way the results were provided. The authors decided to consider the '+LPRF +/- BG' group as the intervention group and the '-LPRF +/- BG' group as the control group, as the former always included the intervention (LPRF), while the latter did not. No further outcomes were offered for

separate analysis of the groups, so it is recommended to interpret these findings cautiously.

Results

Study selection

The initial database search yielded a total of 403 records, and further nineteen studies were discovered through registers. Following deduplication, 261 records were screened based on their title and abstract, resulting in the exclusion of 244 records. Seventeen studies underwent full-text screening. Among these, sevenstudies were not yet published, while further seven studies did not meet the eligibility criteria, ultimately leaving three studies for inclusion (Figure 1). The excluded studies and the reasons, as well as the included studies are presented in the extended data[34].

Study characteristics

The characteristics of the included trials are provided in extended data[34]. The three studies were conducted in Italy[41], Belgium[41] and India[40]. The participant numbers ranged from 11 to 50 across the trials, with a relatively balanced distribution of males and females. The mean age of the participants varied between 28 and 47 years. In the study by Angerame *et al.* (2015), platelet-rich fibrin was used as the intervention, while Dhamija *et al.* (2020) employed platelet-rich plasma, and Meschi *et al.* (2020) utilized leucocyte- and platelet-rich fibrin +/- Bio-Glide membrane.

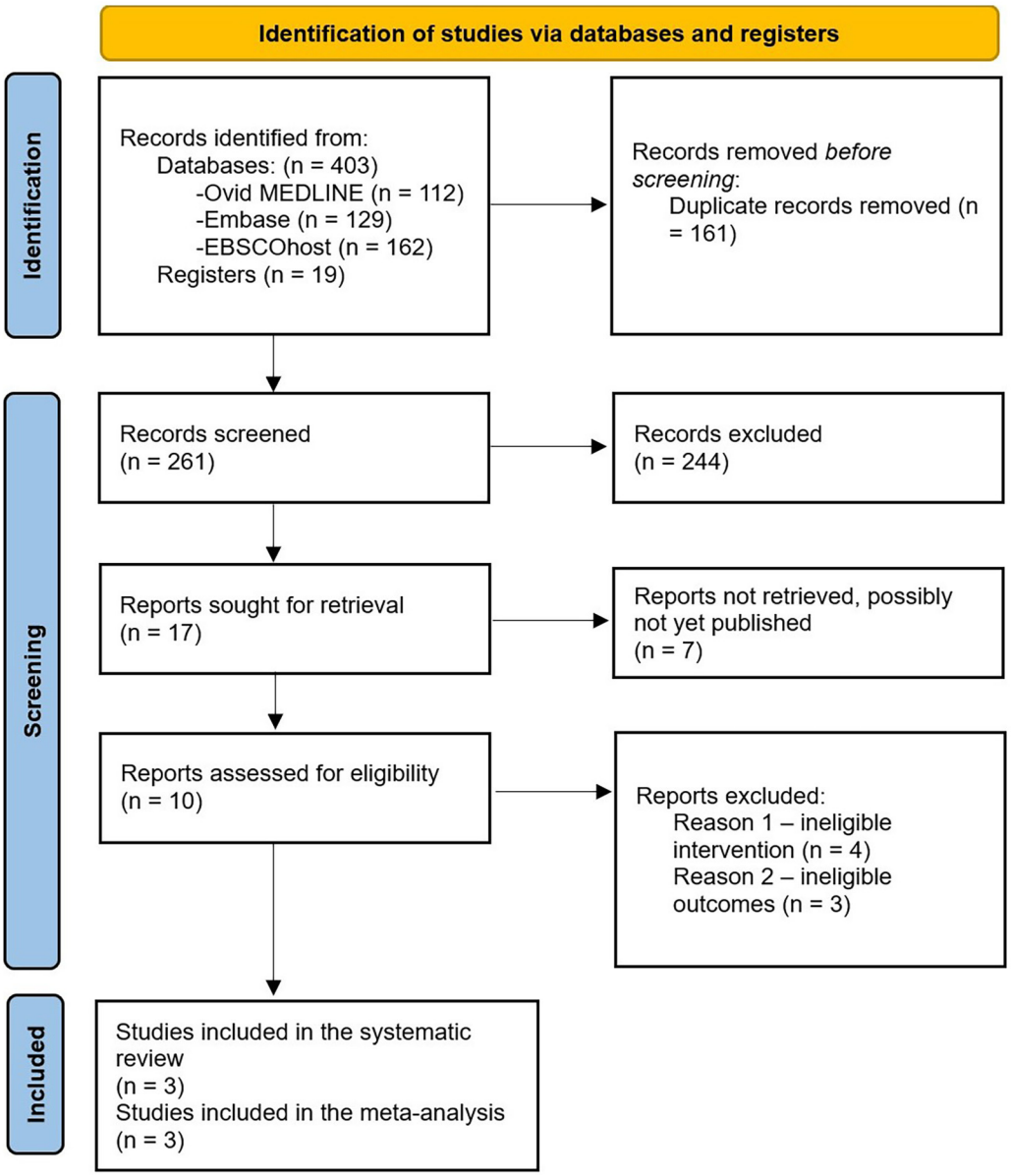

Figure 1. PRISMA 2020 flow diagram.

In both the Angerame *et al.* (2015) and Dhamija *et al.* (2020) studies, a single operator conducted all procedures. They used appropriate surgical techniques and a microscope, indicating a minimised risk of performance bias influencing the results, aligning with best practice guidelines and ensuring more precise surgical techniques. However, in the Meschi *et al.* (2020) study, two operators—a maxillofacial surgeon and an endodontist—were involved, potentially introducing variability in the procedure. The authors did not provide specific details regarding the experience or training of the operators, further adding to the ambiguity. Moreover, the Meschi *et al.* (2020) study initially used loupes, which was followed by a microscope only at the conclusion of the surgery.

Results of syntheses

Results were converted into Molven's criteria scores, which enabled comparison across different time points, groups, and 2-D results, as presented in Table 2. To facilitate comparison, the results were also dichotomized into success and failure, as shown in Table 3. Among the included studies, Angerame *et al.* (2015) reported an improved success in the BDP group compared to the standard procedure. In the Dhamija *et al.* (2020) study, the BDP group demonstrated a higher rate of complete healing and a lower rate of incomplete healing compared to the control group. However, in the Meschi *et al.* (2020) study, the control group exhibited a higher rate of complete healing, while the BDP group had higher rates of incomplete healing, uncertainty, and non-healing. The average success rate for the control group across all three studies was 86%, whereas the intervention group had an average success rate of 90% at 12 months. However, the sample size in each study was small, limiting the ability to achieve statistical significance.

The meta-analysis was conducted using the random inverse variance model in JBI SUMARI software (https://sumari.jbi.global/) under the guidance of a statistician. The results of the meta-analysis are summarized in Figure 2. For Dhamija *et al.* (2020), the odds ratio for healing with the intervention of BDP was 1.00 (95% CI 0.06 to 17.51). Angerame *et al.* (2015) yielded an odds ratio of 6.43 (95% CI 0.21 to 201.07), while Meschi *et al.* (2020) resulted in an odds ratio of 0.38 (95% CI 0.06 to 2.22). The overall odds ratio was 0.78 (95% CI 0.18 to 3.34), favoring standard procedure. However, it is important to exercise caution in interpreting these findings as the odds ratio for each individual study, as well as the overall ratio, shows variability and crosses the line of no effect. The level of heterogeneity (I^2) was observed to be 7.

Critical appraisal

The critical appraisal summary is displayed in Table 4 using the GRADE approach. Indirectness was classified as 'serious' due to Meschi *et al.* (2020) not providing separate results for

Table 2. Combined Results: Time Points, Groups, and 2-Dimensional Results based on Molven's Criteria.

Time point	Study	Group	Molven's criteria			
			Complete Number (%)	Incomplete Number (%)	Uncertain Number (%)	Unsatisfactory Number (%)
1 month	**Angerame *et al.*, 2015**	**Control**			3 (75)	1 (25)
		PRF			7 (100)	
	Dhamija *et al.*, 2020					
	Meschi *et al.*, 2020					
2 months	**Angerame *et al.*, 2015**	**Control**			4 (100)	
		PRF	6 (86)	1 (14)		
	Dhamija *et al.*, 2020					
	Meschi *et al.*, 2020					
3 months	**Angerame *et al.*, 2015**	**Control**			4 (100)	
		PRF	6 (86)	1 (14)		
	Dhamija *et al.*, 2020					
	Meschi *et al.*, 2020					
4 months	**Angerame *et al.*, 2015**	**Control**	1 (25)	2 (50)	1 (25)	
		PRF	7 (100)			
	Dhamija *et al.*, 2020					
	Meschi *et al.*, 2020					

Time point	Study	Group	Molven's criteria			
			Complete Number (%)	Incomplete Number (%)	Uncertain Number (%)	Unsatisfactory Number (%)
5 months	**Angerame *et al.*, 2015**	**Control**	1 (25)	2 (50)	1 (25)	
		PRF	7 (100)			
	Dhamija *et al.*, 2020					
	Meschi *et al.*, 2020					
6 months	**Angerame *et al.*, 2015**	**Control**	1 (25)	2 (50)	1 (25)	
		PRF	7 (100)			
	Dhamija *et al.*, 2020					
	Meschi *et al.*, 2020	**Control (-LPRF +/- BG)**	14 (64)	1 (4.5)	6 (27)	1 (4.5)
		PRP (+LPRF +/-BG)	11 (50)	1 (5)	8 (36)	2 (9)
12 months	**Angerame *et al.*, 2015**	**Control**	1 (25)	2 (50)	1 (25)	
		PRF	7 (100)			
	Dhamija *et al.*, 2020	**Control**	9 (56)	6 (38)	1 (6)	0 (0)
		PRP	12 (75)	3 (19)	1 (6)	0 (0)
	Meschi *et al.*, 2020	**Control (-LPRF +/- BG)**	18 (90)	0 (0)	2 (10)	0 (0)
		PRP (+LPRF +/-BG)	15 (68)	2 (9)	4 (18)	1 (5)

Table 3. Success and failure rates at 12 months in the three included studies.

Study	Group	Success Number (%)	Failure Number (%)
Angerame *et al.* (2015)	Control	3 (75)	1 (25)
	PRF	7 (100)	0 (0)
Dhamija *et al.* (2020)	Control	15 (94)	1 (6)
	PRP	15 (94)	1 (6)
Meschi *et al.* (2020)	Control (-LPRF +/- BG)	18 (90)	2 (10)
	PRP (+LPRF +/-BG)	17 (77)	5 (23)

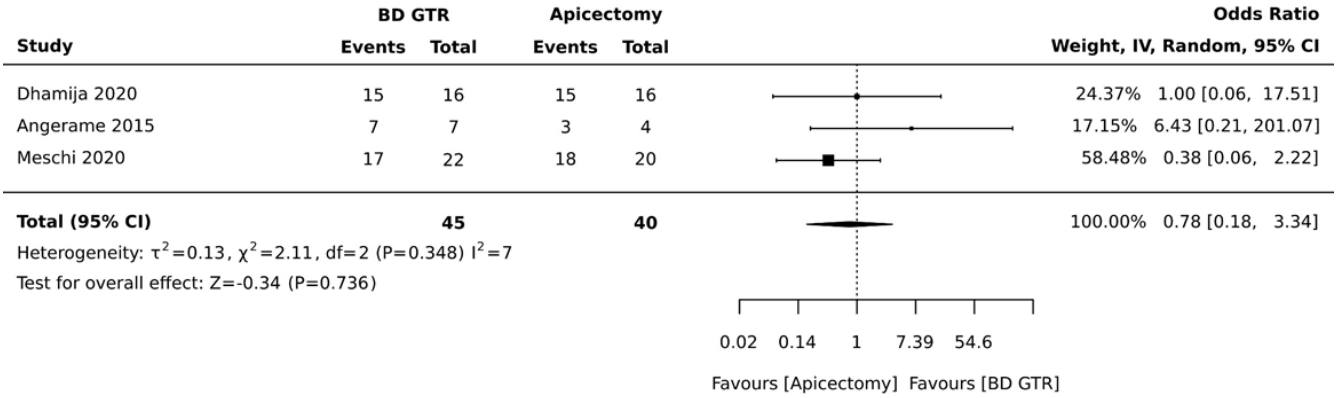

Figure 2. Meta-analysis Summary: Healing Outcome Analysis. Explanations: • The term "apicectomy" is used to designate the standard periradicular surgery procedure in this figure • The term "BD GTR" is used to refer to the standard procedure that incorporates guided tissue regeneration with the use of blood-derived products.

intervention versus control, instead combining the results for intervention group with or without a membrane. Imprecision was downgraded due to the limited sample size across the included trials. Consequently, these factors resulted in a downgrading of the overall certainty level to 'low'. The GRADE summary of findings and synthesis of the systematic review results are presented in Table 5. The interactive summary of findings is included in the supplementary files[34].

The key limitations identified in the studies during the critical appraisal were primarily related to questions addressing blinding during the trials. As the participants and those delivering the treatment were not blinded to the treatment assignment due to the nature of the intervention involving blood collection in the intervention group. Despite these limitations, both reviewers unanimously agreed to include the three trials in the systematic review following the critical appraisal.

Discussion

The use of GTR involving BDPs in periradicular surgery remains debatable and warrants further evidence to support its routine use in clinical practice. While some studies have reported positive outcomes, others question their clinical efficacy and cost-effectiveness. Critics argue that the use of BDPs adds an additional layer of complexity and expense with limited evidence to support their advantage over conventional techniques. Moreover, concerns have been raised about potential associated risks, including infection, allergic reactions, and inconsistent clinical outcomes. Given the lack of consensus and conflicting opinions, this systematic review aimed to shine a light on the clinical outcomes of GTR using BDPs in periradicular surgery.

All three RCTs included in this review had a 1-year follow-up, which has been shown to exhibit a association with the longevity of the outcomes[42,43]. This strengthens the reliability of the results. However, it should be noted that some RCTs compared the standard technique with this comparator but also involved other GTR techniques, such as the use of a membrane, complicating the findings[44]. Furthermore, it is essential to recognise the inherent methodological limitation in such trials where blinding of trial participants was not feasible due to the requirement for blood collection.

Certain limitations of the study should be considered. There were notable differences among the trials which were included, increasing heterogeneity across studies. Firstly, all trials utilised different BDPs and their respective preparations. Angerame *et al.* (2015) employed PRF, Dhamija *et al.* (2020) utilized PRP, and Meschi *et al.* (2020) employed L-PRF as their BDPs. Furthermore, Angerame *et al.* (2015) administered post-operative antibiotics (1g Amoxicillin BD) to both groups for 6 days, whereas the other included trials did not disclose the use of any antibiotics. It is also worth mentioning, as previously explained, that Meschi *et al.* (2020) presented their Molven's criteria as percentages and combined the GTR with BDPs group with the membrane group in some instances, making it difficult to separate and interpret the results, resulting in further ambiguity.

The overall findings of the meta-analysis do not favour the use of GTR involving BDPs in periapical surgery (Figure 2). This may be attributed to the limited number of trials that met the inclusion criteria, as well as limited sample sizes. Alternatively, these findings may indeed reflect the true clinical effect. It is important to note that GTR involving BDPs is a recent advancement. Some studies have reported promising results with the use of GTR and BDPs[45,46], and a case series investigating PRF application after periapical surgery demonstrated improved bone healing at a 6-month follow-up[12]. However, other studies have not found significant improvements in bone repair[47]. One possible reason for this discrepancy is the rapid resorption of blood products, with some studies indicating complete resorption within a few weeks[48,49]. Furthermore, the release of growth factors from BDPs might be limited to 1–2 weeks following application[48,50]. Moreover, blood products primarily improve the healing of dental soft tissues rather than play a significant role in osteogenesis[15]. These factors collectively contribute to the minimal difference observed between the control and intervention

Table 4. The critical appraisal summary of the three RCTs included in the systematic review - GRADE evidence assessment.

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Guided tissue regeneration involving blood derived products	Standard procedure	Relative (95% CI)	Absolute (95% CI)		
Healing (follow-up: 1 years; assessed with: Clinically and radiologically)												
3[a]	randomised trials	not serious	not serious	serious	serious	none	39/45 (86.7%)	36/40 (90.0%)	**OR 0.78** (0.20 to 2.75)	**3 fewer per 100** (from 26 fewer to 6 more)	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **OR**: odds ratio

a In all three studies included in this review, healing was evaluated using Molven's criteria, which categorized the outcomes into 'complete' and 'incomplete' healing groups.

b The indirectness was classified as 'serious' because Meschi *et al.* (2020) did not present separate results for the comparison of blood-derived products (BDP) versus control.

c The imprecision was lowered as a result of the small sample size, consisting of only 85 patients across the three trials.

Table 5. The synthesis of the systematic review results and the summary of findings.

Periradicular surgery involving guided tissue regeneration techniques involving blood derived products compared to standard procedure						
Patient or population: Adult patients undergoing periradicular surgery **Setting:** Dental practice or dental hospital **Intervention:** Guided tissue regeneration techniques involving blood derived products **Comparison:** Standard periradicular surgery (or apicectomy) procedure						
Outcomes	**Anticipated absolute effects*(95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with standard procedure	**Risk with guided tissue regeneration involving blood derived products**				
Success and failure to heal. Healing assessed clinically and radiologically Follow-up: 1 year	**Study population**		**OR 0.78** (0.20 to 2.75)	85 (3 RCTs)[a]	⨁⨁◯◯ Low[b, c]	
	90 per 100	**87 per 100** (64 to 96)				
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **OR:** odds ratio						
GRADE Working Group grades of evidence: **High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect. **Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.						

a In all three studies included in this review, healing was evaluated using Molven's criteria, which categorized the outcomes into 'complete' and 'incomplete' healing groups.

b The indirectness was classified as 'serious' due to the fact that Meschi *et al.* (2020) did not present separate results for the comparison of blood-derived products (BDP) versus control.

c The imprecision was downgraded as a result of the small sample size.

groups in this systematic review. While currently there is not enough evidence to support the routine use of BDPs in periradicular surgery, further exploration with larger trials is warranted to determine if GTR involving BDPs can reliably change clinical outcomes of periapical surgery.

Currently, extraction followed by dental implant placement is a popular treatment option for teeth with a poor prognosis. Consequently, a significant portion of current research focuses on implantology. GTR involving BDPs is being investigated in implantology to promote long-term stability of the implant. However, it is worth noting that only natural teeth possess a periodontal ligament with proprioceptors, which contribute to a more natural sensation during function and serve as protection against fractures (e.g., when biting into hard objects like popcorn kernels). In contrast, implants lack a periodontal ligament and do not possess these natural attributes. This raises the argument that clinicians may be too hasty in opting for extraction and replacement, overlooking the potential to salvage natural teeth that still have the capacity to provide these unique sensory experiences and protective mechanisms. This trend towards dental implants may be influenced by factors such as patient preferences for the perceived modernity of implants or the notion that implants are more durable than natural teeth when properly maintained. Therefore, further research exploring strategies to preserve existing teeth rather than automatically resorting to replacement with implants would be advantageous.

Conclusions

According to the findings of the reviewed studies, the use of GTR involving BDPs does not seem to yield improved clinical outcomes for patients undergoing periradicular surgery. It is important to note that the inclusion criteria of this systematic review were met by only three RCTs, indicating a limited pool of evidence. To further investigate the efficacy of BDPs in the healing of periradicular tissues, additional large-scale prospective trials are warranted.

Recommendations

The results of this systematic review indicate no substantial difference observed between the standard periapical surgery technique with or without the use of GTR involving BDPs. The additional procedures associated with GTR using BDPs have not demonstrated significant improvement in patient outcomes

thus far. Based on these results, the authors do not recommend the routine use of GTR involving BDPs as an adjunct to the standard surgical technique.

Data availability

Underlying data

The data for this article consists of bibliographic references, which are included in the References section.

Extended data

Open Science Framework: Supplementary Data: Guided tissue regeneration involving blood-derived products, https://doi.org/10.17605/OSF.IO/NJYSE[34].

This project contains the following extended data

- Search strategy
- Studies excluded at full text, including the reasons for exclusion
- Summary of Included Studies: Results and Characteristics
- JBI Critical Appraisal Tool for Randomised Controlled Trials
- Summary of Findings Generated with GRADE Pro Software (gradepro.org)

Reporting guidelines

Open Science Framework: PRISMA checklist for: Guided tissue regeneration involving blood-derived products, https://doi.org/10.17605/OSF.IO/NJYSE[34].

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Open Peer Review

Current Peer Review Status: ✔ ✔

Version 2

Reviewer Report 20 March 2024

https://doi.org/10.21956/materialsopenres.19002.r27180

✔ **Malik Ali Hassan Sajid**
FMH College of Medicine and Dentistry, Lahore, Pakistan

This systematic review adheres to the current guidelines and is well-written. The subject of the review matters to the practice of oral surgery. The objectives & the rationale have been stated with clarity and methods are given with adequate details. The conclusion reached is sufficiently substantiated by the results in the review. I would like to propose a few small changes:

Introduction:
However, periapical surgery is mainly considered when a necrotic tooth is accompanied by a persistent periapical lesion, resulting in contamination of the periapical region, and complicating the healing process. Therefore, disinfection of the periapical area is paramount to eliminate bacterial load and enable the effective application of GTR principles.**kindly consider to add reference*

Discussion:
GTR involving BDPs is being investigated in implantology to promote long-term stability of the implant.**kindly consider to add reference*

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Yes

Are the conclusions drawn adequately supported by the results presented in the review?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Oral & Maxillo-Facial Surgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 01 March 2024

https://doi.org/10.21956/materialsopenres.18943.r27183

Muhammad Ali Malik
[1] Great Western Hospital NHS Foundation Trust, Swindon, UK
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This is a well-written systematic review and follows the contemporary guidelines. The topic is relevant to clinical oral surgical practice. I would suggest some minor language amendments.

Abstract

- Background: “Therefore, the aim of this review was to analyse the outcomes of root-end surgery compared to periapical surgery incorporating GTR using blood-derived products”.
- Revise to: “Therefore, the aim of this review was to analyse the outcomes of periradicular with GTR using blood-derived products compared to standard periradicular surgery”.

Methods

- “This review involved randomised controlled trials exploring the comparison between GTR utilising blood-derived products and the conventional periapical surgery”.
- Revise to: “This review was based on randomised controlled trials comparing periradicular surgery in conjunction with GTR with blood-derived products and the standard periapical surgery”.
- “The databases Embase, MEDLINE, Cochrane CENTRAL, and Dentistry and Oral Sciences Source were searched, with the most recent search conducted on December 16th, 2022”.
- Revise to: “The databases searched included Embase, MEDLINE, Cochrane CENTRAL, and Dentistry and Oral Sciences Source, with the most recent search conducted on December 16th, 2022”

Introduction

- Consequently, the objective of this systematic review and meta-analysis was to evaluate whether the implementation of GTR techniques involving BDPs during periapical surgery leads to improved outcomes in comparison to employing standard periapical surgery procedure.

- Revise to: The aim of this systematic review and meta-analysis was to evaluate whether the use of GTR techniques involving BDPs during periradicular surgery leads to improved outcomes in comparison to employing standard surgery.

Discussion

- The use of GTR involving BDPs in periradicular surgery remains debatable and warrants further evidence to support its routine use in clinical practice.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

Yes

Are the conclusions drawn adequately supported by the results presented in the review?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Oral and Maxillofacial surgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.