Duramater Healing Following Decompression And Posterior Stabilization Using Platelet Rich Plasma And Platelet Rich Fibrin: A Systematic Review

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KEYWORDS

Durameter, Posterior Stabilization, Platelet Rich Fibrin, PRP

ABSTRACT

Background: Platelet-rich plasma (PRP) applications have the potential to play adjunctive roles in a variety of regenerative medicine treatment plans. PRP therapy is based on the fact that platelet growth factors (PGFs) support the three phases of wound healing and repair cascade. This systematic review evaluates the efficacy of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in enhancing duramater healing and reducing complications, particularly cerebrospinal fluid (CSF) leaks, following spinal surgeries. Incidental dural tears are a common complication in lumbar spine surgeries, leading to significant postoperative challenges.
Methods: The review included randomized controlled trials comparing PRP and PRF with conventional treatments, sourced from databases such as PubMed, ScienceDirect, ProQuest, and Cochrane Library.
Results: PRP and PRF are rich in growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-beta (TGF-β), all of which play crucial roles in wound healing.
Conclusion: Both PRP and PRF significantly improve duramater healing, with PRF offering a more sustained release of growth factors, thereby enhancing watertight dura closure and reducing CSF leakage.

1. Introduction

Incidental tears of the dural sac are considered to be the most commonly encountered complication of lumbar spine surgery, with a reported prevalence that varies from 1.8% to as high as 17.2% in some reports.1,2,10 Incidental dural tears (DTs) can be noticed either intraoperatively, with the identification of an obvious tear, a leak of cerebrospinal fluid or both or can be suspected retrospectively due to the postoperative appearance of postural headaches, as well as a persistent clear drainage.1,10,13 Complication that could arise from this leakage of cerebrospinal fluid is eruption and damage of nerve filaments.11 Another complication related to incidental DT is epidural fibrosis.12 The increased incidence of incidental durotomy (ID) is related to epidural fibrosis, which is induced by previous operation and advanced spinal degenerative changes, such as ossified yellow ligament.1,3,4 Beside direct dural laceration, other intraoperative mechanisms causing dural tear are excessive nerve root traction during removal of the disc extrusion and excessive force during removal of the adherent yellow ligament.2

Platelet-rich plasma (PRP) applications have the potential to play adjunctive roles in a variety of regenerative medicine treatment plans. PRP therapy is based on the fact that platelet growth factors (PGFs) support the three phases of wound healing and repair cascade (inflammation, proliferation, remodelling) at the time was being used as a transfusion product in thrombocytopenic patients.3,4,5 Since then it has been applied in multiple fields including plastic surgery, paediatric surgery, cardiac surgery, gynaecology, urology and ophthalmology.6,7 However, it is within the musculoskeletal field where there has been a surge of PRP use for multiple pathologies, largely due to widespread commercial interest following PRP use in professional sport. Current recommendation for PRP usage in musculoskeletal injuries are as treatment for rotator cuff tear, osteoarthritis, tendinopathies, and plantar fasciitis.14,15 Moreover, PRP usage in these conditions has shown positive result with good outcomes and little-to-zero adverse effects.15,16,17 Besides such conditions, PRP has also seen usage in spinal diseases. Studies have mentioned that PRP is able to give positive effects on aiding neuronal healing after spinal cord injury, promotes bone fusion on spinal fusion surgery, and other spinal diseases.25 However, PRP is not without its disadvantage; for example, PRP requires considerably advanced technique to be created due to its complex preparation and chemical manipulation compared

to the newer platelet-rich fibrin (PRF).19 Moreover, some legal restrictions on blood handling make the usage of PRP more difficult. Hence, a newer solution was proposed.20

The second generation of blood concentrates, i.e., platelet-rich fibrin (PRF), is prepared by a one-step centrifugation without the application of any anticoagulants [29].18 PRF consists of platelets, leukocytes and their subgroups embedded in a fibrin matrix with plasma proteins [21]18. The first protocol of PRF applies a comparably lower, but still high RCF (≈710×g) [30]. This protocol was called leukocytes-rich platelet-rich fibrin (L-PRF), mainly because it contains more leukocytes compared to the first-generation blood concentrates PRP.24 PRF has many benefits over PRP, including easy handling, low cost, and the lack of anticoagulant or bovine thrombin, which reduces biochemical alteration and risks associated with the use of bovine thrombin5,18. For about three decades, PRF has been used for regenerative purposes in dentistry [6]. Additionally, PRF has the potential to be used in fields other than dentistry, such as maxillofacial surgery and orthopaedic surgery. 6,7,8,9 Recent studies have shown the usage of PRF in musculoskeletal injuries give positive result, such as in meniscal tear, tendon repair, cartilage regeneration, and other sports-related injury.21,22,23

Only minimal research has been done in this field especially using this blood products following a procedure. Given the aforementioned problem and treatment above, comparison of the efficacy and efficiency in utilizing different blood products to enhance the recovery speed of dural tear after underwent spinal surgery should be a concern. Therefore, this systematic review was conducted with the aim to determine which treatment can further improve the patient condition following decompression and posterior stabilization.

2. Methodology

This systematic review was conducted based on methodological guideline of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for more transparent and comprehensive systematic review. The study protocol was registered in the PROSPERO International Prospective Register of Systematic Reviews. Data Source and Search Strategy Three reviewers (DK, JN, DGN) searched published studies using online search engineering from four databases including PubMed, ScienceDirect, ProQuest, and Cochrane Library. The terms used were as follows ‘dural tear’, ‘Spinal Surgery’, ‘Platelet-Rich Plasma’, ‘Platelet-Rich Fibrin injection’, ‘dura mater healing’. We adapted the search terms to fit the requirements of each database. A protocol for our review was registered online with Prospero No. CDR42024581227;

Studies included in our study are randomized controlled trials (RCTs) that include patients with dural tear. The intervention groups receive Platelet-Rich Plasma injection and the control groups receive Platelet-Rich Fibrin injection. Only English and Indonesian literature, as well as last 10-year studies, were reviewed for this study. We excluded studies in case series, commentary, review articles, conference abstracts, editorial letters, and brief reports. Full articles that failed to be retrieved were also excluded. Study Selection Studies are identified using keywords used during the search. After removing duplicates using Rayyan.ai, retrieved articles were screened based on their titles and abstracts by three independent reviewers (DK, JN, DGN). Potentially full-text articles were thoroughly assessed using the eligibility criteria described above. Consensus among reviewers would be held if there were any emerging discrepancies that need to be resolved.

The appropriate risk of bias assessment tool according to our study was utilized using Review Manager 5.4.1. This tool measured the risks of bias in selection, performance, detection, attrition, and outcome reporting of our systematic review qualitatively. Results are then classified into high risk, low risk, or unclear risk in risk of bias. We evaluated the risk of bias independently and discussed it together to form a summary. Data Extraction Data from each study is collected and then inputted into a table. Extracted data included: 1) first author and publication year; 2) study design; 3) number of participants; 4) intervention; 5) control; 6) outcomes; and 7) significancy (P-value).

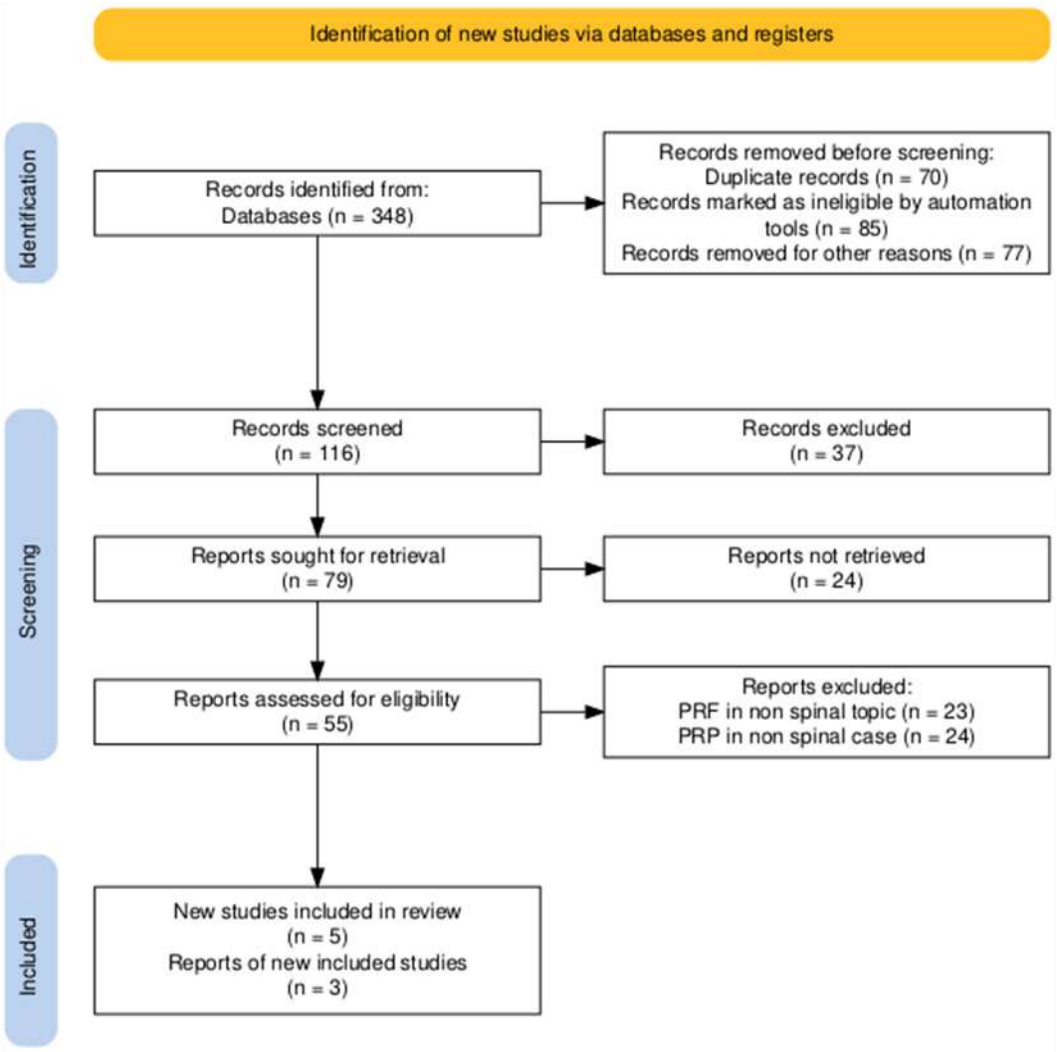

Figure 1. PRISMA flow chart

3. Result and Discussion

Paksoy K et al. conducted a study on albino female rats to assess the difference in thickness of dura mater after applying PRP compared with the conventional suturing technique. The firrst group had a dural incision without repair. A dural incision was closed with suturing (10/0 Vicryl) in the second group, and PRP was applied over the sutured dura in the third group. There were no significant differences in dura mater thickness and surface area between Group 1 and Group 2. However, the third group observed a significant increase in dura mater thickness and surface area. New bone areas and new vasculature were observed more frequently in the PRP rooms group. The PRP-treated group also displayed a higher occurrence of new bone areas secondary to increased osteoblastic activity and high vascularity due to increased angiogenesis. Providing the regeneration of dura mater in defect situations will contribute to the protection of the barrier feature. In line with this idea, it is thought that PRP can be beneficial for us to reach this goal.1

Vasilikos et al. developed an in vitro testing apparatus for hydrostatic assessment of water-tight dura closure. Using freshly harvested bovine dura mater, a standardised 20-mm incision was closed with a running suture, and the leak pressure was measured first without (primary leak pressure) and then with PRF augmentation (secondary leak pressure). The secondary leak pressure was measured following the introduction of PRP augmentation. In all cases, liquid PRF fully covered the surface of the chamber and the underlying PRF membrane. The PRP augmentation consistently strengthened the closure, with a four times higher leak pressure compared to standard running suture technique. Autologous platelet

rich fibrin augmentation reliably reinforced watertight closure of the dura mater to a > 4-fold increased leak pressure after failure of the initial standard running suture technique.2

Coucke et al., conducted a single-blinded, prospective randomized controlled interventional trial using Patients undergoing cranial neurosurgery (supratentorial and infratentorial) with intentional opening of the dura. Patients are randomized in a 1:1 fashion comparing L-PRF to commercially available fibrin sealants. The surgery is performed by a team of trained neurosurgeons according to local standards. The dura is primarily closed with sutures, and additional grafts can be used to close the remaining defects. For patients allocated to treatment with L-PRF, no commercially available fibrin sealants may be used for dural closure, but they can be used for hemostasis or to fixate Teflon® or vessels during microvascular decompression. L-PRF and liquid L-PRF glue are prepared during surgery. The primary endpoint is the success rate of both techniques, which means the absence of a clinically relevant CSF leak at 12 weeks after surgery, i.e., any leak that needs surgical revision or any other intervention, e.g., puncture or aspiration, longer hospitalization, or repeat imaging. Secondary endpoints include an analysis of peri- and postoperative complications (CSF leakage, both clinically relevant (incisional leakage) and not clinically relevant (swelling, pseudomeningocele), surgical site infection and treatment-site bleeding in particular), as well as a cost-effectiveness evaluation. In addition, the study will compare the efficiency of L-PRF in supratentorial and infratentorial surgery, based on surgical approach and technique.

Table 1. Inclusion Studies Characteristics

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Study	Study design	Population	Study Groups	No of cases	Objective	Outcome
Paksoy et al., 2021[1]	Experimental Design	Wistar Albino female rats were randomly allocated into three groups	Group 1 (Control group): Craniectomy + dural incision Group Group 2 (only suturing group): Craniectomy + dural incision + suturing (The dura was sutured with 10/0 Vicryl) Group Group 3 (PRP group): Craniectomy + dural incision + suturing + PRP (The dura was sutured with 10/0 Vicryl and PRP was applied over sutured dura.)	30	To compare the histopathological effects of dural suture technique with combined suturing and topically applied PRP on dural healing in a rat model of dural injury and cerebrospinal fluid leakage.	No significant difference was observed in the thickness and surface areas of dura mater in group 1 and group 2. Significant increase was observed in the thickness and surface areas of dura mater in the PRP applied group (Group 3) compared to other groups. New bone areas and new vasculature were observed more frequently in the PRP rooms group (Group 3). Mean volumes of dura mater in Groups 1, 2 and 3 were calculated as 14616000 (455705) micrometers cubed (µm3), 15558400 (264649) µm3 and 44515200 (327769) µm3, respectively. The statistical analysis shown a significant difference was observed between Group 1 and Group 3 (p> 0.05), a significant difference was observed between both Group 1 and Group 3 and between Group 2 and Group 3 (p <0.05).
Vasilikos, 2019[2]	Experimental Design	In vitro study where the watertight dura mater closure could hydrostatically assess.	Group A: Dura-closure with runningsuture only, Group B: PRF augmented group	26	The effect of applying PRF in reinforcing the watertight dura mater closure	The “running suture only group” had a mean pressure of 10.5 ± 1.2 cmH2O while the “PRF-augmented group” had a significantly higher mean value of 47.1 ± 2.6 cm H2O (p < 0.001; paired t test) The concentration of Fibrin on each PRF-application was not evaluated during this study, neither the serum-Fibrin levels of each volunteer. Group A had a leak pressure of 10.5 ± 1.2 cmH2O while Group B had a leak pressure of 47.2 ± 2.6 cm H2O. (p < 0.0001)

Coucke, 2024[3]	A single-blinded, prospective, randomized controlled interventional trial	Patients undergoing elective cranial neurosurgery	Subject were randomly assigned to receive either L-PRF (active treatment) or commercially available fibrin sealants (control) for dural closure in a 1:1 ratio	350	The noninferiority of L-PRF compared with commercially available fibrin sealants in preventing postoperative CSF leakage in supra- and infratentorial cranial surgery, with secondary outcomes focused on CSF leakage risk factors and adverse events	Six patients (5 in the control group, 1 in the L-PRF group) presented with CSF leakage requiring any intervention (relative risk [RR] 0.20, one-sided 95% CI -∞ to 1.02, p = 0.11), confirming noninferiority. 1 of 6 patient (control group) presented with CSF leakage requiring revision surgery. No risk factors for reconstruction failure in combination with L-PRF were identified. RRs for adverse events such as infection (0.72, 95% CI -∞ to 1.96) and meningitis (0.36, 95% CI -∞ to 1.25) favored L-PRF treatment, although L-PRF treatment showed slightly more bleeding events (1.44, 95% CI -∞ to 4.66).
Qureshi et al., 2017[4]	Case report	Patient with severe headaches post lumbar puncture, who was treated with epidural injection of PRP	-	1	Report of patient treated with epidural injection of PRP.	Patient reported complete resolution of headaches immediately after the procedure and minor pain in lower back at site of needle insertion
Gunaydin et al. 2017 [5]	Case report	A healthy 34-year-old term parturient (172 cm, 91 kg) suffering from severe PDPH after epidural labor.	-	1	To report successful utilization of an epidural patch with PRP for persistent post-dural puncture headache refractory to standard epidural blood patch.	She was discharged home 6 h after the epidural patching with PRP. She was instructed to carefully avoid extreme movements in her daily life. She was interviewed by daily phone calls. The resolution of headache was gradual and slight clinical improvement was obtained after 3 days. One week after the epidural patch procedure, she was admitted to repeat MRI. MRI after the epidural patch procedure reveals apparent radiological improvement with decreased pachymeningeal contrast enhancement. The patient was still free of symptoms 35 days after the epidural patch with PRP was performed. She was called for a further 6-month follow-up.
Soldatova et al., 2017[6]	Retrospective Studies	Patients underwent endoscopic endonasal resection of sellar, parasellar, and suprasellar lesions with the application of LPRF membranes during the skull base reconstruction at two surgical centers.	47 patients, 22 males and 25 females, with mean age of 51, underwent EEA resection of various pituitary and suprasellar masses with L-PRF membrane application during the skull base defect reconstruction at two surgical centers. Following institutional review board approval, their postoperative records were retrospectively reviewed to evaluate the rate of CSF leaks and postsurgical healing.	47	Investigate the effect of leukocyte–platelet-rich fibrin (L-PRF) on the postoperative healing after endoscopic skull base surgery	21 days following the surgery, 17/41 patients (42%) demonstrated improvement in the crusting score as compared with their 7 day postoperative examination. Ten of these patients (23%) showed no crusting. Fourteen (34%) patients had no change in the crusting score. Six patient records were incomplete. A total of 4/47 cases (8.5%) had postoperative cerebrospinal fluid leak requiring surgical repai

Arabacı et al., 2023[7]	Retrospective Studies	40 infants with a diagnosis of MMC who were operated on at our neurosurgery clinic	PRP was administered to 20 of the patients, and 20 were followed up without PRP. In the PRP group, 10 of the 20 patients underwent primary defect repair and 10 underwent flap repair. In the non-PRP group, 14 patients underwent primary closure and 6 underwent flap closure	40	To minimize cerebrospinal fluid leakage and accelerate the healing of the immature pouch tissue following corrective surgery for meningomyelocele by administering Platelet-rich plasma.	In the PRP group, CSF leakage occurred in one (5%) patient, and none developed meningitis. Partial skin necrosis occurred in three (15%) patients and wound dehiscence in three (15%) patients. In the group that did not receive PRP, CSF leakage occurred in nine (45%) patients, meningitis in seven (35%), partial skin necrosis in 13 (65%), and wound dehiscence in seven (35%) patients. The rate of CSF leakage and skin necrosis in the PRP group was significantly (p<0.05) lower than that in the PRP group. Furthermore, wound closure and healing were also improved in the PRP group

Qureshi et al. reported a case of a patient with headache secondary to a lumbar puncture performed to exclude meningitis. The patient showed complete resolution of symptoms after receiving injectable PRP. Another case report showed the successful utilization of a PRP patch in a patient with post-dural puncture headache (PDPH) after a failed standard epidural blood patch. The headache gradually decreased and completely resolved after 3 days. The 1-week follow-up MRI revealed apparent radiological improvement with decreased pachymeningeal contrast enhancement. The patient was reported to be free of symptoms at the last follow-up of about one month. The fibrinogen in PRP may be activated to form a fibrin matrix and platelets aggregate along the fibrin fibers during clotting creating an effective seal in the extradural space. 4

Gunaydin et al. reported a case of 4-year-old term parturient suffering from severe PDPH after epidural labor analgesia who received first EBP within 48 hours. Then, the parturient was offered a second epidural patch with PRP. Then, epidural patching using 10 ml of autologous PRP was performed in the sitting position at the first attempt between the L 2–3 intervertebral space. She was discharged home 6 h after the epidural patching with PRP. he resolution of headache was gradual and slight clinical improvement was obtained after 3 days. One week after the epidural patch procedure, she was admitted to repeat MRI. MRI after the epidural patch procedure reveals apparent radiological improvement with decreased pachymeningeal contrast enhancement The patient was still free of symptoms 35 days after the epidural patch with PRP was performed. In conclusion, epidural patch with PRP seems to be a successful procedure after failed EBP in this particular parturient with persistent PDPH refractory to standard medical and/or invasive treatment.5

Soldatova et al., conducted a retrospective study with 47 patients underwent endoscopic endonasal resection of sellar, parasellar, and suprasellar lesions with the application of LPRF membranes during the skull base reconstruction at two surgical centers. 22 males and 25 females, with mean age of 51, underwent EEA resection of various pituitary and suprasellar masses with L-PRF membrane application during the skull base defect reconstruction at two surgical centers. Following institutional review board approval, their postoperative records were retrospectively reviewed to evaluate the rate of cerebrospinal fluid (CSF) leaks and postsurgical healing. Crusting scale score was used as an indicator of healing progression. Healing was assessed during routine follow-up using a clinically intuitive scale based on sinonasal endoscopy. After the surgery, this studies found the improvement in the crusting score. But fourteen of paitents had no change in the crusting score. This study demonstrates the potential utility of L-PRF membranes for skull base defect reconstruction. Future studies will be conducted to better assess the role of L-PRF in endoscopic skull base surgery.6

Arabacı et al., conducted a retrospective study with 40 babies who had surgery with the diagnosis of meningomyelocele, 20 patients received PRP after surgical repair, and 20 were followed up without

PRP. In the PRP group, 10 of the 20 patients underwent primary defect repair, the other 10 underwent flap repair. In the group that did not receive PRP, primary closure was performed in 14 patients and flap closure in six. CSF leakage occurred in 10 patients and mostly from non PRP treatment. Local infection and skin necrosis also was observed in mostly patient with non PRP group PRP treatment of postoperative meningomyelocele infants facilitates showed better healing and lowers the risk of CSF leakage, meningitis, and skin necrosis.7 This is in line with theory said Platelet-rich plasma (PRP), a platelet-rich form of plasma extracted from venous blood, is a blood-derived product. Alpha granules contain a large number of cytokines, such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor, platelet factor 4 (PF-4), insulin-like growth factor-1 (IGF-1), and transforming growth factor-β (TGF-β). These growth factors allow stem cell proliferation and angiogenesis, promote bone regeneration, improve the local microenvironment, and enhance tissue regeneration capacity and functional recovery.8

The reviewed studies collectively suggest that both platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) could significantly enhance the healing of duramater following spinal surgery, particularly in reducing cerebrospinal fluid (CSF) leakage and promoting tissue regeneration. These findings are consistent with the broader body of literature that underscores the regenerative potential of platelet concentrates in various surgical contexts. PRP and PRF are rich in growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-beta (TGF-β), all of which play crucial roles in wound healing. These factors not only promote cell proliferation and angiogenesis but also aid in the formation of a more robust extracellular matrix, which is essential for effective tissue repair and regeneration. One of the key advantages of PRF over PRP, as highlighted in the literature, is its ability to maintain a sustained release of growth factors over time due to its fibrin matrix. This sustained release could explain why PRF has been shown to provide a more durable seal in duramater repair, as it supports prolonged healing processes, reducing the risk of complications like CSF leaks. This aligns with findings from other surgical fields where PRF has been successfully used, such as in maxillofacial and dental surgeries.

However, while the results are promising, it is important to recognize the limitations and variability among the studies. For instance, the preparation protocols for PRP and PRF can differ significantly, which may influence their effectiveness. Moreover, the studies reviewed varied in terms of design, population, and outcome measures, making direct comparisons challenging. Future research should focus on standardizing PRP and PRF preparation techniques and conducting larger, multicentre randomized controlled trials to better understand their efficacy and optimize their use in clinical practice. Additionally, the economic aspect of using PRP and PRF in spinal surgery warrants consideration. While these therapies offer potential clinical benefits, their cost-effectiveness compared to traditional methods such as suturing and commercial fibrin sealants needs thorough evaluation. The financial implications are particularly relevant in healthcare systems with constrained resources, where cost-benefit analyses could determine the broader adoption of these techniques.

In conducting this systematic review, several limitations were identified that may impact the interpretation and generalizability of the findings. Factors such as lack of blinding, incomplete outcome data, and selective reporting were prevalent, potentially influencing the results and the conclusions drawn.The sample sizes in several studies were relatively small, reducing the statistical power and reliability of their findings. To address these limitations, future research should focus on conducting well-designed, large-scale randomized controlled trials with rigorous methodology. Efforts should be made to minimize bias, ensure adequate sample sizes, and use direct clinical outcomes. Including studies from diverse populations and settings will also enhance the generalizability of the findings.

4. Conclusion and future scope

In conclusion, the use of PRP and PRF in enhancing duramater healing post-spinal surgery appears to offer significant benefits, particularly in reducing CSF leakage and promoting tissue regeneration. While current findings are encouraging, further research is necessary to standardize these therapies and

establish their cost-effectiveness. If these challenges are addressed, PRP and PRF could become standard adjuncts in spinal surgery, improving patient outcomes and reducing postoperative complications.

Conflict Of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper. No financial, commercial, legal, or professional relationships with other organizations or individuals have influenced the research presented in this study. All authors have disclosed any potential conflicts of interest and affirm that the integrity of the research has been maintained

Ethical Considerations

This study was conducted in accordance with ethical principles and guidelines to ensure the protection of participants' rights, safety, and well-being. Ethical approval was obtained from the Institutional Review Board (IRB) of Hasanuddin University prior to the commencement of the study.

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Author Contribution

All authors have made significant contributions to this study. [Author 1] was responsible for the conceptualization and design of the study. [Author 2] conducted the data collection and performed the experiments. [Author 3] carried out the statistical analysis and interpretation of the data. [Author 4] drafted the initial manuscript, and [Author 5] provided critical revisions for important intellectual content. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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