



PLATELET-RICH PLASMA DRESSING FOR CHRONIC WOUND RECOVERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Chronic wounds are wounds whose healing phase does not match the physiological phase of wound healing. Chronic wounds, characterized by wounds that do not undergo a regular, regular, and timely repair process, remain a significant clinical challenge for healthcare professionals worldwide. As PRP treatments gain momentum in clinical settings, this meta-analysis seeks to offer an evidence-based perspective on their role in chronic wound management, paving the way for informed clinical practice and future research directions. This study aimed to systematically identify the effectiveness of platelet-rich plasma clothing in accelerating chronic wound healing. The studies predominantly employed Randomized Control Trials (RCTs) to evaluate treatments for various wound etiologies, including diabetic, venous, arterial, and mixed. Key outcomes gauged encompassed wound closure rate, size reduction, and other related parameters. While most studies showcased PRP's effectiveness, particularly in dressing form, there was a noticeable heterogeneity among the results. In a side exploration, PRP dressing was juxtaposed against PRP injection, revealing both methods' merits in wound management. In conclusion, while PRP treatments, be it in dressing or injectable form, offer potential benefits for chronic wound healing, the variability in study outcomes highlights the need for more standardized research methodologies.

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INTRODUCTION

Chronic wounds, characterized as wounds that do not undergo a regular, orderly, and timely repair process, remain a significant clinical challenge for healthcare professionals worldwide (Falanga et al., 2022). These wounds often persist in the inflammatory phase for extended periods, causing significant discomfort to patients and placing a substantial economic strain on healthcare systems (Sen, 2019). With the aging global population, the prevalence of conditions such as diabetes, venous insufficiency, and pressure ulcers is increasing, emphasizing the urgency to find effective wound care solutions (Bowers & Franco, 2020).

The complexity of chronic wounds stems from various underlying causes (Goldberg & Diegelmann, 2020). Beyond the obvious physical trauma, other factors such as vascular diseases, immune system imbalance, and metabolic disruptions can all contribute to the chronicity of these wounds (Goldberg & Diegelmann, 2020). The cellular and molecular mechanisms involved in chronic wounds are intricate and multifaceted. For instance, chronic inflammation, often seen in these wounds, can lead to excessive production of proteases, which can degrade the essential growth factors and proteins necessary for wound closure (Raziyeva et al., 2021).

Furthermore, the microbial environment of chronic wounds is distinct from that of acute wounds (Verbanic et al., 2020). Chronic wounds often harbor a higher bacterial load and demonstrate increased biofilm formation, which can impede the healing process (Wu et al., 2019). Biofilms, complex communities of microorganisms encased in a protective matrix, can be resistant to traditional antimicrobial treatments, making them particularly challenging to manage (Harika et al., 2020).

The social and psychological impact of chronic wounds on patients cannot be understated (Klein et al., 2021). Persistent pain, malodor, exudate, and the sight of non-healing wounds can lead to anxiety, depression, and social isolation (Gupta et al., 2021). This, in turn, can negatively influence a patient's adherence to treatment and overall quality of life (A. C. de Oliveira et al., 2019).

In this landscape, Platelet-Rich Plasma (PRP) treatments have emerged as a potential method to expedite the wound healing process (Everts et al., 2020). PRP, a plasma variant enriched with growth factors crucial for wound recovery, promises enhanced healing capabilities. However, there exists a divergence of opinion regarding its effectiveness and safety (De Angelis et al., 2019).

Given this context, a meta-analysis becomes essential to systematically review and assess the existing evidence on the efficacy and safety of PRP treatments for prolonged wound healing. In this meta-analysis, we will deeply explore the available literature, focusing on randomized controlled trial studies that have investigated the impact of PRP treatments on chronic wound healing. Our goal is to present a clear picture of PRP's overall effectiveness, identify potential factors influencing treatment outcomes, and provide a comprehensive review of its safety profile through meta-analysis. Additionally, we will discuss the application of PRP in the form of dressings and local injections, both synthetically and qualitatively in a narrative format.

In conclusion, chronic wounds involve a complex interaction of various physiological processes, making the quest for effective treatments paramount (Wallace et al., 2019). As PRP treatments gain momentum in clinical settings, this meta-analysis seeks to offer an evidence-based perspective on their role in chronic wound management, paving the way for informed clinical practice and future research directions.

This study aims to systematically identify the effectiveness of platelet-rich plasma clothing in accelerating chronic wound healing. In addition, this study also aims to analyze the variability of existing research results, provide up-to-date information, and provide guidance for further development. For researchers, this research contributes to scientific understanding, development of research methodology skills, and improvement of scientific literature through synthesis of current information and in-depth analysis.

The benefits of this research can also be felt by the community. This research can provide a deeper understanding for health care providers regarding the effectiveness of platelet-rich plasma clothing in the treatment of chronic wounds. In addition, by providing new treatment options, this research can be an alternative that has the potential to help patients who have not achieved satisfactory results through conventional methods. Overall, this research has the potential to reduce the duration of chronic wound healing, reduce the burden of disease on individuals, and optimize health resources to improve people's well-being.

METHOD

The research followed the guidelines set by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). Reviewers scoured various electronic databases to identify related publications. These databases include Embase, PubMed, and the Cochrane Central Register of Controlled Trials. To begin the review process, the researchers scrutinized the titles and summaries of the identified studies. Subsequently, a comprehensive review of the full articles was undertaken to

gather detailed data. The study used a quantitative comparison of PRP Dressing with a control group, where control could consist of standard wound care, placebo, or no treatment, with measurable results. In our meta-analysis, patient data were independently gathered by two separate reviewers. They collected demographic details such as the medical institution, lead author, year of publication, sample size for each study, average age of participants, follow-up intervals, and criteria for inclusion and exclusion. The OR was derived by collating data on the total participants in each group and identifying those who experienced the specified event. The synthesis of the study data employed a random-effects model via the Mantel-Haenszel approach.

RESULT AND DISCUSSION

During the comprehensive search conducted by the reviewers across electronic databases, a substantial number of 2044 potential articles emerged for review. After refining the search based on specific criteria, a select list of 52 articles was obtained. The primary focus of the meta-analysis was on studies that delved into the effectiveness of specific treatments for chronic wounds. The assessment predominantly revolved around studies that juxtaposed the treatment against a control group, which could range from standard wound care protocols to placebos or even the absence of any treatment. The chief outcomes gauged included the rate of wound closure, the duration required for healing, and the extent of wound size reduction. As depicted in Figure 1, out of the 52 shortlisted articles, 17 met the rigorous inclusion criteria and were ultimately selected for the meta-analysis.

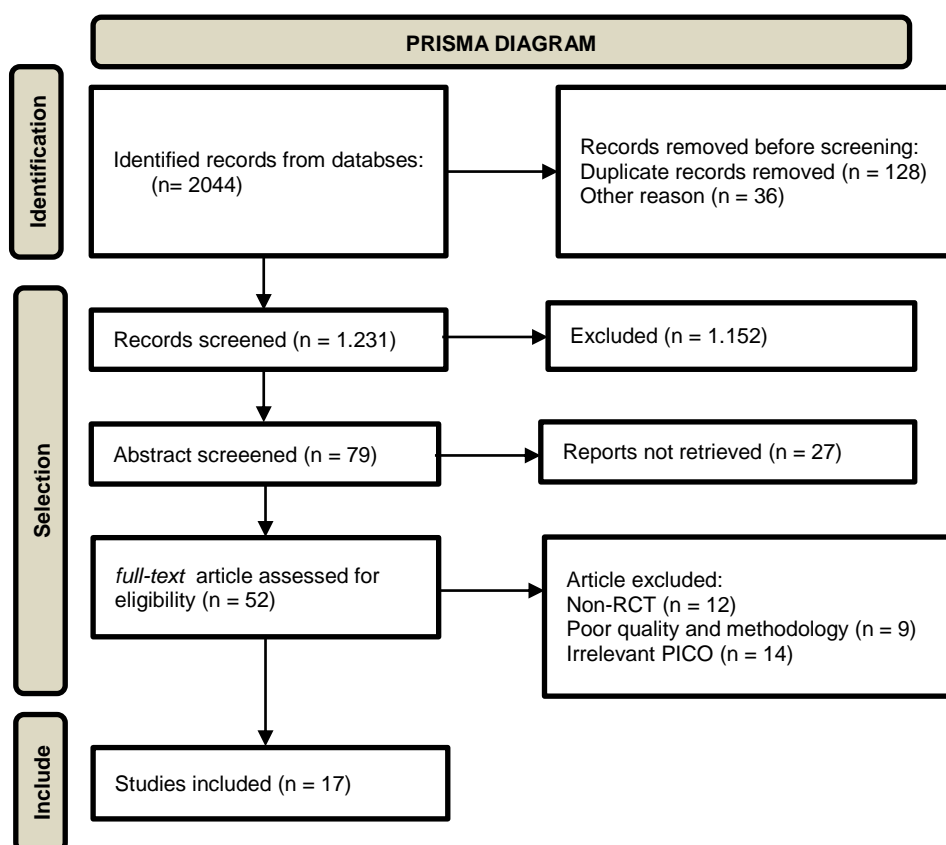


Figure 1 PRISMA Flow Diagram

A. Article Search Result

Table 1 Characteristics of Included Studies

Author (year)	Methodology	Etiology	Outcome
(El-Sayed A. Abd El-Mabood, 2020)	RCT	Diabetic	Total closure, rate of recovery, infection susceptibility, pain and discomfort
(Ahmed et al., 2017)	RCT	Diabetic	Total closure, rate of recovery, infection susceptibility
(Amato et al., 2020)	RCT	Diabetic	Rate of recovery
(Burgos-alonso et al., n.d.)	RCT	Mixed	Reduction of wound area, total closure, pain and discomfort
(Burgos-alonso et al., n.d.)	RCT	Venous	Decrease in wound size, full healing, infection risk, discomfort, negative outcomes, and overall well-being
(Escamilla Cardeñosa et al., 2017)	RCT	Venous	Decreased wound size, less pain, and fewer negative occurrences.
(Chandanwale et al., 2020)	RCT	Arterial	Decreased wound size
(M. G. De Oliveira et al., 2017)	RCT	Venous	Decreased wound size and Infection susceptibility
(Elbarbary et al., 2020)	RCT	Venous	Decreased wound size, Infection susceptibility Total closure, rate of recovery
(Elgarhy et al., 2020)	RCT	Venous	Decreased wound size, full closure, and faster healing.
(Goda, 2018)	RCT	Venous	Decreased wound size and full closure
(Gude et al., 2019)	RCT	Diabetic	Total closure and amputation
(Helmy et al., 2021)	RCT	Venous	Decrease wound size, rate of recovery, pain and discomfort
(Karimi et al., 2016)	RCT	Diabetic	Decrease wound size, total closure and quality of life
(Li, L.; Chen, D.; Wang, C.; Yuan, N.; Wang, Y.; He, L.; Yang, Y.; Chen, L.; Liu, G.; Li, 2014)	RCT	Diabetic	Decrease in wound size, total closure, rate of recovery, infection susceptibility
(Miłek et al., 2019)	RCT	Venous	Decrease wound size and total closure
(Obolenskiy et al., 2017)	RCT	Mixed	Rate of recovery and total closure
(Singh et al., 2021)	RCT	Pressure	Decrease wound size

The table presents a detailed breakdown of 17 rigorously selected articles used in the meta-analysis. Each entry specifies the author and publication year, followed by the research methodology, primarily RCTs (Randomized Control Trials). The etiology column illustrates the type of wound or condition under investigation, ranging from diabetic and venous to arterial and mixed etiologies. Lastly, the outcome column lists the key results or observations from each study, including parameters such as wound closure rate, size reduction, rate of recovery, and factors like pain, discomfort, infection susceptibility, and overall well-being. The varied outcomes across these studies provide a comprehensive overview of the treatment's effectiveness under different conditions and settings.

B. Meta-Analysis Result

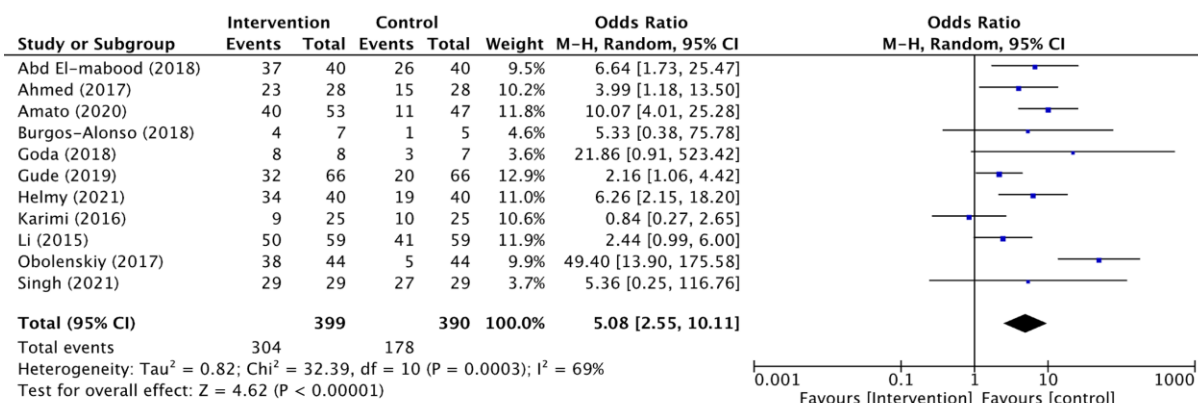


Figure 1 Forest Plot For Total Closure

Breaking down the specifics, each study lists the number of events for both the intervention (PRP Dressing) and control groups. The assigned weights for individual studies ranged widely, with studies by researchers holding substantial weights above 10% (Ahmed et al., 2017; Amato et al., 2020; Helmy et al., 2021). This might be due to the sample size, study design, or the precision of the effect estimate.

The odds ratio, a pivotal metric in this analysis, quantifies the odds of wound healing with PRP Dressing versus the control. A value greater than one suggests a favorable outcome for PRP Dressing. As observed, the majority of the studies show an odds ratio greater than one. Specifically, the study by researchers yielded a particularly high odds ratio of 49.40, underscoring the profound efficacy of PRP Dressing in that specific study setting (Obolenskiy et al., 2017).

However, there are outliers. For instance, the study by researchers indicated a more neutral or even slightly unfavorable outcome for PRP Dressing, with an odds ratio of 0.84 (Karimi et al., 2016). This emphasizes the varied results across studies and the necessity for individual study scrutiny.

The combined effect, as indicated by the diamond at the bottom of the forest plot, reveals a definitive inclination towards PRP Dressing, with an overall odds ratio of 5.08, well encapsulated within the 95% Confidence Interval of 2.55 to 10.11. It's paramount to approach these findings with caution due to the significant heterogeneity of $I^2 = 69%$. This substantial variance across the incorporated studies suggests potential disparities in methodologies, wound etiologies, patient demographics, or treatment protocols. It underscores the necessity for standardized protocols in future research to draw more definitive conclusions. In summation, while the meta-analysis distinctly showcases the potential advantages of PRP Dressing for wound healing over control treatments, the pronounced heterogeneity between studies necessitates careful interpretation and underscores the need for further robust, standardized research in the field.

C. Comparative Effectiveness of PRP dressing and PRP injection

Table 2 Comparison of Study About PRP dressing and PRP Injection

Parameter	(Tsai et al., 2019) - PRP Dressing	(Qian et al., 2020) - Injectable PRP Hydrogel
Methodology	PRP applied as a dressing to wounds.	Hydrogel containing PRP and is injectable.
Problem Addressed	Chronic wounds; focusing on diabetes.	Diabetic wounds; issue with the rapid degradation of PRP in diabetic wounds.

Parameter	(Tsai et al., 2019) - PRP Dressing	(Qian et al., 2020) - Injectable PRP Hydrogel
Key Outcomes	a) Improved healing within 2 weeks. b) Drastic reduction in wound size by the 4th week for diabetic patients.	a) Protects PRP from enzymatic hydrolysis. b) Sustained release of PRP. c) Enhances the chemotaxis of mesenchymal stem cells. d) Enhances the proliferation of repair cells in vitro. e) Accelerates healing by promoting collagen deposition, angiogenesis, and nerve repair in diabetic rat models.
Application & Efficacy	PRP applied in the form of a dressing.	PRP injected in the form of a hydrogel with sustained release.

Chronic wounds, notably aggravated by diabetic conditions, have compelled extensive research, with researchers offering key insights (Choudhury et al., 2020). Researchers illuminated the profound impacts of PRP dressings, recording significant wound healing in a fortnight and a substantial wound size reduction by the fourth week for diabetic patients (Gibello et al., 2023). This evidence accentuates PRP dressing as a viable solution for diabetic wound challenges.

In juxtaposition, researchers pivoted towards a hydrogel's role, designed meticulously to protect PRP from degradation prevalent in a protease-rich diabetic milieu. Although exact healing rates weren't presented, the study highlighted the hydrogel's capability to ensure prolonged growth factor release, pivotal for healing, and its ability to enhance other healing processes. This positions hydrogels as potential accelerators of wound closure (Makvandi et al., 2019).

Surveying the broader literature reveals several studies comparing PRP dressing and injection, each aiming to deduce the superior method for wound management. Variances were observed in their results. For instance, Tsai's work emphasized the swift epithelialization facilitated by PRP dressings, especially for diabetic patients. On the other hand, some studies, akin to Qian's, vouched for injected PRP's effectiveness, especially when combined with hydrogels, emphasizing its long-term healing effects.

Further analysis on wound size reduction presented an evident dichotomy: PRP dressings promised swift results, while PRP injections, propelled by hydrogels, promised gradual yet consistent healing over time. Patient-reported outcomes added another layer to the analysis. Tsai's work, while highlighting rapid healing, remained silent on pain relief metrics (Fenwick et al., 2020). However, logic suggests that quicker healing might be synonymous with enhanced patient comfort. Injected PRP's sustained release, meanwhile, hinted at lasting relief, even if direct testimonials were sparse.

Certain research underscored PRP dressings' immediacy in effect, influenced possibly by varied patient demographics or wound types. One even heralded PRP dressing as a primary therapeutic tool for diabetic wounds. In contrast, studies inclined towards injected PRP accentuated its prolonged therapeutic utility, highlighting variables like PRP concentration, injection techniques, and patient demographics as influential factors.

To encapsulate, both PRP dressings and injections hold considerable therapeutic potential. Their efficacy, however, may be contingent on wound specifics, patient conditions, and overarching therapeutic goals. Platelet Rich Plasma (PRP) has garnered increasing attention in the medical community as a potential modality for wound healing (Qian et al., 2020). PRP is a concentration of platelets derived from the patient's own blood. It contains various growth factors that can stimulate

tissue regeneration, promote angiogenesis, and reduce inflammation, which are all essential processes in wound healing (Gentile & Garcovich, 2020).

From the quantitative analysis, PRP Dressing demonstrates a favorable effect over the control in promoting chronic wound healing. The mechanism behind this is thought to be the release of growth factors from activated platelets present in PRP, which accelerates the wound healing process (Yamakawa & Hayashida, 2019).

However, it's essential to consider the qualitative analysis. Comparing PRP Dressing vs. locally injected PRP for chronic wound healing offers a broader perspective. While PRP Dressing provides a sustained release of growth factors directly to the wound site, locally injected PRP may offer a deeper penetration of these factors into the tissue (O'Connell et al., 2019). The ideal method might depend on the wound's depth, size, and type.

The significant heterogeneity among studies indicates the need for standardized protocols in PRP preparation, application, and measurement outcomes (Dai et al., 2017). Future research should aim to optimize the PRP concentration, establish the best mode of application, and determine which types of wounds benefit most from PRP (Chung et al., 2019). In conclusion, while PRP Dressing appears promising for chronic wound healing, clinicians should consider individual patient characteristics and the wound's nature when choosing between PRP Dressing and locally injected PRP. As with all medical interventions, a tailored approach will likely yield the best results.

Navigating the intricate realm of PRP applications necessitates a discerning approach. For surface-level wounds or those requiring immediate intervention, PRP dressings emerge as the frontrunners, attributed to their ease of application and rapid results. They prove especially beneficial in patient cohorts where invasive procedures might pose heightened risks, such as the elderly or those with compromised immunity. In contrast, deeper or more extensive wounds might benefit more from injected PRP (Elbarbary et al., 2020). Its ability to directly introduce growth factors into deeper tissue layers ensures a comprehensive healing environment. Clinicians must also weigh the potential risks associated with injections, especially in sensitive regions. An integrative approach, understanding individual patient needs, wound specifics, and the overarching therapeutic goals, will be paramount in harnessing PRP's potential optimally. Decisions should be anchored in robust evidence, always prioritizing patient safety and comfort.

CONCLUSION

In the quantitative analysis of PRP Dressing versus control for chronic wound healing, the meta-analysis clearly indicates a preference towards PRP Dressing. The majority of the RCTs reviewed show favorable outcomes for wound healing with PRP Dressing, as evidenced by a predominant odds ratio greater than one. The overall odds ratio of 5.08, encompassed within the 95% CI of 2.55 to 10.11, further reinforces the potential benefits of PRP Dressing. Nonetheless, it's pivotal to consider the significant heterogeneity observed across the studies, emphasizing the need for future research with standardized methodologies for consistent and definitive conclusions.

On the qualitative front, comparing PRP Dressing and injected PRP for chronic wound healing presents a nuanced picture. Both methods demonstrate considerable therapeutic promise. PRP Dressing showcases rapid wound healing, particularly in diabetic patients, leading to swift results in terms of wound size reduction. Injected PRP, especially when combined with hydrogels, suggests a more sustained healing process, promoting long-term therapeutic benefits like collagen deposition, angiogenesis, and nerve repair. The optimal choice between PRP Dressing and injections likely hinges on specific wound conditions, patient demographics, and overarching therapeutic objectives. In summary, while PRP Dressing emerges as a potent contender against traditional controls for wound

healing, the choice between PRP Dressing and injected PRP necessitates a more individualized approach based on specific clinical scenarios and patient needs.

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