Review

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Protocols, Clinical Effects, and Safety of Platelet-Rich Plasma for Diabetes-Related Foot Ulcers: A Systematic Review with Narrative Synthesis

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Abstract

Introduction. Platelet-rich plasma (PRP) has been investigated as an adjunctive therapy for diabetes-related foot ulcers, but heterogeneity in preparation and application protocols limits interpretation of the evidence. This review aimed to analyze current evidence on PRP, focusing on protocols, clinical effects, safety, and standardization gaps.
Methods. This systematic review with narrative synthesis followed PRISMA 2020, the Cochrane Handbook, and SWiM guidance. Searches were conducted between September and October 2025 in MEDLINE/PubMed, LILACS, BDENF, CUMED, the Cochrane Library, Web of Science, and Scopus. Primary human studies published from 2021 to 2025 evaluating PRP or related platelet-derived products were included. Two reviewers independently screened studies and extracted data. Meta-analysis was not performed because of substantial clinical and methodological heterogeneity.
Results. Of 907 records identified, 34 studies involving 3,597 participants were included. PRP was administered through different modalities, including dressings, gels, topical applications, injections, platelet-rich fibrin, and combinations with other wound-care technologies. Some studies reported favorable findings for complete ulcer closure, wound area or volume reduction, shorter healing time, granulation, re-epithelialization, and fewer local complications. Complete healing rates ranged from 55.3% to 95%, while healing time was most often between four

and 16 weeks. However, methodological heterogeneity, moderate methodological quality, risk-of-bias concerns, and incomplete safety reporting limited interpretation of the findings.

Discussion. PRP showed potential as an adjunctive treatment for diabetes-related foot ulcers, with favorable findings for tissue regeneration and wound healing in several studies. Its minimally invasive nature and relatively simple application may support clinical feasibility. However, heterogeneity among protocols, risk of bias, and incomplete safety reporting preclude definitive conclusions regarding its clinical effectiveness and safety.

Keywords: Diabetic Foot, Foot Ulcer, Platelet-Rich Plasma, Platelet-Rich Fibrin, Wound Healing, Treatment Outcome

Introduction

Diabetes-related foot ulcers (DFU) are among the most frequent, severe, and costly complications of diabetes and are associated with infection, hospitalization, amputation, mortality, reduced quality of life, and increased health care costs. Global estimates indicate an approximate prevalence of 6.3% for foot ulcers among people with diabetes, with higher occurrence among individuals with type 2 diabetes, older age, and longer disease duration (Zhang et al., 2017). Beyond the individual clinical burden, these ulcers remain a persistent challenge for health services because of their chronicity, recurrence, and need for prolonged multidisciplinary follow-up (Armstrong et al., 2017).

Conventional treatment for diabetes-related foot ulcers is based on local wound care, debridement, infection control, maintenance of a moist wound environment, pressure offloading, metabolic control, vascular management, and multidisciplinary follow-up. Although these components remain essential, some ulcers show slow or insufficient healing, particularly in the presence of neuropathy, peripheral arterial disease, infection, persistent inflammation, cellular response imbalance, and extracellular matrix impairment. In this context, adjunctive therapies have been investigated to support tissue repair and shorten the time required for wound closure. International guidelines emphasize that interventions intended to enhance wound healing should be supported by evidence of efficacy, safety, feasibility, and cost-effectiveness when used in addition to standard care (Chen et al., 2023).

Among these interventions, platelet-rich plasma has received increasing attention. Platelet-rich plasma (PRP) is a biological product generally obtained from the patient's own blood through processing that concentrates platelets in a reduced volume of plasma. When activated, platelets release growth factors, cytokines, and bioactive molecules involved in different phases of wound healing, including hemostasis, inflammation, angiogenesis, cell proliferation, extracellular matrix formation, granulation, and re-epithelialization. Thus, platelet-rich plasma has been proposed as an adjunctive strategy to modulate the wound microenvironment and support the repair of chronic ulcers (Chicharro-Alcantara et al., 2018; Deng et al., 2023).

Recent clinical studies have assessed different uses of PRP in diabetes-related foot ulcers, including topical application, gel formulations, dressings, intralesional or perilesional injections, platelet-rich fibrin, and combinations with secondary dressings, negative pressure therapy, or other wound care technologies. This diversity is clinically relevant because application frequency, preparation method, route of administration, type of platelet-derived product, ulcer severity, comparator intervention, and follow-up duration may influence the observed outcomes (Muthu et al., 2022; OuYang et al., 2023).

Recent systematic reviews and meta-analyses suggest that platelet-rich plasma may improve healing rate, shorten healing time, and support ulcer area reduction compared with conventional treatment. A meta-analysis of randomized controlled trials identified favorable effects of autologous platelet-rich plasma on healing

rate, healing time, ulcer area reduction, and amputation rate, without a significant increase in adverse events compared with conventional therapy (Deng et al., 2023). Another meta-analysis reported improved healing rate and shorter healing time, whereas a systematic review emphasized the need for standardized platelet-rich plasma preparation and additional clinical data on efficacy and safety outcomes (OuYang et al., 2023; Peng et al., 2024).

Despite these promising findings, the incorporation of PRP into clinical practice still requires caution. The International Working Group on the Diabetic Foot recommends that, except for the autologous leukocyte, platelet, and fibrin patch, autologous platelet therapies should not be routinely used as adjunctive therapy to standard care for healing diabetes-related foot ulcers because of the low certainty of the available evidence (Chen et al., 2023). This position highlights an important tension between favorable findings from some clinical studies and the need for greater standardization, higher methodological quality, cost-effectiveness evaluation, and clearer identification of the patient profiles most likely to benefit from these interventions (OuYang et al., 2023; Peng et al., 2024).

Therefore, the relevance of a new review is not merely to restate whether PRP has clinical benefits, but to critically organize recent evidence on preparation and application protocols, forms of use, frequency, treatment duration, comparators, healing outcomes, safety, costs, and methodological gaps. Such a synthesis may support health professionals, researchers, and wound care teams in interpreting the clinical applicability of PRP and in designing more standardized future studies.

Accordingly, this systematic review with narrative synthesis aims to analyze current evidence on the use of PRP as adjunctive therapy for diabetes-related foot ulcers, considering application protocols, clinical effects, safety, and standardization gaps.

Methods

Study design and reporting guidelines

This systematic review with narrative synthesis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al., 2020) and was guided by the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2022). Given the expected clinical and methodological heterogeneity across the included studies, findings were synthesized without meta-analysis and reported according to the Synthesis Without Meta-analysis (SWiM) reporting guideline (Campbell et al., 2020).

The review protocol was registered in a public database (PROSPERO: CRD420261465693). However, the review question, eligibility criteria, information sources, search strategy, outcomes of interest, and synthesis plan were defined a priori by the research team.

Review question and PICOS framework

The guiding question was: What is the current evidence on the use of platelet-rich plasma as adjunctive therapy for diabetes-related foot ulcers, considering application protocols, clinical effects, safety, and standardization gaps? The question was structured using the PICOS framework, according to:

- Population (P) comprised adults with diabetes-related foot ulcers;
- Intervention (I) included platelet-rich plasma and related platelet-derived products, including autologous platelet-rich plasma, platelet-rich fibrin, platelet gel, lysed plasma gel, or other platelet-derived products used as adjunctive therapy;
- Comparison (C) included standard care, conventional dressings, saline dressings, other adjunctive therapies, or no comparator group, depending on study design.
- Outcomes (O) included complete ulcer healing, time to healing, reduction in ulcer area or volume, granulation, re-epithelialization, infection, local complications, amputation, pain, adverse events, costs, hospitalization, and resource use;
- Study designs (S): the inclusion of different types of studies was carried out, following JBI guide for mixed methods studies (Lizarondo et al., 2020). Eligible study designs included randomized clinical trials, quasi-experimental studies, comparative studies, prospective or retrospective observational studies, and case series including at least 10 participants.

Information sources and search strategy

Searches were conducted between September

and October 2025 in MEDLINE via PubMed; LILACS, BDENF, and CUMED via the Virtual Health Library; the Cochrane Library; Web of Science; and Scopus. Controlled descriptors and free-text terms in Portuguese, English, and Spanish were used, based on Medical Subject Headings (MeSH) and Health Sciences Descriptors (DeCS), combined with the Boolean operators AND and OR.

The main search terms included "Diabetic Foot," "Diabetic Foot Ulcer," "Foot Ulcer," "Foot Wounds," "Wound Healing," "Platelet-Rich Plasma," "Platelet-Rich Fibrin," "platelet gel," "plasma rico em plaquetas," "fibrina rica em plaquetas," and "pé diabético." No language restrictions were applied. A publication date limit from 2021 to 2025 was used to map recent clinical evidence on protocols, applicability, and safety of platelet-rich plasma for diabetes-related foot ulcers. The complete search strategies are provided in Supplementary Table S1.

Eligibility criteria

Primary studies involving human participants were included, available in full text and published between 2021 and 2025, which investigated plasma rich in platelets or related platelet-derived products as adjuvant therapy for the healing of diabetic foot ulcers. Studies that have evaluated various application modalities (including gel, topical dressings, intra-perilesian or injectable applications, platelet-rich fibrin, cord blood products, or combinations with other wound care technologies) were eligible, provided that the effect of the platelet derivative could be identified.

Duplicate records, grey literature, non-available full-text articles, preprints, conference summaries, in vitro studies, animal studies, review articles, clinical trial protocols, review protocols, guidelines, editorials, commentaries, letters to the editor, books, book chapters, patents, retractions, experience reports and case series or reports with fewer than 10 participants were excluded. Studies that did not present specific data on diabetic foot ulcers or did not evaluate platelet-rich plasma as a therapeutic intervention were also excluded.

Study selection process

Retrieved records were exported to Rayyan, which was used to manage screening and identify duplicates (Ouzzani et al., 2016). After duplicate removal, two reviewers independently and blindly screened titles and abstracts. Potentially eligible studies were then assessed in full text by the same reviewers. Disagreements were resolved by consensus and, when necessary, by a third reviewer. Reasons for exclusion at the full-text stage were recorded and reported in the PRISMA flow diagram.

Data extraction

Data extraction was performed independently by two reviewers (F.S.L.I and R.C.Q.S) using a standardized form developed a priori by the research team. The following information was extracted: author and year of publication, country, study design, sample size, participant characteristics, clinical characteristics of the ulcers, type of platelet-derived product, product source, preparation method when reported, route of administration, application frequency, intervention duration, comparator, cointerventions, follow-up period, outcomes assessed, main findings, adverse events, complications, costs, and information on funding or conflicts of interest when available. Discrepancies in data extraction were resolved by consensus between the two initial reviewers and a third reviewer (D.C.O). Missing or unclear information was recorded as not reported.

Outcomes of interest

The primary outcomes of interest were complete ulcer healing, time to healing, and reduction in ulcer area or volume. Secondary outcomes included granulation tissue formation, re-epithelialization, exudate reduction, infection control, local complications, need for debridement, amputation, pain, patient satisfaction, adverse events, length of hospitalization, costs, and resource use. When studies used different instruments or assessment time points, results were extracted as reported by the original authors and organized narratively and in tables.

Data synthesis

A meta-analysis was not performed due to substantial heterogeneity across studies in study design, type of platelet-derived product, preparation method, route of administration,

application frequency, treatment duration, follow-up period, ulcer severity, comparators, and outcome measures. Therefore, results were synthesized narratively and tabulated according to recommendations for synthesis without meta-analysis (Campbell et al., 2020) by two reviewers (F.S.L.I and R.C.Q.S).

The synthesis was organized into clinical and operational domains: characteristics of the included studies; types of platelet-derived products and application protocols; effects on complete healing, time to healing, and reduction in ulcer area or volume; effects on granulation, re-epithelialization, and tissue repair; safety, adverse events, infection, complications, and amputation; costs, hospitalization, treatment burden, and resource use; and gaps in protocol standardization. When available, absolute values, percentages, means, medians, measures of dispersion, effect estimates, confidence intervals, and p-values reported in the primary studies were presented.

Critical appraisal of the included studies

The level of evidence of the included studies was classified according to the hierarchy proposed by Melnyk and Fineout-Overholt (2005) (Melnyk et al., 2005): Level I, systematic reviews or meta-analyses of randomized controlled trials; Level II, randomized controlled trials; Level III, quasi-experimental studies; Level IV, descriptive, observational, or qualitative studies; Level V, case reports or case series; and Level VI, expert opinion or consensus.

Three distinct but complementary methodological dimensions were assessed. The Melnyk and Fineout-Overholt hierarchy was used exclusively to classify the level of evidence according to study design. Risk of bias was assessed using RoB 2 (Sterne et al., 2019) for randomized controlled trials and ROBINS-I (Sterne et al., 2016) for non-randomized intervention studies, with a focus on potential sources of systematic error that could compromise the internal validity of the findings.

Methodological quality was assessed separately using the design-specific JBI Critical Appraisal Checklists for randomized controlled trials (Barker et al., 2023), cohort studies (Moola et al., 2020), case series (Munn et al., 2020), and quasi-experimental studies (Barker et al., 2024). Thus, level of evidence, risk of bias, and methodological quality were treated as related but non-equivalent assessments. These assessments informed the interpretation and narrative synthesis of the evidence and were not used as criteria for excluding studies from the review.

Ethical Considerations

Ethical approval was not required because this systematic review analyzed data from previously published studies and did not involve direct participation of human subjects or access to identifiable individual-level data.

Results

Study selection

The database search identified 907 records. After removal of 404 duplicates, 503 records were screened by title and abstract. At this stage, 456 records were excluded because they did not meet the eligibility criteria, mainly due to topic divergence, incompatible study design, in vivo or in vitro design, protocols, reviews, case reports with fewer than 10 participants, abstracts, editorials, guidelines, or publication outside the predefined time frame. Six studies were not available in full text, so forty-one articles were retrieved and evaluated for eligibility, and 7 were excluded: five did not answer the review question, one was a summary and the other was a letter to the editor. Thus, 34 studies were included in the narrative synthesis. The study selection process is presented in Figure 1.

General characteristics of included studies

The final sample comprised 34 primary studies involving 3,597 people with diabetes-related foot ulcers. The included primary studies are summarized in the review tables (Jain et al., 2025; Marram et al., 2025; Nasr et al., 2025; Zhen et al., 2025; Azam et al., 2024; Lambadiari et al., 2024; Jain et al., 2024; Das et al., 2024; Ohura et al., 2024; Jin et al., 2024; Sheng et al., 2024; Vannan & Sivapriya, 2024; Tabanjeh et al., 2023; Rani et al., 2023; Huang et al., 2023; Izzo et al., 2023; El-Leithy et al., 2023; Patel et al., 2023; Kanber & Gulmez, 2023; Fibrini & Lister, 2023; Kamineni & Tupkar, 2023; Gowsick et al., 2023; Arora et al., 2022; Hossam et al., 2022; Ullah et al., 2022; Wang et al., 2022; Saad et al., 2022; Du et al., 2022; Mandadap, 2022; Orban et al.,

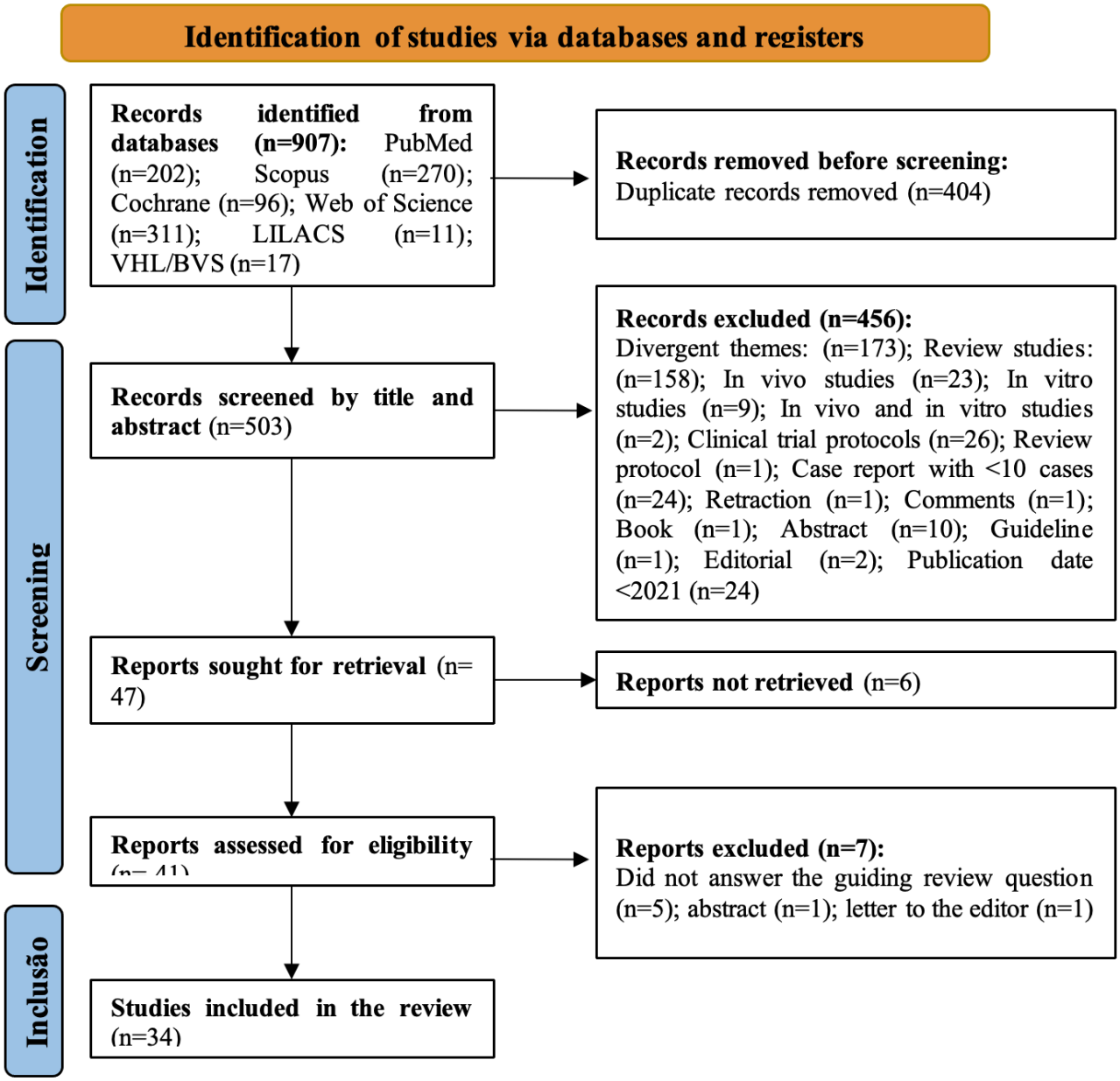

Figure 1. PRISMA 2020 flow diagram for study selection.

2022; Meamar et al., 2021; Alamdari et al., 2021; Rajendran et al., 2021; Gupta et al., 2021). The studies were published between 2021 and 2025, with the highest concentration in 2023 (n = 10), followed by 2022 (n = 8), 2024 (n = 8), 2021 (n = 4), and 2025 (n = 4). Studies were conducted predominantly in Asian countries, especially India (n = 12), China (n = 6), Egypt (n = 5), Pakistan (n = 3), and Iran (n = 2). The remaining studies were conducted in Greece, Japan, Italy, Turkey, Indonesia, and Saudi Arabia, with one study in each country.

Regarding the types of studies, the articles that make up the final sample included randomized clinical trials (n=22), quasi-experimental studies (n=8), case series (n=3) and observational study (n=1). According to the hierarchy proposed by Melnyk and Fineout-Overholt (2005) (Melnyk et al., 2005), 22 studies were classified as level II, eight as level III, and four as level IV.

The risk of bias of randomized controlled trials was assessed using the RoB - 2 tool, which evaluates five domains: bias arising from the randomization process (D1), deviations from intended interventions (D2), missing outcome data (D3), outcome measurement (D4), and selection of the reported result (D5). Overall judgments are classified as low risk of bias, some concerns, or high risk of bias. Among the 22 randomized studies, some concerns were the most frequent overall judgment (n = 12), followed by high risk of bias (n = 9) and low risk of bias (n = 1) (Figure 2).



Figure 2. Risk of bias assessment of randomized controlled trials using the RoB-2 tool.

The risk of bias of quasi-experimental studies was assessed using the ROBINS-I tool, which evaluates seven domains, including confounding, participant selection, intervention classification, deviations from intended interventions, missing data, outcome measurement, and selection of the reported result. Overall judgments are classified as low, moderate, serious, or critical risk of bias. Among the eight quasi-experimental studies, seven were judged to have a moderate risk of bias, and one was classified as having a serious risk of bias (Figure 3).

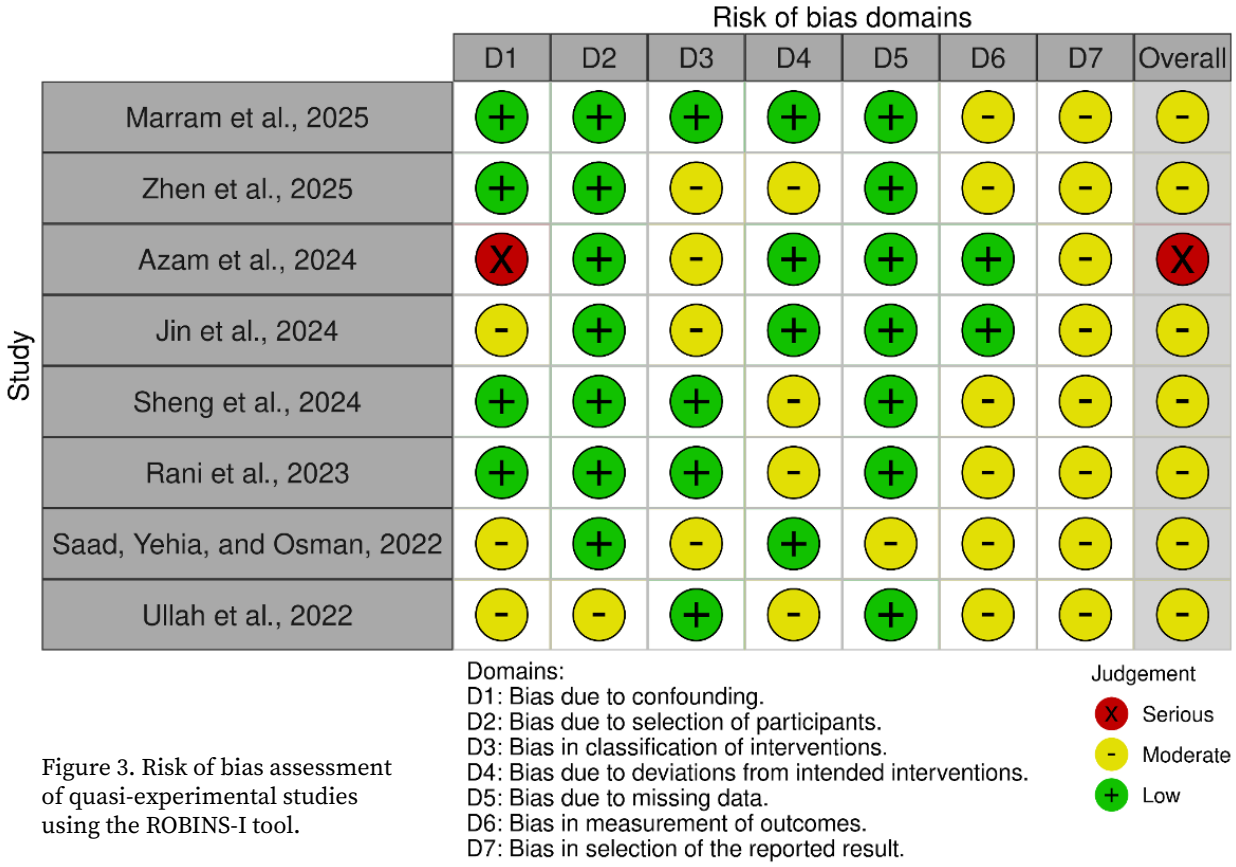

Figure 3. Risk of bias assessment of quasi-experimental studies using the ROBINS-I tool.

The methodological quality was assessed using the appropriate JBI Critical Assessment Checklists, according to the study design. Among the three case series, two were classified as having moderate methodological quality and one as high quality (Figure 4).

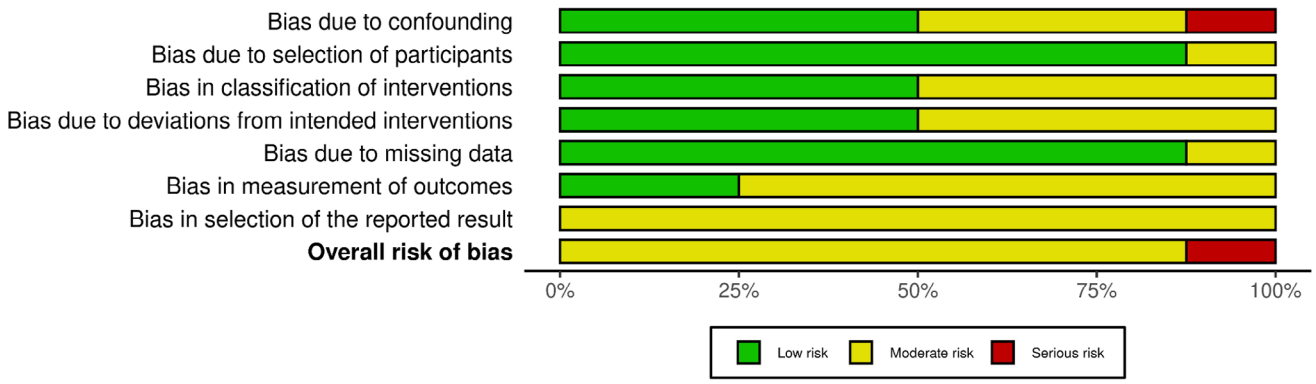

Figure 4. Methodological quality assessment of case series using the JBI Critical Appraisal Checklist.

The single cohort study was classified as having moderate methodological quality (Figure 5).

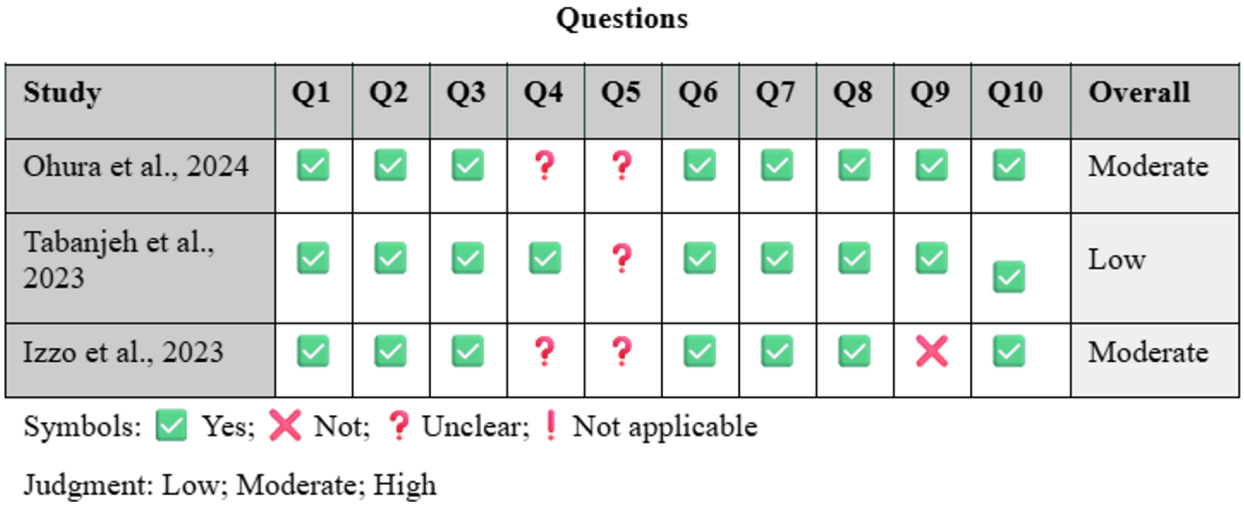

Figure 5. Methodological quality assessment of the cohort study using the JBI Critical Appraisal Checklist.

Of the eight quasi-experimental studies evaluated with the JBI checklist, six were classified as high methodological quality and two as moderate methodological quality (Figure 6).

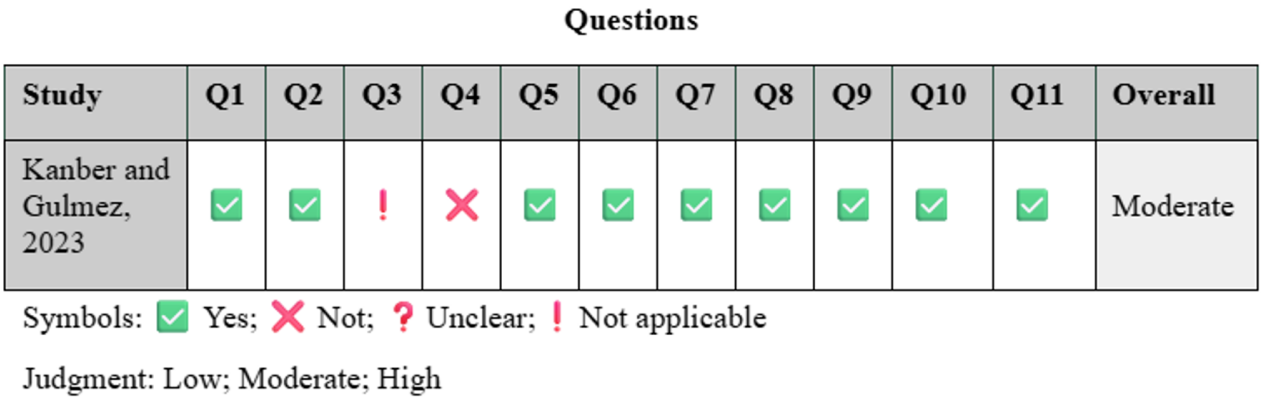

Figure 6. Methodological quality assessment of quasi-experimental studies using the JBI Critical Appraisal Checklist.

The 22 randomized controlled trials were also assessed for methodological quality (Figure 7). Overall, a high frequency of "unclear" ratings was observed across several methodological domains, indicating insufficient information to adequately judge specific criteria. In contrast, most studies fulfilled the criteria related to outcome measurement and statistical analysis. Therefore, considering the overall appraisal, all studies were classified as having moderate methodological quality.

The predominance of studies with moderate methodological quality and some concerns about the risk of bias was due to the work not presenting the type or description of the randomization process and/or not reporting on the blinding of participants, applicators or evaluators. This methodological diversity supports the use of narrative synthesis and requires cautious interpretation of the findings.

Table 1 provides the summary of the 34 articles included in the review, as well as their characterization as a sample, country risk of bias, type of study, risk of bias and methodological quality

PRP formulations, routes of administration, and comparators

Platelet-rich plasma interventions were

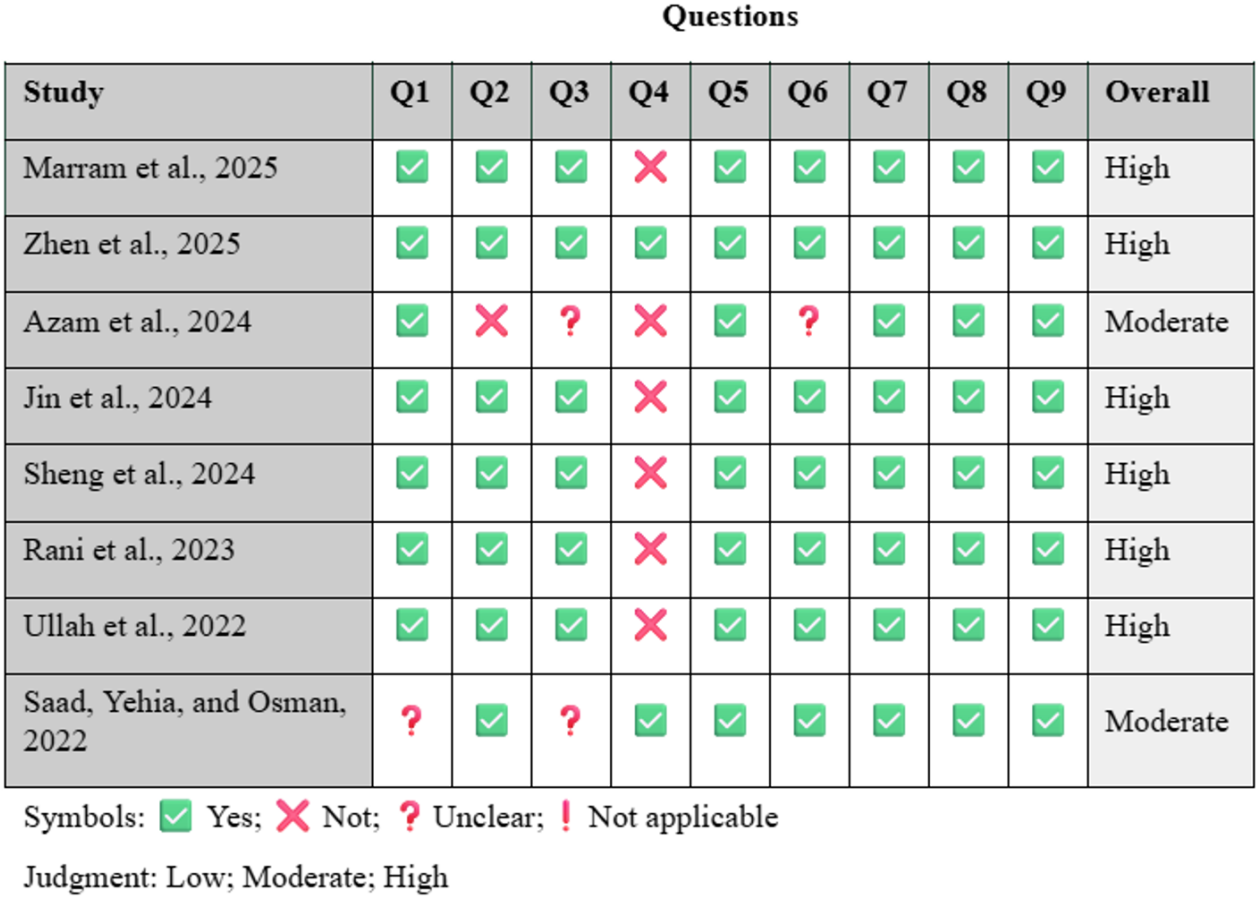

Figure 7. Methodological quality assessment of randomized controlled trials according to the JBI Critical Appraisal Checklist.

heterogeneous in formulation, route of administration, application frequency, and follow-up duration. The main modalities described were PRP dressings or wound coverings, PRP gel, intralesional, perilesional, or subcutaneous injections, topical application, combined injection and gel protocols, activated PRP, umbilical-cord-blood-derived platelet gel, and interventions combined with other technologies, such as negative pressure wound therapy, grafting, mesenchymal stem cells, or nanofibers.

In most studies, PRP application was preceded by wound cleansing, saline irrigation, debridement of devitalized tissue, and coverage with sterile dressing or petrolatum gauze. Comparators included conventional dressings, saline dressings, standard care, negative pressure wound therapy, grafting, mesenchymal stem cell gel, shockwave therapy, topical insulin, and other adjunctive strategies. Most studies were organized into two groups - PRP versus control - or three comparative groups when different PRP modalities or adjunctive therapies were assessed simultaneously.

Table 2 presents the mode of application of PRP, protocol of application used, benefits and main results achieved with the use of this therapy.

Duration of protocols and application frequency

Protocol duration varied widely across studies. Overall, PRP application ranged from approximately two to 24 weeks, although some studies used longer follow-up to assess complete wound closure or clinical progression. Application frequency also varied, including weekly, biweekly, twice-weekly, every three or four days, or cycles defined according to clinical evaluation of the ulcer.

This variability is one of the main findings of the review because it limits direct comparison across studies and prevents definition of a standardized protocol for clinical use. Nevertheless, most protocols described PRP as an adjunct to standard care rather than as a replacement for conventional ulcer management, including debridement, infection control, dressings, offloading, and clinical monitoring.

Table 1 (part 1). Characteristics of the studies included in the review.

Authors/year	Aim	Sample and location	Study design / level of evidence	Instrument/ Risk of bias	Instrument/ Methodological quality
Jain et al. (2025) (Jain et al., 2025)	To compare platelet-rich plasma with normal saline dressing for promoting healing of diabetes-related foot ulcers and reducing complications among people with diabetes.	50 patients / India	Prospective single-site randomized clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Marram et al. (2025) (Marram et al., 2025)	To evaluate the efficacy of PRP for non-healing diabetes-related foot ulcers compared with conventional dressings.	120 patients / Pakistan	Quasi-experimental comparative study / III	ROBINS- 1/ Moderate	JBI Quasi-Experimental/ High
Nasr et al. (2025) (Nasr et al., 2025)	To compare the clinical and histological efficacy of injected PRP, topically applied PRP, and traditional treatment for diabetes-related foot ulcers.	60 patients / Egypt	Randomized controlled clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Zhen et al. (2025) (Zhen et al., 2025)	To compare tibial transverse transport and PRP for healing diabetes-related foot ulcers, evaluate clinical efficacy, and explore effects on lower-limb circulation.	60 patients / China	Comparative quasi-experimental study / III	ROBINS-1/ Moderate	JBI Quasi-experimental/ High
Azam et al. (2024) (Azam et al., 2024)	To evaluate the efficacy of PRP therapy for healing non-healing diabetes-related foot ulcers.	80 patients / Pakistan	Quasi-experimental study / III	ROBINS-1/ Serious	JBI Quasi-experimental/ Moderate
Lambadiari et al. (2024) (Lambadiari et al., 2024)	To evaluate the efficacy and safety of human umbilical-cord-blood-derived PRP lysate gel compared with regular saline dressing in diabetes-related foot ulcers.	120 patients / Greece	Prospective, open, controlled, randomized clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Jain, Jain, and Malik (2024) (Jain et al., 2024)	To evaluate autologous PRP dressing for healing chronic diabetes-related foot ulcers compared with conventional saline dressing.	50 patients / India	Randomized controlled clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Das et al. (2024) (Das et al., 2024)	To compare PRP and saline dressings, both combined with total contact casting, for diabetes-related foot ulcers.	108 patients / India	Randomized controlled clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Ohura et al. (2024) (Ohura et al., 2024)	To evaluate wound-healing outcomes of PRP gel prepared with Aurix in difficult-to-heal diabetes-related foot ulcers after inadequate response to at least four weeks of standard care.	54 patients / Japan	Study case series, open, single-arm, multicenter / IV	-	JBI Case Series/ Moderate
Jin et al. (2024) (Jin et al., 2024)	To compare PRP gel and umbilical-cord mesenchymal stem cell gel for treating diabetes-related foot ulcers.	30 patients / China	Comparative quasi-experimental study/ III	ROBINS-1/ Moderate	JBI Quasi-experimental/ High
Sheng et al. (2024) (Sheng et al., 2024)	To explore the effect of autologous platelet-rich gel combined with continuous vacuum-sealed drainage and recombinant human acidic fibroblast growth factor on healing of diabetes-related foot ulcers.	90 patients / China	Comparative quasi-experimental study/ III	ROBINS-1/ Moderate	JBI Quasi-Experimental/ High
Vannan and Sivapriya (2024) (Vannan & Sivapriya, 2024)	To investigate the therapeutic role of PRP in healing diabetes-related foot ulcers.	50 patients / India	Comparative, prospective, single-site randomized clinical trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate
Tabanjeh et al. (2023) (Tabanjeh et al., 2023)	To demonstrate positive therapeutic outcomes of PRP in diabetes-related foot ulcers.	14 patients / Saudi Arabia	Clinical case series / IV	-	JBI Case Series/ High
Rani et al. (2023) (Rani et al., 2023)	To evaluate autologous PRP for diabetes-related foot ulcers and compare topical PRP with perilesional PRP injections.	60 patients / India	Prospective quasi-experimental study / III	ROBINS-1/ Moderate	JBI Quasi-Experimental/ High
Huang et al. (2023) (Huang et al., 2023)	To compare the higher cost-performance ratio of conventional treatment, PRP, and graft treatment groups.	63 patients / China	Comparative randomized clinical trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate
Izzo et al. (2023) (Izzo et al., 2023)	To evaluate ulcer size reduction and complete healing rate six months after treatment initiation.	12 patients / Italy	Case series / IV	-	JBI Case Series/ Moderate
El-Leithy et al. (2023) (El-Leithy et al., 2023)	To compare shockwave therapy, PRP injection, and topical insulin therapy for healing diabetes-related foot ulcers.	60 patients / Egypt	Comparative randomized clinical trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate
Patel et al. (2023) (Patel et al., 2023)	To verify the effects and benefits of PRP in treating diabetes-related foot ulcers.	60 patients / India	Comparative randomized clinical trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate
Kanber and Gulmez (2023) (Kanber & Gulmez, 2023)	To evaluate factors affecting PRP success in treating diabetes-related foot ulcers.	182 patients / Turkey	Prospective observational study / IV	-	JBI Cohort/ Moderate
Fibrini and Lister (2023) (Fibrini & Lister, 2023)	To evaluate the safety and efficacy of systemic and local autologous PRP for healing diabetes-related foot ulcers and effects on serum HbA1c.	10 patients / Indonesia	Randomized clinical trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate
Kamineni and Tupkar (2023) (Kamineni & Tupkar, 2023)	To evaluate PRP dressing versus normal saline dressing for managing diabetes-related foot ulcers.	64 patients / India	Prospective controlled randomized clinical trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate
Gowsick et al. (2023) (Gowsick et al., 2023)	To compare autologous PRP instillation and conventional saline/povidone-iodine dressing in diabetes-related foot ulcers.	174 patients / India	Randomized controlled clinical trial / II	ROB-2/ Low	JBI Randomized controlled trials/ Moderate
Arora et al. (2022) (Arora et al., 2022)	To evaluate topical PRP combined with vacuum-assisted closure compared with topical PRP alone in diabetes-related foot ulcers.	100 patients / India	Randomized clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Hossam et al. (2022) (Hossam et al., 2022)	To evaluate autologous PRP for promoting healing of non-ischemic diabetes-related foot ulcers.	80 patients / Egypt	Randomized controlled clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Ullah et al. (2022) (Ullah et al., 2022)	To investigate injectable PRP as treatment for diabetes-related foot ulcers compared with conventional dressing.	160 patients / Pakistan	Prospective quasi-experimental study / III	ROBINS-1/ Moderate	JBI Quasi-experimental/ High
Wang et al. (2022) (Wang et al., 2022)	To explore risk factors for morbidity and mortality of diabetes-related foot ulcers and investigate negative pressure therapy combined with PRP.	1,163 patients / China	Randomized clinical trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate

Table 1 (part 2). Characteristics of the studies included in the review.

Authors/year	Aim	Sample and location	Study design / level of evidence	Instrument/ Risk of bias	Instrument/ Methodological quality
Saad, Yehia, and Osman (2022) (Saad et al., 2022)	To assess the net outcome and potency of local PRP gel.	45 patients / Egypt	Quasi-experimental study / III	ROBINS-1/ Moderate	JBI Quasi-experimental/ Moderate
Du et al. (2022) (Du et al., 2022)	To evaluate the clinical efficacy and safety of autologous platelet-rich gel combined with conventional treatment and traditional Chinese medicine for diabetes-related foot ulcers.	60 patients / China	Open and parallel randomized clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Mandadap (2022) (Mandadap, 2022)	To evaluate PRP dressing compared with conventional dressing for diabetes-related foot ulcers.	48 patients / India	Prospective comparative randomized controlled trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate
Orban et al. (2022) (Orban et al., 2022)	To evaluate autologous PRP for treating diabetes-related foot ulcers.	72 patients / Egypt	Prospective comparative randomized controlled trial / II	ROB-2/ High	JBI Randomized controlled trials/ Moderate
Meamar et al. (2021) (Meamar et al., 2021)	To investigate nanofibers loaded with human placenta-derived mesenchymal stem cells plus PRP for healing diabetes-related foot ulcers.	28 patients / Iran	Randomized clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Alamdari et al. (2021) (Alamdari et al., 2021)	To evaluate the clinical benefit of PRP in the healing process of clean diabetes-related foot ulcers.	90 patients / Iran	Randomized clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Rajendran et al. (2021) (Rajendran et al., 2021)	To evaluate autologous PRP application for chronic non-healing diabetes-related foot ulcers compared with normal dressings.	120 patients / India	Randomized clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate
Gupta et al. (2021) (Gupta et al., 2021)	To evaluate local PRP application in relation to healing rate and ulcer area reduction in diabetes-related foot ulcers.	60 patients / India	Randomized controlled clinical trial / II	ROB-2/ Some concerns	JBI Randomized controlled trials/ Moderate

Note. DFU = diabetes-related foot ulcer; PRP = platelet-rich plasma.

Table 2 (part 1). Platelet-rich plasma protocols, application modalities, reported benefits, and main findings

Study	PRP modality	Application protocol	Reported benefits	Main finding
Jain et al. (2025) (Jain et al., 2025)	PRP dressing	Biweekly PRP dressing for four weeks.	Accelerated healing and fewer complications.	PRP showed better tissue regeneration and ulcer closure than saline dressing, with mean ulcer-area reduction of 17.6 mm^2 and fewer complications (3/6% vs. 24/48%).
Marram et al. (2025) (Marram et al., 2025)	PRP injections	After ulcer cleansing, PRP was injected at 1 mL/cm^2 into the base and margins on days 7, 14, 30, and 45; follow-up was 60 days.	Accelerated healing and fewer complications.	Autologous PRP performed better than conventional dressings for ulcer-grade reduction (88.8% vs. 46%), local complications (6.6% vs. 26.6%), complete healing (80% vs. 23.3%), and patient satisfaction (88.3% vs. 43.6%).
Nasr et al. (2025) (Nasr et al., 2025)	Injected and topical PRP	After surgical debridement, PRP was injected biweekly at 1 mL/cm^2 into the margins/base or applied topically and covered with petrolatum gauze and sterile dressing; follow-up twice weekly for 12 weeks or until complete healing.	Higher healing rate, shorter healing time, and no reported safety concerns.	Injected or topical PRP improved DFU healing compared with traditional treatment; 87.5% of PRP-treated patients achieved complete healing versus 55% in the traditional-treatment group.
Zhen et al. (2025) (Zhen et al., 2025)	PRP dressing	Topical autologous PRP dressing after debridement; sterile dressings were changed every seven days during long-term follow-up.	Improved DFU healing and closure time.	PRP achieved an 80% healing rate in severe DFUs, with mean healing time of 6.04 +/- 0.85 months and improved arterial blood-flow velocity in the lower limbs.
Azam et al. (2024) (Azam et al., 2024)	Autologous PRP injections	PRP was injected subcutaneously into and around the ulcer periphery; dressings were changed after treatment and then weekly during four weeks of follow-up.	Accelerated healing.	PRP therapy healed 51 ulcers (63.7%). Ulcers of shorter duration healed more quickly, and healing was more frequent in participants with normal BMI.
Lambadiari et al. (2024) (Lambadiari et al., 2024)	PRP lysate gel	After debridement and saline cleansing, human umbilical-cord-blood PRP lysate gel was applied and covered with sterile gauze and a noncompressive bandage; dressings were changed every three days for one month.	Accelerated healing and reduced mean ulcer area.	PRP gel reduced ulcer area over time. Complete healing occurred in 55.3% of the PRP group versus 16.3% of the saline-dressing group, with mean healing time of 16 versus 24 weeks.
Jain, Jain, and Malik (2024) (Jain et al., 2024)	PRP dressing	PRP was applied directly to ulcers in two sessions, with debridement as needed.	Accelerated healing, reduced complications, treatment burden, and pain.	PRP patients required fewer debridements and dressings, had shorter hospital stay (5.5 vs. 35.6 days), and achieved complete healing in 72% of cases within four weeks.
Das et al. (2024) (Das et al., 2024)	PRP dressing	After cleansing and debridement, PRP was applied to the ulcer bed, covered with sterile gauze, and combined with total contact casting/offloading; follow-up every 15 days for three months.	Improved healing, healing time, and ulcer size.	At day 90, PRP showed greater ulcer-size reduction and greater improvement in PUSH scores; mean healing time was shorter with PRP (11.17 +/- 2.73 weeks) than with saline (13.78 +/- 1.66 weeks).
Ohura et al. (2024) (Ohura et al., 2024)	PRP gel	PRP gel was applied to the target ulcer and covered with petrolatum gauze for at least 24 hours; eligible patients received PRP gel twice weekly for eight weeks.	Potentially effective and safe for difficult-to-heal DFUs; improved area/volume reduction and closure time.	High reductions in ulcer area (72.8%) and volume (92.7%) were observed. Complete closure at final assessment was achieved in 27 patients (57.4%).
Jin et al. (2024) (Jin et al., 2024)	PRP gel	After debridement, 10 mL of PRP gel was applied to the ulcer surface and covered with foam dressing; healing was assessed every 10 days until complete closure.	Improved neuropathic/vascular symptoms, inflammatory response, and healing rate.	Both PRP and umbilical-cord mesenchymal stem cell gel were effective. PRP achieved a healing rate of 77.2% and complete closure in 37.73 days.
Sheng et al. (2024) (Sheng et al., 2024)	PRP gel	Gel was sprayed on the ulcer surface or injected into deep fistulas; petrolatum gauze was applied, and dressings were changed every three days.	Shorter healing time, improved healing, and fewer dressing changes.	PRP gel combined with negative pressure drainage and fibroblast growth factor reduced dressing-change frequency and healing time compared with other treatment combinations.
Vannan and Sivapriya (2024) (Vannan & Sivapriya, 2024)	PRP injection	Approximately 2 mL of PRP was injected about 3/4 cm from the ulcer margin using an insulin syringe; dressings were changed every four days for six weeks.	Faster healing rate, greater ulcer-size reduction, and safe therapy.	Mean percentage ulcer-area reduction was greater in the PRP group than in the control group (33.746 +/- 3.968 vs. 12.822 +/- 1.916; $p < .001$), and mean healing duration was shorter (4.488 +/- 0.409 vs. 6.188 +/- 0.391 weeks; $p < .001$).
Tabanjeh et al. (2023) (Tabanjeh et al., 2023)	PRP injection	PRP was injected subcutaneously into ulcer margins and granulation tissue from edge to center, with injections spaced 3-5 mm apart; the procedure was repeated every 7-10 days.	Improved DFU healing and contributed to complete closure.	Treatment lasted 3-14 weeks; two to three autologous PRP doses were generally needed to achieve complete healing or maximum closure, with complete closure occurring between weeks 3 and 15.
Rani et al. (2023) (Rani et al., 2023)	Perilesional and topical PRP	Fresh autologous PRP was applied topically or injected perilesionally once weekly for four weeks; volume was calculated according to ulcer size.	Perilesional PRP had better healing than topical PRP with minimal side effects.	After three months, topical PRP reduced ulcer size by 69.57%, whereas perilesional PRP reduced it by 82.69% ($p < .001$); complete healing occurred in four perilesional and three topical PRP patients.
Huang et al. (2023) (Huang et al., 2023)	PRP dressing	After routine treatment, debridement, and negative pressure therapy, PRP was applied evenly to the DFU surface and covered with sterile gauze.	Increased cumulative incidence of healed DFUs and reduced ulcer size and healing time.	At 12 weeks, complete re-epithelialization occurred in 70% of the PRP group, 43.5% of conventional treatment, and 65% of graft treatment; PRP and graft groups had more favorable healing time and cumulative healing rates.
Izzo et al. (2023) (Izzo et al., 2023)	PRP injection	Ulcers were disinfected, debrided, disinfected again, and treated with 3 mL of PRP injected into the ulcer bed and margins every three weeks until healing or up to 12 weeks.	Improved healing process, complete healing rate, and ulcer-size reduction.	Eight patients achieved complete healing (66.67%); four had partial healing with >50% ulcer-size reduction.
El-Leithy et al. (2023) (El-Leithy et al., 2023)	PRP gel	PRP gel was applied to the ulcer and covered with a sterile nonabsorbent dressing; one weekly PRP session was provided for four weeks.	Improved healing.	PRP was compared with extracorporeal shockwave therapy, topical insulin, and standard care; all groups showed significant reductions in mean PUSH scores at weeks 4 and 12 versus baseline.
Patel et al. (2023) (Patel et al., 2023)	PRP injection	Fresh PRP was injected at each dressing session, approximately 2 mL about 3/4 cm from the ulcer margin, using an insulin syringe; dressings were changed every four days.	Facilitated DFU contraction and may be used as adjunctive treatment.	In the PRP group, 73.3% of ulcers showed contraction between 15 and 25 cm^2, whereas most standard-care ulcers had 5.1-15 cm^2 contraction; PRP was associated with shorter time to contraction and fewer problems, infection, exudate, and discomfort.
Kanber and Gulmez (2023) (Kanber & Gulmez, 2023)	PRP dressing	Dead tissue and hyperkeratotic areas were debrided; saline irrigation was followed by PRP application and petrolatum gauze, sterile gauze, and noncompressive bandage. Cycles were performed twice weekly for up to 24 weeks.	Accelerated healing.	Among patients receiving PRP, 141 (77.5%) achieved ulcer healing; the original report also mentioned variables such as BMI as factors related to treatment success.
Fibrini and Lister (2023) (Fibrini & Lister, 2023)	Autologous activated PRP injection and systemic infusion	Activated autologous PRP was injected at 10 points around the ulcer (1 mL) and the remaining PRP was infused intravenously over 10-15 minutes; treatment lasted two weeks in addition to debridement and antidiabetic therapy.	Increased healing rate and reduced serum HbA1c.	The aaPRP group showed a higher healing rate than controls, although not statistically significant ($p = .136$), and greater reduction in serum HbA1c during the first treatment week ($p = .030$).
Kamineni and Tupkar (2023) (Kamineni & Tupkar, 2023)	PRP dressing	PRP dressing was applied to the ulcer and changed every four days for six weeks.	Increased healing rate.	PRP showed higher ulcer-healing rates than normal saline at weeks 1, 2, and 3. After four weeks, PRP showed higher ulcer contraction and area reduction.

Note. The table summarizes information reported by the included studies. PRP = platelet-rich plasma; DFU = diabetes-related foot ulcer; VAC = vacuum-assisted closure; PPP = platelet-poor plasma; HbA1c = glycated hemoglobin; PUSH = Pressure Ulcer Scale for Healing; hPMSCs = human placenta-derived mesenchymal stem cells; aaPRP = autologous activated platelet-rich plasma.

Table 2 (part 2). Platelet-rich plasma protocols, application modalities, reported benefits, and main findings

Study	PRP modality	Application protocol	Reported benefits	Main finding
Gowsick et al. (2023) (Gowsick et al., 2023)	PRP injection	PRP was injected into ulcer margins after surgical debridement and covered with a nonabsorbent dressing once weekly for 12 weeks.	Higher DFU healing rate in shorter time compared with traditional treatment.	At 12 weeks, the PRP group showed 86% ulcer-area reduction and 65.1% complete healing; the control group showed 61% reduction and 42.7% healing.
Arora et al. (2022) (Arora et al., 2022)	Autologous PRP injections and aPRP dressing with VAC	After debridement, one group received peripheral aPRP injections plus sterile foam dressing; another received aPRP dressing sealed and connected to VAC at 125 mmHg intermittently.	Reduced ulcer area, earlier granulation, lower infection, and shorter hospitalization.	aPRP + VAC achieved faster tissue coverage and lower infection, exudate, and persistent pain than topical aPRP alone; 86% required skin grafting in aPRP + VAC versus 90% in aPRP.
Hossam et al. (2022) (Hossam et al., 2022)	PRP injection	PRP was injected into the healing edge and ulcer floor with mechanical activation, followed by PPP gel applied to the ulcer and covered with saline dressing. The process was repeated every two weeks up to three times over 12 weeks.	Accelerated healing, better cost-effectiveness than standard treatment, and lower local infection rate.	Complete healing occurred in 95% of PRP patients by week 6 versus 77.8% of controls by week 9 ($p < .001$).
Ullah et al. (2022) (Ullah et al., 2022)	PRP injection	PRP was applied at 1 mL/cm^2 around the margins and base; three injections were administered at two-week intervals on days 0, 14, and 28.	More effective than conventional treatment and improved healing rate.	PRP reduced ulcers in 64 patients (80%), compared with 37 patients (46.25%) receiving conventional dressing ($p < .0001$).
Wang et al. (2022) (Wang et al., 2022)	PRP dressing combined with negative pressure therapy	After saline treatment and debridement, PRP dressing was combined with negative pressure therapy; negative pressure was applied for 5-7 days and PRP twice over 14 days, followed by paraffin gauze.	Accelerated healing and reduced mortality-risk rate.	PRP + negative pressure healed ulcers faster than negative pressure plus traditional dressings; healing rates were 93.8% versus 53.3%, and mortality risk related to DFU decreased by 6.3% in the combined group.
Saad, Yehia, and Osman (2022) (Saad et al., 2022)	PRP injections and PRP gel	After debridement, PRP injections were applied 2-3 cm from ulcer edges, or PRP gel was applied to the ulcer surface and covered with moist contact, moisture-retentive, and secondary absorptive dressings.	Improved healing and reduced ulcer area.	PRP injection produced greater ulcer-area reduction and higher complete healing (12/15; 80%) than PRP gel (10/15; 66.7%) and classic standard treatment (7/15; 46.7%).
Du et al. (2022) (Du et al., 2022)	Autologous platelet-rich gel	After debridement, PRP gel was applied over the ulcer, covered with petrolatum gauze, and supported with pressure bandage and conventional care. Traditional Chinese medicine was also administered three times daily for six weeks.	Accelerated healing and increased healing rate.	PRP gel plus conventional therapy and traditional Chinese medicine showed faster healing than conventional therapy plus traditional Chinese medicine; effective healing was 83.3% at week 12 in the PRP group versus 43.3% in controls.
Mandadap (2022) (Mandadap, 2022)	PRP dressing	Before dressing, debridement and antiseptic application were performed. Dressings were changed every four days for three weeks and then once weekly.	Improved healing and reduced infection compared with conventional dressings.	After five weeks, healing occurred in 91.66% of PRP cases versus 50% of controls.
Orban et al. (2022) (Orban et al., 2022)	PRP injection	Debridement and offloading were performed as needed. PRP was injected around and under the ulcer base, with another portion applied to the base to form gel; dressings were changed every two days, with weekly PRP until healing or up to 10 applications.	Improved healing rate and shorter healing time.	Ulcer healing occurred in 31 PRP patients (86.11%) versus 23 controls (63.89%). Mean healing time was 10.90 +/- 3.40 weeks with PRP and 13.48 +/- 3.37 weeks with conventional treatment ($p = .01$).
Meamar et al. (2021) (Meamar et al., 2021)	PRP gel plus hPMSC-loaded nanofibers	Ulcers were first coated with PRP gel and then dressed with nanofibers loaded with human placenta-derived mesenchymal stem cells; dressings were changed twice weekly until healing, with follow-up up to 12 weeks.	Accelerated healing.	At 12 weeks, PRP + hPMSCs reduced ulcer area by 71%, with 21% completely healed; by 16 weeks, ulcer size had decreased by 80%.
Alamdari et al. (2021) (Alamdari et al., 2021)	PRP gel	Clean ulcers were assessed, classified, debrided, and treated with PRP gel twice weekly for three weeks, covered with a sterile nonabsorbent dressing, and irrigated with saline at each dressing change.	Accelerated healing, increased healing rate, and shortened healing time.	PRP gel produced a higher healing rate and reduced healing time to 53.3 +/- 10.6 days, but did not significantly affect the need for amputation or amputation grade.
Rajendran et al. (2021) (Rajendran et al., 2021)	PRP dressing	Activated PRP was applied after adequate surgical debridement and covered with a nonabsorbent dressing once weekly for six weeks.	Easy, low-cost, and minimally invasive application; reduced ulcer size, hospital stay, and patient costs.	Mean weekly healing rate was significantly better with PRP (5.49 cm^2) than with normal dressing (0.83 cm^2). Complete healing occurred in 40 PRP patients (66.7%), while no control patient achieved complete healing.
Gupta et al. (2021) (Gupta et al., 2021)	Intralesional PRP injections	Fresh PRP was injected weekly into the ulcer margin and base; remaining PRP was applied over the ulcer and covered with sterile cotton gauze. Patients were followed weekly for six weeks or until complete healing.	Lower patient costs, improved performance, and reduced lesion area.	The mean healing rate did not differ significantly between groups (0.71 +/- 0.46 vs. 0.64 +/- 0.36 cm^2/week; $p = .734$). At six weeks, healed area was 85.98% +/- 13.42% in the PRP group and 81.72% +/- 17.2% in controls.

Note. The table summarizes information reported by the included studies. PRP = platelet-rich plasma; DFU = diabetes-related foot ulcer; VAC = vacuum-assisted closure; PPP = platelet-poor plasma; HbA1c = glycated hemoglobin; PUSH = Pressure Ulcer Scale for Healing; hPMSCs = human placenta-derived mesenchymal stem cells; aaPRP = autologous activated platelet-rich plasma.

Duration of protocols and application frequency

Protocol duration varied widely across studies. Overall, PRP application ranged from approximately two to 24 weeks, although some studies used longer follow-up to assess complete wound closure or clinical progression. Application frequency also varied, including weekly, biweekly, twice-weekly, every three or four days, or cycles defined according to clinical evaluation of the ulcer.

This variability is one of the main findings of the review because it limits direct comparison across studies and prevents definition of a standardized protocol for clinical use. Nevertheless, most protocols described PRP as an adjunct to standard care rather than as a replacement for conventional ulcer management, including debridement, infection control, dressings, offloading, and clinical monitoring.

Effects on complete closure, healing time, and ulcer area reduction

Some comparative studies reported differences between PRP and conventional treatment; however, the certainty of these findings is limited by the methodological weaknesses identified in the risk-of-bias assessment. One trial reported greater ulcer-area reduction and fewer complications with PRP than with saline dressing (Jain et al., 2025). Another study associated umbilical-cord-blood-derived PRP lysate gel with greater ulcer-area reduction and a higher proportion of complete healing than saline dressing (Lambadiari et al., 2024). Studies using injectable PRP also reported higher closure rates, shorter time to 50% wound-area reduction, and earlier complete healing than control groups (Hossam et al., 2022; Ullah et al., 2022; Orban et al., 2022). These findings indicate a possible clinical benefit but do not establish consistent effectiveness across settings or protocols.

Accordingly, the findings should be interpreted as signals of possible clinical benefit rather than definitive evidence of effectiveness. Differences in ulcer severity, comparators, PRP formulations, administration routes, application frequency, concomitant therapies, follow-up duration, methodological quality, and risk of bias prevent firm conclusions or direct generalization to routine clinical practice.

Granulation, re-epithelialization, infection, and local complications

In addition to complete wound closure, several studies reported improvements in intermediate tissue-repair outcomes, such as granulation, re-epithelialization, exudate reduction, ulcer area contraction, and wound-assessment scores. Some studies also described fewer local complications, reduced infection, less pain, lower need for debridement, or fewer dressing changes compared with control groups or conventional therapies.

These outcomes are clinically relevant because they suggest that PRP may influence not only final wound closure but also intermediate stages of tissue repair. However, not all studies used the same assessment instruments, and many reported intermediate outcomes descriptively. This limitation reduces comparability across studies and highlights the need for standardized outcomes in future research.

Safety, adverse events, and tolerability

Safety reporting was heterogeneous across studies. In general, studies that reported adverse events or complications did not identify serious events directly attributable to PRP. Some studies described fewer local complications, infections, pain, or discomfort in PRP-treated groups compared with controls. However, not all studies provided systematic adverse-event monitoring, clear causality criteria, or standardized safety follow-up.

Therefore, the absence of reported adverse events should not be interpreted as evidence of complete safety. Assessment of PRP tolerability remains limited by methodological heterogeneity and incomplete adverse-event reporting, particularly in observational studies, single-arm studies, and case series.

Costs, resource use, and clinical feasibility

Some studies suggested potential reductions in costs or resource use associated with PRP, particularly when shorter healing time, fewer dressing changes, reduced need for debridement, shorter hospital stay, or fewer complications were reported. However, the economic evidence was limited because few studies performed formal cost-effectiveness analyses.

Thus, cost-related findings should be

interpreted cautiously. The review suggests that PRP may indirectly reduce resource use in specific clinical contexts, but it does not allow the conclusion that PRP is consistently more cost-effective than standard care across different health systems.

Synthesis of findings

Overall, the certainty of the evidence was limited by methodological heterogeneity, inconsistent intervention protocols, and the risk-of-bias concerns identified across the included studies. Within this context, the available studies reported possible improvements in complete closure, ulcer-area reduction, healing time, and intermediate markers of tissue repair. These clinical findings should therefore be interpreted in light of the limitations of the underlying evidence rather than as confirmation of effectiveness.

The main contribution of this review is the organization of the available clinical findings alongside the methodological limitations that affect their interpretation. Insufficient standardization remains regarding PRP preparation, application modality, frequency, treatment duration, patient selection, outcome definition, and safety monitoring. These limitations should guide both clinical interpretation and the design of future studies.

Discussion

This systematic review with narrative synthesis suggests that PRP may be associated with favorable clinical outcomes as an adjunctive treatment for DFU, particularly increased ulcer closure rates, reduction in wound area, shorter healing time, and improvement in local parameters such as granulation and re-epithelialization.

However, these findings should be interpreted with caution because the included studies showed substantial heterogeneity in study design, type of platelet-derived product, preparation method, route of administration, frequency of use, follow-up duration, comparators, and ulcer severity. Therefore, the main contribution of this review is not only to reiterate the potential benefits of PRP, but also to critically organize how this therapy has been used, which outcomes have been reported, and which gaps still limit its clinical standardization.

Main findings and clinical interpretation

The studies analyzed indicated a favorable trend for PRP as an adjunctive therapy compared with conventional care, particularly in studies assessing complete ulcer closure, wound area reduction, healing time, and local complications. Positive findings were reported in clinical trials and comparative studies using PRP as gel, dressings, topical application, intralesional or perilesional injections, and combinations with other wound care technologies, such as negative pressure wound therapy, total contact casting, or growth factors (Jain et al., 2025; Marram et al., 2025; Nasr et al., 2025; Lambadiari et al., 2024; Das et al., 2024; Huang et al., 2023; Alamdari et al., 2021; Rajendran et al., 2021).

Overall, these findings are consistent with recent systematic reviews and meta-analyses in which PRP was associated with higher healing rates and shorter healing time compared with conventional treatment (Deng et al., 2023; OuYang et al., 2023; Peng et al., 2024; Syafira et al., 2024; Xu et al., 2025). Nevertheless, this convergence does not eliminate uncertainty. Recent meta-analyses have also emphasized clinical and methodological heterogeneity, a limited number of robust trials, differences in preparation and application protocols, and the need for greater standardization of outcomes (Deng et al., 2023; OuYang et al., 2023).

In the present review, the clinical benefit of PRP appeared more evident when outcomes were related to local wound healing responses, such as ulcer area reduction, granulation tissue formation, re-epithelialization, and complete closure. In contrast, harder and more clinically consequential outcomes, such as amputation, ulcer recurrence, hospitalization, severe infection, mortality, and quality of life, were measured less frequently or reported heterogeneously. This distinction is important because improvement in local wound healing should not be automatically interpreted as a proven reduction in amputations or other complex clinical events.

Biological plausibility of PRP in chronic wound healing

The biological plausibility of PRP is based on platelet concentration and the release of growth factors, cytokines, and bioactive molecules involved in different phases of

wound healing. These mediators may promote cellular chemotaxis, angiogenesis, fibroblast proliferation, collagen synthesis, extracellular matrix remodelling, granulation, and re-epithelialization (Smith & Rai, 2024; Verma et al., 2023; Wilkinson & Hardman, 2020). In DFU, this rationale is particularly relevant because the wound microenvironment is often characterized by persistent inflammation, impaired angiogenesis, cellular dysfunction, neuropathy, ischemia, infection, and delayed tissue repair.

Beyond the effect on growth factors, experimental and translational studies suggest that platelet-derived products may influence cell migration, keratinocyte and fibroblast proliferation, expression of cell cycle–related proteins, and tissue regeneration (Smith & Rai, 2024; Kim et al., 2013). However, translating these mechanisms into clinical practice depends on important operational variables, such as platelet concentration, presence or absence of leukocytes, product activation, time between preparation and application, delivery matrix, wound conditions, and association with standard care. Thus, biological plausibility supports therapeutic interest in PRP, but it does not replace the need for standardized, high-quality clinical evidence.

Application protocols as a central axis for interpreting the findings

One of the most relevant aspects of this review is the diversity of protocols used across studies. The included studies employed autologous PRP gel, PRP dressings, intralesional or perilesional injections, topical application after debridement, platelet-rich fibrin, lysed plasma derived from umbilical cord blood, and combinations with conventional dressings, negative pressure wound therapy, total contact casting, grafts, or other biological products (Nasr et al., 2025; Lambadiari et al., 2024; Das et al., 2024; Jin et al., 2024; Sheng et al., 2024; Huang et al., 2023; Arora et al., 2022; Wang et al., 2022; Du et al., 2022).

This diversity broadens the understanding of the field but also limits direct comparison. PRP, platelet-rich fibrin, platelet gel, lysed plasma, and autologous leukocyte, platelet, and fibrin patches should not be treated as equivalent interventions. Each product may differ in composition, platelet density, leukocyte content, fibrin matrix, growth factor release, and mechanical properties. Consequently, synthesis of the evidence should avoid generic conclusions such as "PRP is effective" and instead prioritize interpretation by product type, route of administration, frequency, duration, and clinical context.

The route of administration also deserves attention. Studies using topical or gel application suggested improvements in wound area and ulcer closure, whereas studies using intralesional or perilesional injections reported favorable findings in specific contexts (Nasr et al., 2025; Rani et al., 2023; Orban et al., 2022; Alamdari et al., 2021; Gupta et al., 2021). However, not all studies showed statistically significant differences. For example, Gupta et al. (Gupta et al., 2021) did not observe a significant difference in the mean healing rate when comparing intralesional PRP with control treatment, despite reporting percentage improvement in healed area. This type of finding reinforces that the effect of PRP is not uniform and may depend on ulcer characteristics, patient profile, and protocol design.

Comparison with guidelines and recent meta-analyses

The overall interpretation of this systematic review with narrative synthesis is limited by substantial heterogeneity, the predominance of moderate methodological quality, and relevant risk-of-bias concerns in several included studies. Within these constraints, PRP was associated in some studies with favorable healing-related outcomes, including ulcer closure, wound-area reduction, shorter healing time, granulation, and re-epithelialization.

These findings do not provide sufficient certainty to establish the clinical effectiveness or safety of PRP for diabetes-related foot ulcers. The studies differed in design, platelet-derived product, preparation method, route and frequency of administration, follow-up duration, comparator, and ulcer severity. Accordingly, this review primarily clarifies how PRP has been investigated, which outcomes have been reported, and which methodological gaps prevent standardized clinical recommendations.

Recent meta-analyses support the potential effect of PRP but also reinforce the need for greater methodological quality. Peng et al. (Peng et al., 2024) reported higher healing rates and shorter healing time with PRP compared with conventional care. Similarly, Deng et al. (Deng

et al., 2023), OuYang et al. (OuYang et al., 2023), Syafira et al. (Syafira et al., 2024), and Xu et al. (Xu et al., 2025) reported favorable effects for different outcomes, although with reservations related to heterogeneity and the need for larger, better standardized clinical trials. Therefore, the contribution of this review is to map recent protocols and outcomes, showing that the current question should not be only whether PRP works, but for whom, how, with which product, at what frequency, for how long, and for which clinically meaningful outcomes.

Safety, adverse events, and tolerability

The risk-of-bias assessment and methodological appraisal indicate that the clinical findings must be interpreted cautiously. Many studies had incomplete reporting of randomization or blinding, moderate methodological quality, or relevant risk-of-bias concerns. Against this background, some studies reported a favorable trend for PRP as an adjunctive therapy compared with conventional care, particularly for complete ulcer closure, wound-area reduction, healing time, and local complications (Jain et al., 2025; Marram et al., 2025; Nasr et al., 2025; Lambadiari et al., 2024; Das et al., 2024; Huang et al., 2023; Alamdari et al., 2021; Rajendran et al., 2021). The direction of these findings is clinically relevant, but their magnitude and consistency remain uncertain.

Nevertheless, the absence of reported adverse events should not be interpreted as definitive evidence of safety. In many studies, adverse-event monitoring was poorly described, and standardized criteria for infection, pain, bleeding, wound deterioration, local reactions, recurrence, or amputation were not consistently reported. In addition, PRP preparation and application require careful attention to blood collection, processing, aseptic technique, timing of use, storage, and biosafety. Therefore, the available evidence suggests a favorable safety profile, but one that remains insufficiently standardized and documented.

Importantly, safety reporting was highly heterogeneous across the included studies, limiting confidence in the available evidence regarding the safety of PRP. Although several studies reported that no serious adverse events occurred, many did not clearly describe how adverse events were defined, monitored, classified, or attributed to the intervention. Moreover, follow-up for safety assessment varied considerably, and several studies did not specify whether adverse-event surveillance was conducted prospectively or systematically.

Consequently, the apparently favorable safety profile of PRP may partly reflect underreporting or inconsistent reporting rather than the true absence of complications. Future clinical trials should adopt standardized safety-reporting frameworks, including predefined adverse-event definitions, severity grading, causality assessment, and adequate follow-up, to enable more reliable comparisons across studies and strengthen confidence in the safety profile of PRP.

Costs, feasibility, and applicability in health services

Some included studies reported reduced costs, fewer dressing changes, shorter hospital stays, or lower treatment burden in groups treated with PRP (Jain et al., 2024; Huang et al., 2023; Rajendran et al., 2021; Gupta et al., 2021). These findings are relevant for health services, particularly in settings with high demand for chronic wound care. In addition, recent economic analyses have suggested that PRP may be cost-effective in specific contexts when compared with standard care (Russo et al., 2022; Russo et al., 2025).

However, claims of "low cost" should be used cautiously. The real cost of PRP depends on laboratory infrastructure, kits or centrifugation systems, trained personnel, preparation time, number of applications, follow-up logistics, type of product used, and the health system in which the intervention is implemented. Therefore, although PRP may reduce indirect costs related to slow healing, hospitalization, or prolonged dressing use, the evidence on cost-effectiveness is not yet sufficiently generalizable. Economic studies conducted across different countries and health systems are needed before broad adoption can be recommended on the basis of cost.

Implications for clinical practice and multidisciplinary care

From a clinical perspective, the current evidence does not support a definitive recommendation for routine use of PRP in diabetes-related foot ulcers. PRP may warrant consideration only as an adjunct within comprehensive standard care and after individual assessment of perfusion,

infection, ulcer depth, necrosis, glycemic control, neuropathy, adherence to offloading, and access to multidisciplinary follow-up. This cautious interpretation reflects the heterogeneity, methodological limitations, and risk-of-bias concerns identified in the available studies.

For nursing and wound care teams, this review reinforces the need for clear protocols for ulcer assessment, wound bed preparation, photographic recording, standardized area measurement, infection control, selection of secondary dressings, and monitoring of adverse events. Future studies should report not only healing rates but also patient experience, pain, number of dressing changes, adherence, need for debridement, treatment burden, quality of life, and return to daily activities.

Limitations of the included evidence

The evidence synthesized in this review has important limitations. First, the included studies comprised different methodological designs, ranging from randomized clinical trials to quasi-experimental studies, observational studies, and case series, which reduces comparability across findings. Second, many studies had small samples, short follow-up periods, and incomplete reporting of randomization, blinding, sample size calculation, control of co-interventions, and losses to follow-up.

Another relevant limitation is the heterogeneity of the platelet-derived products themselves. Not all studies sufficiently described final platelet concentration, applied volume, number of centrifugation steps, leukocyte content, activation method, time between preparation and use, or standardization of application. The absence of these details limits reproducibility and makes comparisons across studies difficult.

There was also diversity in the outcomes assessed. Some studies prioritized complete closure, whereas others used area reduction, healing time, the Pressure Ulcer Scale for Healing, photography, software-based measurement, ulcer volume, granulation, re-epithelialization, infection, complications, or costs. This variability justifies narrative synthesis and limits the possibility of establishing robust quantitative recommendations without meta-analysis stratified by intervention type, comparator, and outcome.

Limitations of this review

This review also has limitations. The restriction to studies published in the last five years allowed the review to map recent evidence, but it may have excluded earlier studies that are relevant to understanding the historical development of the intervention. Including different study designs broadened the evidence base but increased methodological heterogeneity. Furthermore, because gray literature, preprints, and conference abstracts were excluded, publication bias and selective reporting cannot be ruled out. Unpublished or non-significant findings may therefore be underrepresented, and selective publication may have contributed to the predominance of favorable outcomes in the available literature. In addition, the absence of meta-analysis prevented estimation of pooled effects for outcomes such as complete healing, healing time, or ulcer area reduction.

Future research should prioritize multicenter randomized clinical trials with adequate sample sizes, detailed description of PRP preparation, standardization of platelet concentration, frequency of application, type of associated dressing, inclusion criteria according to ulcer severity, and clinically relevant outcomes. Results should also be stratified by ischemia, infection, neuropathy, ulcer depth, duration of the lesion, and metabolic control.

In addition, long-term outcomes should be incorporated, including recurrence, amputation, hospitalization, quality of life, pain, patient satisfaction, adverse events, and cost-effectiveness. Standardization of these elements would allow more consistent comparison across studies and would help define the role of PRP in the care pathway for DFU.

Conclusion

Based on the available evidence, platelet-rich plasma has shown potentially favorable healing-related findings as an adjunctive approach for diabetes-related foot ulcers. However, substantial heterogeneity among interventions, methodological limitations, and the considerable risk of bias identified in several included studies preclude firm conclusions regarding its clinical effectiveness and safety. The available findings should therefore be interpreted as preliminary and should not be used to support routine clinical adoption outside comprehensive standard care.

Further well-designed, adequately powered, and standardized multicenter clinical trials are needed. Future studies should provide detailed intervention protocols, systematic safety monitoring, economic evaluation, and long-term assessment of recurrence, amputation, hospitalization, quality of life, and other clinically meaningful outcomes.

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