Ann Ist Super Sanità 2026 | Vol. 62, No. 1: 16-31
DOI: 10.4415/ANN_26_01_05

Expert Consensus on the use of autologous platelet-rich plasma in the context of regenerative medicine: moving forward to good clinical practice

Massimo Danese[1], Vittoria D'Esposito[2], Rosario Miranda[3], Vincenza Dolo[4], Ilaria Giusti[4], Alessio Borean[5], Donato Rosa[6], Bruno Amato[6], Anna Rughetti[7], Valentina Del Greco[7], Laura Mazzucco[8], Antonio Aversa[9], Valter Cassutti[10], Francesco Casabona[11], Alfonso Maria Irollo[12], Carlo Setacci[13], Eugenio Caradonna[14], Andrea Ascoli Marchetti[15], Gaetano Caloprisco[16], Michele Angelo Farina[17], Pietro Formisano[18], on behalf of SIMCRI Expert Consensus Group*

[1]Medicina Rigenerativa, Azienda Ospedaliera San Giovanni Addolorata, Rome, Italy
[2]Istituto degli Endotipi in Oncologia, Metabolismo e Immunologia "G. Salvatore" (IEOMI), Consiglio Nazionale delle Ricerche, Naples, Italy
[3]Azienda Sanitaria Locale Napoli 3 Sud, Naples, Italy
[4]Dipartimento di Medicina Clinica, Sanità Pubblica, Scienze della Vita e dell'Ambiente, Università degli Studi dell'Aquila, L'Aquila, Italy
[5]Servizio di Medicina Trasfusionale, ULSS 1 Dolomiti, Belluno, Italy
[6]Dipartimento di Sanità Pubblica, Università degli Studi di Napoli Federico II, Naples, Italy
[7]Servizio di Immunoematologia e Trasfusionale, Azienda Sanitaria Locale 1 Abruzzo, L'Aquila, Italy
[8]SC Medicina Trasfusionale, AOU SS Antonio e Biagio e Cesare Arrigo, Alessandria, Italy
[9]Dipartimento di Medicina Sperimentale e Clinica, Università degli Studi di Catanzaro "Magna Graecia", Catanzaro, Italy
[10]Società Italiana di Medicina e Chirurgia Rigenerativa Polispecialistica, Terni, Italy
[11]Chirurgia Plastica Ricostruttiva ed Estetica, Gruppo Multimedica, Milan, Italy
[12]Unità di Medicina Rigenerativa Ginecologica, Chianciano Salute, Chianciano Terme, Italy
[13]Dipartimento di Scienze Mediche, Chirurgiche e Neuroscienze, Università di Siena, Siena, Italy
[14]Dipartimento di Medicina di Laboratorio, Centro Diagnostico Italiano, Milan, Italy
[15]Dipartimento di Biomedicina e Prevenzione, Università di Roma "Tor Vergata", Rome, Italy
[16]Poliambulatorio Bellunomedica, Belluno, Italy
[17]Centro di Medicina Rigenerativa, Studio Medico Farina, Caserta, Italy
[18]Dipartimento di Scienze Mediche Traslazionali, Università degli Studi di Napoli Federico II, Naples, Italy
**The members of the SIMCRI Expert Consensus Group are reported in the Acknowledgments*

Abstract

Introduction. This paper summarizes the conclusions of the Expert Consensus (EC) on the use of platelet-rich plasma (PRP) in regenerative medicine. The initiative aimed to promote appropriate and effective clinical use of PRP based on current scientific evidence and expert experience. The main objectives are: to define a flexible operative range for PRP, allowing for personalized application; to establish principles for standardized clinical practice.

Methods. The methods used to develop this EC involved the scientific literature review, the data quality assessment, the evaluation of practical experiences, the critical summary of reviewed literature, the development of questions for expert panel and the drafting of consensus statements.

Results. Recommendations emphasize compliance with legislation, proper device use and operator training. Adequate platelet load is essential for therapeutic efficacy; platelet

Key words
- regenerative medicine
- platelet-rich plasma
- Expert Consensus

Address for correspondence: Pietro Formisano, Dipartimento di Scienze Mediche Traslazionali, Università degli Studi di Napoli Federico II, Via Pansini 5, 80131 Naples, Italy. E-mail: fpietro@unina.it.

recovery should be considered as quality standard. PRP has demonstrated effectiveness in managing diabetic and venous ulcers, osteoarthritis, and tendinopathies, although variability in protocols and inconsistent reporting limit the strength of evidence. Emerging applications include vasculitis, mucositis, and urogenital conditions, although further research is needed.

Conclusions. The EC encourages multicentre research, strict publication standards, and international collaboration to strengthen scientific foundations for PRP use in regenerative medicine.

INTRODUCTION

In recent years, the use of platelet-rich plasma (PRP) has seen significant advancements and has been applied across numerous clinical scenarios. Platelets serve as a critical reservoir of soluble mediators, including cytokines and growth factors. Upon activation, platelets release these molecules, which act locally to promote tissue repair processes and modulate immune and inflammatory responses. Recently, it has been shown that activated platelets also release extracellular vesicles rich in various molecules, including miRNAs, and transfer functional mitochondria to other cells, thus sustaining all the processes of tissue regeneration [1-4]. This has formed the basis for the use of platelet concentrates in various medical and surgical applications.

In Italy, the use of PRP is regulated by law (Ministry of Health Decree, published in the Official Gazette "*Gazzetta Ufficiale*" on December 28, 2015, n. 300, and amended on August 1, 2019). The decree mandates a platelet concentration of 1×10^6/µL ±20% in the final product.

In 2012 Italian Society of Transfusion Medicine and Immunohematology (Società Italiana di Medicina Trasfusionale e Immunoematologia, SIMTI) guidelines referred to this concentration range (Raccomandazioni SIMTI sugli emocomponenti per uso non trasfusionale, available from: https://www.aovr.veneto.it/documents/20182/286958/Raccomandazioni+SIMTI.pdf/93e9ba10-931b-49b7-a26d-412b78f56f73); however, based on reported references, the concentration is not explicitly indicated as a mandatory standard, but rather as an observed value.

One of the earliest documented uses of PRP was in maxillofacial surgery [5], where a minimum platelet concentration of 1×10^6/µL ±20% was established as the baseline threshold for efficacy.

In 2016, the Cochrane Database [6] on platelet concentration mentioned: *"Because most individuals have a baseline blood platelet count of 200,000 (±75,000)/µL, a platelet count of 1 million/µL has been postulated as the ideal therapeutic dose of PRP"*. This statement refers to Marx's 2004 work as the sole bibliographic source [7]. *In vitro* studies have demonstrated a correlation between platelet concentration and activation, and the resulting levels of growth factors [8]. Other studies have explored the efficacy of various platelet concentrations on different cell types (endothelial cells, fibroblasts, mesenchymal stem cells) in terms of proliferation, vasculogenesis, and motility [9-12]. Nevertheless, specific studies on tenocytes have indicated better outcomes at lower platelet concentrations (500,000/µL) [13]. Thus the "regenerative" effect of platelet appears to be dependent on cellular targets.

It is important to emphasize that PRP is a biological product classified as Substance of Human Origin (SoHO), and treatment based on SoHO have been recently regulated by the European Union (Regulation EU 2024/1938 of the European Parliament and of the Council of June 13, 2024, on standards of quality and safety for substances of human origin intended for human application, which repeals Directives 2002/98/EC and 2004/23/EC). PRP is characterized by significant variability in platelet content and soluble factors. Inter-individual variability depends on platelet endowment and possible pathological conditions (e.g., platelet dysfunctions or systemic diseases) that may affect platelet features. Despite potential platelet dysfunction, several cases of patients with such conditions have benefited from autologous PRP treatment, suggesting that altered platelet function does not necessarily compromise treatment efficacy [14]. Additionally, plasma molecule concentrations (e.g., growth factors, cytokines) may vary depending on lifestyle, metabolic conditions, and inflammatory states [15, 16]. Finally, the clinical context in which PRP is applied (e.g., tissue type, damage extent, and local inflammation) represents another important variable, needing personalization of therapeutic plans. Factors such as delivery method, concentration and volume, number of applications, intervals between treatments, and synergistic approaches (e.g., hyaluronic acid, antibiotics, ozone therapy, photobiomodulation) should be carefully tailored.

While encouraging results in PRP applications have been reported, key issues remain:

- variability in platelet production and activation processes due to different commercial devices;
- difficulty comparing studies in the literature due to methodological inconsistencies;
- insufficient sample sizes in many studies, limiting robust statistical comparisons;

  poorly designed studies that are often incomparable.

Thus, acknowledging the complexity of PRP applications in regenerative medicine, this Expert Consensus (EC) aims to:

- define operational "freedom" within minimal evidence-based ranges for current indications;
- establish clear methodological models for significant and comparable scientific studies to enrich autologous PRP use as an adjunct therapy;
- address production, biological qualification, and storage challenges to suggest practices aligned with existing regulations;

- guide the development of standardized operating procedures based on best clinical practices.

This document seeks to serve as a rigorous and shared reference for practitioners in the field. It does not claim to be definitive but rather represents a step in the ongoing evolution of regenerative medicine and its integration with other synergistic methodologies under development.

METHODS

The methods used to develop this EC involved the following steps:

- scientific literature review: examination of recent publications using scientific databases such as PubMed, Scopus, and others;
- data quality assessment: evaluation of data quality based on critical analysis of study results and bibliometric indices (e.g., citation count, journal Impact Factor);
- evaluation of practical experiences: consideration of real-world applications and expert experiences in the field;
- critical summary of reviewed literature: synthesis of findings from the analysed studies into a comprehensive critical summary;
- development of questions for expert panel: formulation of targeted questions to be addressed by a panel of experts;
- drafting of consensus statements: preparation of statements reflecting agreement among the experts based on evidence and discussion.

RESULTS

Critical evaluation of PRP preparation techniques

Clinical PRP preparations enable the local delivery of active molecules (e.g., >300 growth factors and cytokines) to injured tissues. Preparation methods significantly influence PRP quality and efficacy, particularly platelet yield. Double-spin techniques typically yield higher concentrations and superior platelet capture rates than single-spin systems [12, 17]. Recent approaches emphasize the load of platelets applied, measured as absolute platelet count, enabling better standardization and outcome reproducibility.

These considerations might explain why conflicting results have been published regarding PRP therapy: specifically, in studies that used protocols with low collection volumes, single-spin methods, and low capture rates, the insufficient number of administered platelets might have compromised adequate management. Another complication for standardization is the deliberate or accidental inclusion or exclusion of the leukocyte component, as it introduces highly active biological variables in the repair process, such as involvement in angiogenic and inflammatory processes, which are critical for initiating and maintaining the reparative process [18].

Recent scientific evidence has also demonstrated the involvement of other blood components in coagulation processes, inflammation modulation, and wound healing. Many studies have evaluated the clinical effects of fibrin scaffolds, monocytes/macrophages [19, 20], and stem cells [21, 22]. Some authors have clinically used the application of whole blood clots, in which all blood corpuscular elements are incorporated into a fibrin network that facilitates cellular migration and modulates the release of growth factors. Red blood cells, which are almost completely excluded during centrifugation to obtain PRP, play a role in coagulation, but little is known about the potential therapeutic effects of whole blood red clots and the role of red blood cells in the healing process [23-26]. This highlights the need to introduce additional parameters for classifying and assessing the quality of PRP, particularly in terms of presence of blood cell populations. A brief mention is warranted regarding the long-term preservation of PRP, which facilitates repeated treatments over time in authorized facilities. Although platelet-derived growth factors have a relatively short half-life, some studies have demonstrated the efficacy of PRP in the form of platelet lysates stored for nine months at –80 °C [27]. Future research should focus on identifying the optimal temperature and time range for preserving sufficient regenerative activity in PRP components.

Another aspect to evaluate is the type of anticoagulant. EDTA alters platelet structure and function, causing irreversible damage with the destruction of platelet granules [28]. Citrate-dextrose solution (ACD) has been widely used in clinical practice for years. It has an acidic pH [29, 30], which may induce pain and reduce platelet functionality, and contains D-glucose, which could facilitate inflammatory reactions [31]. However, its dilution in blood and removal from PRP (particularly in its platelet gel form) renders it safe, with no significant pain reported from its use. Sodium citrate (SC) has a basic pH [32, 33] and shows better platelet recovery efficiency [34].

Overall, the literature reports mainly encouraging findings with PRP in a wide spectrum of clinical conditions; however, studies with negative or inconclusive outcomes should not be disregarded. Despite the complexity of the underlying biological mechanisms and the heterogeneity of the treated pathologies, it is noteworthy that studies reporting limited efficacy frequently utilized PRP preparations characterized by a low total platelet content and, in most cases, a leukocyte-poor composition.

Critical evaluation of PRP treatment in diabetic foot ulcers

The use of autologous PRP in the treatment of diabetic foot ulcers has become standard practice and represents a significant therapeutic tool. The literature is rich in studies, most of which have been conducted in developing countries, primarily India, Pakistan, Iran, and Egypt. This trend likely reflects the high interest in low-cost, self-prepared treatments in these regions, in contrast to high-income countries, where the availability of advanced wound care products reduces the incentive for similar research. The literature includes [35-51]: a double-blind randomized controlled trial (RCT) using platelet lysate [37], open-label RCTs [39, 40, 44, 46-49], non-randomized controlled studies [35, 36, 51], a non-randomized controlled study comparing two PRP

administration methods [43], case reports [45], case series [38], and prospective comparative studies between patient subgroups [41, 42].

All studies included adult patients of both sexes. In some cases, lower and upper age limits were specified. To be included, ulcers had to be non-responsive to conventional therapy. The definition of non-responsiveness varied across studies and included ulcer durations exceeding from 4 weeks to 6 months [35-41]. In some studies, the criteria for defining non-responsiveness were not clearly specified [42], or the inclusion was based solely on the presence of diabetic ulcers [43]. Some studies established additional inclusion criteria, such as ulcer diameter [39, 43], area [37, 44], number [36, 40], or anatomical location [44]. Most studies excluded ulcers involving tendons, bones, or ligaments, as well as those with gangrene. Notably, some studies also excluded patients undergoing anticoagulant or antiplatelet therapy [38, 39, 42]. Thrombocytopenia or platelet disorders were also exclusion criteria in several other studies [37-41, 43].

Blood volumes used for PRP preparation ranged from 20 to 50 mL. All studies used sodium citrate or ACD as anticoagulant. A two-step centrifugation process was employed in nearly all studies, except for one that used a single centrifugation step [45]. Most studies [35, 38, 41, 43] reported centrifugation time and rpm, or, less frequently, time and acceleration (g-force). In some cases, these parameters were not specified [36, 40]. One study [39] used a specialized kit with syringes that fit directly into a dedicated centrifuge and specified both the duration and speed for double centrifugation. When performed, activation was achieved using calcium gluconate [39, 40] or chloride [35, 45]. However, most studies did not report the activation method or explicitly stated that platelet concentrate was used without preactivation. Only a limited number of studies reported platelet concentration in the final PRP product, noting a low leukocyte content and thus clearly identifying the product as P-PRP. Among these, one uncontrolled prospective study [38] and two case reports [41, 45] documented a platelet concentration slightly above 1×10^6/µL. The remaining studies did not specify either the final platelet concentration or leukocyte content.

In some studies, PRP was injected perilesionally and intralesionally without being used as a dressing over the wound [36, 38, 42, 46]. One study involved only perilesional injection [37], although it used platelet lysate rather than PRP. The exclusive use of PRP as a topical dressing – without injection – was reported in a large group of studies [40, 41, 44, 47-50]. Other publications described combined application methods, with PRP used both as a dressing and injected intra- and perilesionally [39, 45]. A single prospective comparative study included two non-randomized arms – one receiving perilesional injections and the other receiving topical PRP application (method of topical application not specified). The study concluded that injected PRP was superior [43]. A limited number of studies [38, 43] specified the injected volume, which ranged from 0.4 to 10.2 mL. Another study that mentioned the volume (5 mL) used a platelet lysate instead of PRP [37].

Treatment is generally performed over multiple sessions, with only one study reporting a single administration [41]. In studies where PRP was used exclusively via injection, sessions were scheduled every two weeks [36, 37] or every three weeks [38]. Only one study reported a more frequent injection schedule – on days 1, 5, 10, and 20 [35]. Another study included two injections spaced three days apart [42]. In studies employing both injection and topical dressing, the treatments were administered concurrently, either weekly until complete healing [45] or for up to four [43] or ten sessions [39]. In studies using PRP exclusively as a dressing, applications were typically twice per week for up to three [48], eight [47], or twenty weeks [40]. One study did not specify treatment duration [50], and only two studies used weekly dressing applications [41, 49]. Another study did not indicate the timing at all [44]. The scoping review by Kunder *et al.* [50] analysed this aspect and found that twice-weekly applications appeared to be more effective than once-weekly.

Excluding case reports, some studies did not clearly define primary endpoints [36, 39, 41]. When specified, primary endpoints were typically wound healing rates, assessed either by the number of wounds completely healed at the end of the observation period or by the percentage reduction in wound area at study completion or during follow-up [35, 40, 42, 43, 47]. In one study involving platelet lysate [37], the primary endpoint was safety, while secondary endpoints included complete healing or wound status at 12 weeks.

Only a limited number of studies compared PRP with a standard reference treatment. Studies comparing PRP with other innovative wound therapies (e.g., adipose tissue grafts) or combined grafting techniques were excluded. The reference treatment included: platelet-poor plasma (PPP) [37], silver sulfadiazine [48], dressings with or without collagenase [46], saline-moistened gauze [36, 39, 40, 44], which corresponds to the outdated *wet-to-dry* technique. Other studies generically referred to "standard treatment" [35, 51] or "antiseptic dressing" [50]. None of the studies used modern advanced dressings based on wound bed preparation principles as a comparator.

Most controlled studies concluded that PRP treatment was significantly superior to the control in terms of number of wounds completely healed and degree of wound surface area reduction (in non-healed wounds or at specific observation times). One open-label RCT [44], however, found no significant difference between PRP and saline-moistened gauze.

The literature also includes several meta-analyses and reviews [50, 52-59], all confirming the utility of autologous PRP in treating diabetic foot ulcers.

Su's meta-analysis of 17 studies on diabetic foot ulcers found that PRP was significantly more effective than standard of care (OR: 2.11; 95% CI: 1.55 to 2.86). PRP also appeared to significantly shorten complete healing time (mean duration: –19.04 days; 95% CI: –20.46 to 17.61) [52], Deng's meta-analysis confirmed higher efficacy of PRP (RR: 1.42; 95% CI: 1.30 to 1.56; $p<0.001$) [54], OuYang's review supported this (OR: 4.37; 95% CI: 3.02 to 6.33; $p<0.001$) [55]. Meznerics' meta-

analysis, which included ulcers of different aetiologies, showed PRP superiority in the diabetic ulcer subgroup (OR: 2.26; CI: 1.50 to 3.41; I^2=12%), though the effect was less marked than in venous ulcers. No significant difference was observed between injectable and topical PRP (though this was based on all ulcer types) [57]. Qu's meta-analysis, also covering ulcers of various aetiologies, reaffirmed PRP's superiority [58]. Thanigaimani's network meta-analysis, which included three trials on diabetic ulcers of various types, also supported PRP efficacy (RR: 9.69; 95% CrI: 1.37 to 103.37) [56]. Finally, Platini *et al*., confirmed the superiority of topically applied PRP gel over controls, identifying Wagner grade 2 (RR=2.12, 95% CI: 1.01 to 0.44; p=0.05) and grade 3 (RR=1.36, 95% CI: 0.70 to 2.64; p=0.37) ulcers as the stages where PRP treatment is most beneficial [53].

The review by Napit *et al*. [59], which analysed 7 studies (4 of which were on diabetic ulcers), noted that none of the studies reported hazard ratios (HR). Deng's meta-analysis [54], which included 19 studies, found a statistically significant reduction in healing time compared to conventional treatment (MD=–3.13 days, 95% CI: –5.86 to –0.39, p<0.001). Similarly, Ou Yang's review [55] reported a significant result (MD=–3.21 days, 95% CI: –3.83 to –2.59, p<0.001).

Napit [59] highlighted the heterogeneity in how healing rates were reported across the 7 studies analysed. While a trend toward faster healing in the PRP group emerged, the heterogeneity prevented statistical pooling or definitive conclusions. Platini [53], in his meta-analysis on topical platelet gel, found a 16.97-day reduction in wound duration (95% CI: –32.64 to –1.29; p<0.00001). However, no statistically significant difference was found when wound duration was expressed in weeks (MD=–5.60 weeks, 95% CI: –18.92 to 7.72; p=0.41). The authors concluded that PRP accelerates tissue growth, but its effect on healing time may not emerge clearly due to high study heterogeneity.

Napit's review [59] noted that, except for one study, no healing occurred in control groups, making statistical comparison infeasible. Deng's meta-analysis [54] showed a significant reduction in wound area with PRP compared to controls (MD=1.02, 95% CI: 0.51 to 1.53, p<0.001). Meznerics *et al*. [57] found PRP to be superior to controls in the diabetic ulcer subgroup (SMD=–0.68, 95% CI: –1.31 to –0.06; I^2=93.64%). Qu's meta-analysis [58], which included both autologous and homologous PRP, also found a significant reduction in ulcer area (SMD=1.37, 95% CI: 0.91 to 1.82; I^2=22.1%) and no difference between autologous and homologous PRP. In contrast, OuYang [55] did not find a statistically significant reduction (MD=5.67, 95% CI: –0.77 to 12.11; p=0.08). Platini [53] concluded that no consistent evidence exists for a significant wound area reduction using topical PRP gel.

Babaei *et al*. [41], in a prospective comparative study, assessed PRP efficacy on ulcers of varying sizes. All wound sizes benefited from PRP, but statistically significant differences in healing times were observed between smaller wounds (2 to 5.5 cm^2) and larger wounds (8.5 to 12.5 cm^2). Thus, supporting the use of PRP especially in smaller lesions.

Overall, both controlled and uncontrolled studies indicate that PRP is safe when used either by injection or as topical dressing. Deng's meta-analysis [54] found no significant difference in adverse events [35-37, 39, 42, 44-46]. Only one study [48] noted a minor local injection-site irritation. A study using injectable platelet lysate [47] reported minor adverse events such as injection site pain, local oedema, infection, bleeding, redness, and warmth. No adverse events were reported in studies using topical PRP as a dressing [40, 41, 44, 47-50].

Meznerics [57] hypothesized a protective effect of PRP against infection, though no quantitative analysis was conducted. Finally, Platini *et al*. [53] found standard treatment to be associated with higher infection risk than PRP at week 1 (RR=0.56, 95% CI: 0.34 to 0.91; p=0.02) and week 2 (RR=0.13, 95% CI: 0.02 to 0.04; p=0.01). However, over time, differences became non-significant.

In addition, no significant difference in amputation rates was found in most of the studies analysed.

However, Deng found PRP to be associated with reduced risk (RR=0.35, 95% CI: 0.15 to 0.83; p<0.001) [54]. In Platini's meta-analysis [53], the amputation rate was significantly higher in the control group (MD=0.36, 95% CI: 0.16 to 0.84; p=0.02).

Overall, the available literature on the use of PRP in diabetic foot ulcers is characterized by substantial heterogeneity, particularly in the criteria used to define chronic or non-healing ulcers. Inclusion thresholds vary widely, encompassing lesions as recent as four weeks to ulcers persisting for up to six months, thus limiting the comparability of study outcomes. Patient selection also differs, with some studies excluding individuals on anticoagulant or antiplatelet therapy, or those with platelet disorders, likely due to concerns about interference with platelet activation or the risk of hematoma formation, even though such medications are common in the diabetic population due to associated cardiovascular risk. The preparation of PRP is inconsistently reported and varies significantly, ranging from single centrifugation procedures reliant on operator expertise to commercial kit-based protocols. This procedural variability undermines reproducibility and reduces the evidentiary strength of the findings, though the safety profile remains generally favourable. Crucial methodological details such as initial and final platelet counts and injection volumes are often omitted, preventing accurate calculation of the administered platelet load, which is increasingly recognized as a fundamental parameter influencing biological activity. The mode of PRP administration also differs, with injectable formulations currently appearing more effective than topical ones, although comparative data are limited and frequently lack key technical specifications, such as platelet concentration and activation status. The frequency and volume of administration are inconsistently reported, further complicating assessment of therapeutic impact. Notably, no studies have incorporated platelet-rich fibrin, which could offer enhanced fibrin stability. The overall quality of study designs remains suboptimal, with a scarcity of double-blind randomized controlled trials; most

evidence derives from non-blinded or non-randomized trials, which carry higher risk of bias. Moreover, control group treatments often rely on outdated standards such as saline-soaked gauze, especially in low-resource settings, and the specifics of standard care are frequently underreported. Endpoints and outcome measures vary widely across studies, ranging from ulcer healing rates and area reduction to healing time, without standardized definitions. This variability significantly hampers cross-study comparisons and the synthesis of data in systematic reviews or meta-analyses.

Critical evaluation of PRP treatment in venous ulcers

The use of PRP in the treatment of venous ulcers is generally reserved for hard-to-heal wounds, which show no signs of healing despite the application of all therapeutic procedures established by international guidelines.

The types of studies reviewed included [60-72]: randomized controlled trials (non-blinded) [63, 67], randomized controlled trials comparing two administration routes [62, 70], non-randomized controlled studies, where the control was a second ulcer in the same patient [65], and case series [66, 72]. Additionally, three studies [60, 61, 64] labelled as prospective controlled trials provided detailed individual patient descriptions but lacked statistical analysis; they can therefore be considered extended case series (dual case series).

One study [60] included only patients with reflux limited to the superficial venous system, but it focused on comparing two treatment approaches to venous insufficiency – "modern" (latest advances in dressings and surgery) *vs* "traditional" – thus its findings are not suitable for comparison with other studies. Another study [61] included ulcers measuring >2 cm² and <100 cm². Some studies also reported ulcer age as an inclusion criterion: 6 weeks [62], 12 weeks [61], or 6 months [63].

Exclusion criteria, when specified, included thrombocytopenia [61] (<150,000 PLT/mm³), treatment with anticoagulants or antiplatelet agents [63], immunosuppressants [64], corticosteroids [61], concomitant arterial disease, diabetes, infection [63, 64], exposed bone or tendon [63], among others.

Blood volumes for PRP preparation are often unspecified; when reported, the standard amount is around 30 ml. Sodium citrate or ACD is used in all studies (though not always explicitly stated). A double-spin protocol is employed in all studies that describe the method [62-64], usually reporting duration and revolutions per minute (rpm) or relative centrifugal force (*g*). Two studies reported 10% calcium chloride at a 1:4 ratio [62, 64] for PRP activation; one study did not activate the PRP [63], and others did not specify activation protocols. Only one prospective comparative study [64] reported the platelet concentration in PRP, which was 5.4 times the baseline level, although leukocyte content was not measured despite labelling the product as P-PRP. In this study, platelet concentration was slightly above 1×10^6 PLT/µl. All other studies did not report final platelet or leukocyte concentrations.

In several studies PRP was injected perilesionally and intralesionally, without topical application [60, 63, 65]. Exclusive use of PRP as a topical dressing without injection was commonly reported [61, 64, 66-69]. No study investigated combined use (injection+dressing). One prospective comparative study [62] included two non-randomized arms: one received perilesional injections, the other topical dressings (topical application method not specified). Results showed a trend toward better outcomes with injections. Notably, dressing changes were performed biweekly in both groups, which may have negatively affected the topical PRP group. Another study [70] comparing the two administration methods found no significant difference between injection and topical groups overall, but topical PRP was more effective in diabetic patients, while injection was preferable for chronic, fibrotic ulcers. Histopathological findings were similar between the two groups [70]. None of the included studies reported the volume of PRP administered. In studies using topical PRP, dressing changes were generally performed weekly for varying durations: up to six weeks [70, 71], nine weeks [68], or one year [64]. One study [61] performed a single application. Many studies did not specify timing. In a comparative study [62], treatment was given every two weeks for a total of 8 sessions, which may have limited the effectiveness of the topical PRP.

Excluding case reports, some studies did not explicitly specify the endpoints [61, 63]. When endpoints were defined [60, 62, 65, 68, 69, 71], primary outcomes included wound healing rate, the number of wounds healed by the end of the observation period, and the percentage reduction in wound size during or at the conclusion of the study. One comparative study between injectable and topical administration based its endpoint on histopathological characteristics of the lesions [70].

It should be noted that studies comparing PRP with other innovative dressings such as adipose tissue or those associating PRP with grafting techniques were excluded. The standard comparator treatment was specified only in some cases: saline-soaked gauze [70], petroleum jelly gauze [67], hydrocolloids [69], while many studies generically referred to a standard treatment without further detail [62, 63, 65, 68, 71]. One study used a calcium chloride solution as control [64]. PRP treatment demonstrated superiority over controls in all studies, for both injectable and topical forms. Direct comparisons between these two methods yielded mixed results: one study [63] found them substantially equivalent, while another [62] reported superiority of the injectable form. However, the latter study performed biweekly dressing changes, which may have disadvantaged the topical method.

A recent review selectively analysed data from randomized controlled trials on venous ulcers, including a total of 20 studies focusing on ulcers rather than patients [73]. It showed that PRP-treated groups had higher complete ulcer closure rates than controls (OR 5.06, 95% CI: 2.35 to 10.89, I^2=58%, p<0.01). Geographic subgroup analysis revealed no significant differences between PRP and control in Asia-Pacific (OR=3.94, 95% CI: 0.53 to 29.59), Europe (OR=1.46,

95% CI: 0.63 to 3.37), or America (OR=1.00, 95% CI: 0.17 to 5.77), but significantly favoured PRP in Africa (OR=14.26, 95% CI: 4.33 to 46.95). The positive effect of PRP remained significant at ≤3 months (OR=9.40, 95% CI: 2.93 to 30.22) and >3 months (OR=2.66, 95% CI: 1.27 to 5.58). Moreover, both injectable (OR=6.69, 95% CI: 3.14 to 14.24) and topical PRP (OR=4.24, 95% CI: 1.75 to 10.26) outperformed controls without significant difference between them (χ^2=0.59, df=1, p=0.44). PRP was more effective for both small (≤10 cm²: OR=8.72, 95% CI: 1.85 to 41.14) and large ulcers (>10 cm²: OR=4.72, 95% CI: 1.68 to 13.29). Few studies assessed pain via VAS scale and only two were included in the meta-analysis [73], with no significant difference between PRP and controls (MD=1.19, 95% CI: –0.67 to 3.04, I^2=52%). In addition, based on two studies, PRP shortened healing time compared to controls (MD=–3.25 days, 95% CI: –4.06 to –2.43, I^2=49%). Recurrence rates, based on limited data, were not significantly different (OR=0.16, 95% CI: 0.05 to 0.50, I^2=18%), nor irritant dermatitis was found (OR=0.38, 95% CI: 0.08 to 1.90, I^2=0%) [73].

Overall, the inclusion criteria for venous ulcer studies are variable and generally do not exclude ulcers associated with post-thrombotic syndrome, while exclusion criteria are more uniform and commonly encompass pregnancy, breastfeeding, coagulation abnormalities, corticosteroid use, immunosuppression, suspected neoplastic ulcers, recent transfusion, and circular ulcers. The frequent exclusion of patients on antiplatelet or anticoagulant therapy, often with the option of temporary suspension, lacks a clearly stated rationale, despite the high prevalence of such therapies in the elderly population typically affected by venous ulcers. The methods used to prepare PRP are frequently underreported, and while double centrifugation appears to be the most adopted technique, insufficient methodological detail weakens the strength of evidence. Crucial parameters such as baseline and final platelet counts, as well as the volume of PRP administered, are rarely specified, preventing accurate estimation of platelet dose per session or across the entire treatment course. This gap may reflect limited expertise in blood component handling, especially when commercial kits are used without critical assessment. Although maintaining a minimum platelet concentration is important, the total platelet dose administered is increasingly regarded as a more relevant indicator of the biological effect. No substantial efficacy differences have yet emerged between injected and topical PRP, although data remain limited. Topical PRP typically requires activation to form a fibrin gel, which is relatively unstable and may necessitate more frequent applications. A comparison with platelet-rich fibrin, which generates a more stable matrix via spontaneous activation, would be of interest. Two non-randomized comparative studies have attempted to evaluate injection versus topical use but lacked essential details such as platelet concentration and delivery mode, underscoring the need for well-designed, double-blind randomized trials. Most studies administered PRP once weekly, though in one comparative study, biweekly injections were employed – potentially disadvantaging the topical group due to rapid degradation of activated PRP gels. The overall quality of the studies is limited by a lack of high-level evidence, with most trials being non-blinded or non-randomized. In several studies, saline-soaked gauze was used as the control treatment, despite its misalignment with contemporary wound care standards, likely due to resource constraints in lower-income settings. Furthermore, standard treatments were often poorly defined and failed to explicitly adhere to principles of moist wound healing or wound bed preparation. Study endpoints were inconsistently reported, further limiting the comparability and interpretability of outcomes.

Critical evaluation of PRP treatment in musculoskeletal disorders

The use of PRP in musculoskeletal disorders has been widely debated over the years for various reasons, including preparation methods, indications for treatment, its efficacy compared to other biological and/or synthetic preparations (hyaluronic acid – HA – and corticosteroids), the number of administrations, and regulatory issues related to the manipulation of blood components. Nevertheless, numerous randomized clinical trials and systematic literature reviews almost unanimously support the efficacy of this treatment, particularly in pain relief and functional restoration in patients with osteoarthritis (OA) and tendinopathies (*Supplementary Table 1 available online*).

In 2023, the ORBIT group of ESSKA (European Society of Sports Traumatology, Knee Surgery and Arthroscopy) established a consensus regarding the use of PRP in patients with osteoarthritis [74]. The consensus includes level I and II studies, as well as prospective studies and meta-analyses, supporting the safety and benefits of PRP compared to both placebo and other infiltrative treatments such as hyaluronic acid and corticosteroids. PRP has proven effective in patients with mild to moderate knee OA (Kellgren-Lawrence – KL ≤3) but offers less benefit in patients with KL 4 OA, for whom it serves mainly as a palliative option in case of refusal or contraindication to surgery.

The consensus also investigated the superiority of PRP over glucocorticoid (GC) infiltrative therapy and the different types of PRP preparations. Regarding comparison with GCs, PRP demonstrated a longer-lasting effect and a better safety profile on chondrocytes, since GCs, especially with repeated injections, exhibit high toxicity. Compared to HA therapy, PRP has a more prolonged efficacy, although the variability of commercially available HA formulations may introduce bias in the evaluated studies.

Based on several meta-analyses, the consensus was unable to reach agreement on the optimal platelet concentration and/or quantity in the preparation or whether Leukocyte-Rich PRP (LR-PRP) or leukocyte-poor PRP (LP-PRP) yields greater patient benefit, suggesting that the beneficial effects of PRP are multifactorial, complex, and not yet fully understood [74].

Thus, in Europe, ESSKA sought to clarify certain aspects of PRP use, while in 2021, the AAOS (American Academy of Orthopaedic Surgeons) published an over-

review confirming the clinical efficacy of PRP compared to placebo but emphasized that PRP outcomes are comparable to other infiltrative therapies, highlighting the need for higher-quality studies to affirm PRP's superiority [75, 76].

Critical evaluation of PRP treatment in vasculitis, mucositis, andrological and gynaecological disorders

Only few studies are available regarding the use of PRP in vasculitis and mucositis. In 2021, a case report described a 46-year-old female patient with leukocytoclastic vasculitis, a vasculitis with various aetiologies affecting the skin and characterized by polymorphic rash with erythema, purpuric skin lesions, necrosis, and ulceration [77]. After 6 months of ineffective conventional treatments, PRP therapy was started, and lesions healed within one month. The frequency and application modalities of PRP were not reported in this study.

Another study [78] is a pilot trial analysing the efficacy of LP-PRP therapy in a group of patients with Behçet's Disease (BD), a chronic immune-mediated vasculitis characterized by mucocutaneous ulcers, ocular involvement, and vascular and neurological alterations. Of 77 patients, only 12 were enrolled because patients with ocular or neurological involvement, those on anticoagulants or immunobiological drugs, or without consent were excluded. Enrolled patients were treated for oral ulcers with nine 3 ml applications over 6 months, with one-year follow-up. Results showed PRP promoted an anti-inflammatory profile characterized by increased regulatory T cells (Tregs) in plasma, decreased activated NK cells, and cytokine profile changes. Clinical improvement was observed with reduced number and faster healing of ulcers.

Several studies [79-81] analysed the efficacy of homologous PRP/Platelet Gel in treating oral mucositis induced by chemotherapy and radiotherapy in oncologic patients. Chemo- and/or radiotherapy can cause oral complications that severely affect quality of life by interfering with essential activities such as eating and communication. Oral mucositis is a frequent and severe complication. PRP use in oral mucositis treatment appears effective in improving oncologic patients' quality of life.

A recent review [82] analysed numerous studies on PRP, alone or combined with adipose-derived stem cells (ADSC), for the treatment of genital female localized Lichen Sclerosus (LS). Safety of PRP and/or ADSC therapy was assessed, with adverse events limited to mild and transient symptoms such as pain and oedema at the injection site. Significant improvements in subjective symptoms (itching, burning, dyspareunia, and sexual function) were reported. Symptom improvement allowed reduction or cessation of topical corticosteroids.

Although few studies exist, available evidence suggests PRP therapy in inflammatory skin and mucosal lesions with difficult healing is effective. Literature shows PRP, delivered in various ways, can rapidly repair oral and oesophageal mucosal damage from the first applications, halt mucositis progression, reduce pain intensity, and restore patients' ability to feed (*Supplementary Table 2 available online*).

PRP use for erectile dysfunction (ED) and Peyronie's Disease (PD) remains still investigational. Regarding ED, 11 studies have enrolled men aged 30 to 75 years, mostly poor responders to conventional oral pharmacotherapy. Only three were placebo-controlled [83-85], with contradictory efficacy results but excellent safety profiles. Despite methodological variability, current studies show promising results in restoring responsiveness to phosphodiesterase type 5 (PDE5) inhibitors. However, the absence of standardized operating procedures renders outcomes highly dependent on the investigators' expertise. Quantification of the platelet concentration administered per session remains necessary, as both treatment intervals (ranging from 4 to 8 weeks) and number of injections (ranging from one to three or more) lack standardization. Notably, only the study by Francomano *et al*. [86] identified mean platelet volume, measured preoperatively, as a potential biomarker of therapeutic efficacy.

Patient selection deserves special attention, with careful evaluation of ongoing therapies and comorbidities to maximize treatment efficacy. The main inclusion criterion for ED should be the presence of a vasculogenic form, confirmed by dynamic penile colour Doppler ultrasound following established protocols [87]. Most studies feature relatively short follow-up periods.

Regarding PD, few studies exist [88-93] and enrolled heterogeneous populations in terms of age, plaques, and deformity. Despite varying methodologies, studies showed promising results in curvature improvement, though techniques varied among authors. The main inclusion criterion should be the absence of anticoagulant therapy, recommending suspension for a suitable period before the procedure if clinically safe. Currently, evidence on PRP effects for all forms of ED is limited and very limited for PD (*Supplementary Table 3 available online*).

The use of PRP in female genital pathologies is also still investigational. Regenerative medicine, particularly PRP with its well-established regenerative, anti-inflammatory, immunomodulatory, and angiogenesis-stimulating properties, is well-suited for application in gynaecology. However, recent studies describing PRP use are limited. The main proposed indications include: chronic pelvic pain (regardless of aetiology), stress urinary incontinence, ovarian insufficiency (e.g., poor ovarian reserve, symptomatic menopause, assisted reproduction scenarios) and endometrial disorders (e.g., failed implantation, recurrent early miscarriage, endometritis).

In the last 5 years, several studies have been published (*Supplementary Table 4 available online*). Current literature and clinical experience highlight PRP's utility in gynaecology. Standardizing protocols and refining patient selection will further strengthen the evidence base.

Key clinical research questions

Q1. Does PRP preparation methodology affect product quality?

Q2. Is there sufficient evidence that platelet concentration affects clinical efficacy?

Q3. Are there robust data supporting specific PRP topical and injectable protocols for defined pathologies?
Q4. What clinical questions remain unanswered?

Expert answers

• *A1: Influence of PRP preparation method on product*

Based on a critical analysis of the literature and the field experience of the expert panel participating in the EC, it is considered that the type of procedure used for product preparation may influence its yield. Numerous devices are currently available for the preparation of PRP for non-transfusional use, most of which are based on the principle of centrifugal separation. Available evidence indicates that protocols involving double centrifugation ensure a higher platelet yield. It should be noted, however, that some of these methods are exclusively available at transfusion facilities. The medical devices (MD) available on the market and primarily used in outpatient or non-hospital settings may produce variable yields compared to the standard indicated in the current transfusion law, which is $1x10^6$/µl ±20%. It is emphasized that such medical devices must be compliant with the medical device class defined by law, and transfusion services are urged to verify the compliance and to employ all necessary measures to ensure the safe use of PRP by healthcare professionals.

Recent scientific literature has highlighted that, in addition to the well-known action of growth factors released by platelets, other mechanisms of intercellular communication are involved in the regenerative and anti-inflammatory effects of PRP. These include the release of extracellular vesicles and the transfer of mitochondria. The practical implication is that "viable" platelets may retain greater regenerative and anti-inflammatory potential. Nevertheless, practical experience and the need to obtain enough platelets suggest that freezing procedures for platelet-derived products can still result in a clinically satisfactory effect.

• *A2: Effect of platelet concentration on PRP efficacy*

Several *in vitro* studies have indicated that the proliferative and differentiative effects of PRP are cell-specific and dependent on the platelet concentration used. Some studies have reported that higher platelet concentrations may paradoxically result in reduced effects compared to lower concentrations, following a bell-shaped dose–response curve. With regard to human application, the concept of concentration should be harmonized with that of "absolute quantity." In other words, in individuals with lower baseline platelet concentrations, a larger blood volume may be required to achieve an effective dose. Although the scientific literature is not entirely consistent or easy to interpret – due to incomplete information on preparation methods and platelet concentrations – three interesting studies [94-96] analysing numerous reports, identified an effective average quantity of 3.2 $x10^9$ platelets, above which all positive results were achieved, while below this threshold, almost all results were negative. This could serve as a starting point for further targeted studies on effective platelet load, tailored to specific tissues/regions, to treat lesions based on their severity and chronicity.

• *A3: Evidence for protocol-specific PRP use*

With regard to diabetic foot ulcers, the extensive scientific literature – despite limitations in the overall quality of studies – is generally consistent in supporting the usefulness of PRP treatment, both when applied as a topical dressing and when administered via peri- and intra-lesional injections. Currently, limited evidence suggests a possible superiority of the injectable form.

For venous ulcers, more evidence is available supporting the use of PRP in topical form as a dressing, whereas fewer studies have evaluated its peri- or intra-lesional injection. These findings are consistent with the recommendations issued by the Italian National Blood Centre (Centro Nazionale Sangue, CNS) in the guideline *Therapeutic indications for the use of blood components for non-transfusional purposes – Third edition, June 2024* which supports the use of PRP in the treatment of both diabetic foot ulcers and venous ulcers (in treatment cycles of 12 applications), with a level of evidence rated 1B, without specifying a preferred route of administration (topical *vs* injectable). It remains to be determined whether PRF (platelet-rich fibrin, obtained through coagulation by contact with glass surfaces without additive agents) may offer similar or superior performance compared to PRP.

Regarding orthopaedic applications, a review of the scientific literature – further reinforced by recent consensus conferences from ESSKA and AAOS – has shown that PRP is effective in patients with mild to moderate knee osteoarthritis (KL grade ≤3) but offers limited benefit in KL grade 4 patients. PRP has also demonstrated superiority over corticosteroid injections, particularly in terms of the duration of therapeutic effects and safety profile with repeated treatments. Superiority over HA has also been reported, although this comparison is affected by the heterogeneity of HA formulations available. The role of leukocytes in PRP preparations remains to be clarified.

These conclusions align with the CNS guidelines, which recently recommended PRP for the treatment of grade 1-3 osteoarthritis of the knee and hip, in treatment cycles consisting of three applications, with a level of evidence rated 1B. The level of evidence for PRP use for other musculoskeletal conditions (ankle osteoarthritis, pseudarthrosis, anterior cruciate ligament lesion/reconstruction, patellar tendinopathy, epicondylitis infiltrative treatment, Achilles tendon inflammation, rotator cuff injury) has been rated 2B.

As for the use of PRP in andrological conditions (ED and PD), in the treatment of vasculitis and mucositis – including those induced by chemotherapy and radiotherapy in cancer patients – and in female genital disorders (chronic pelvic pain, stress urinary incontinence, ovarian insufficiency, endometrial pathologies), the scientific literature remains limited. Nevertheless, despite the small number of published studies, there is broad clinical practice supporting the efficacy and applicability of PRP in these fields. Further research is needed to establish standardized treatment protocols.

- *A4: Unanswered research questions*

The scientific literature shows significant heterogeneity regarding PRP preparation methods. The variability is largely attributable to the use of different devices developed by the industry. These systems, involving minimal manipulation, are designed to simplify the production of platelet concentrate, particularly for users who may lack the manual expertise of transfusion medicine specialists in handling blood products.

Several important issues remain to be clarified:

1. identification of patient-related predictors of clinical outcomes. For example, in the case of diabetic foot ulcers, outcome predictors should consider the relative contribution of ischemic, neuropathic, and infectious components – the three main pathogenic factors involved in lesion development and persistence. Regarding ulcer severity as a prognostic indicator, it would be important to confirm that Wagner grade 1 and 2 lesions show the best therapeutic response. For venous ulcers, it would be necessary to assess blood count parameters and the role of deep or superficial venous insufficiency in lesion development and maintenance;
2. identification of outcome predictors related to the PRP product itself, such as the concentration of specific growth factors or other bioactive mediators;
3. comparison of PRP efficacy with other innovative therapeutic approaches, including advanced wound dressings, synthetic and biological scaffolds;
4. determination of optimal platelet amount, both per session and across the entire treatment cycle, as no definitive clinical data are currently available to establish the most effective total platelet load;
5. clarification of the preferred mode of administration – injection versus topical application;
6. identification of the optimal interval between treatment sessions (both injectable and topical), and the total number of sessions required based on specific pathologies;
7. validation through robust clinical trials of PRP use in less-established applications such as mucositis, vasculitis, ED, PD, stress urinary incontinence, and fertility disorders.

Recommendations from the SIMCRI Expert Consensus Group

In line with previous recommendations and based on the clinical and laboratory experience of the working group members, it has been deemed appropriate to define shared criteria for clinical assessment and PRP preparation procedures. The dual objective is to enhance the therapeutic efficiency of PRP according to the underlying pathology and to promote personalized treatment strategies.

Inspired by the TIMERS framework used in wound care, a dedicated checklist protocol – TAMIS (Tissue, Area, Method, Inflammation/infection, Scheduling) – is proposed to support the clinical use of PRP. The TAMIS protocol guides clinicians in evaluating the following parameters:

- Tissue: identify as bony (e.g., orthopaedic, dental) or soft (e.g., skin, mucosa, muscle);
- Area: define the surface area to be treated;
- Method: choose application mode – e.g., topical gel, injectable (intra-tissue, intra-articular), aerosol, mucosal/ocular;
- Inflammation/infection: determine if adjunct medication is needed (simultaneous or sequential);
- Scheduling: define single dose *vs* cycle, number of sessions, intersession interval, and follow-up maintenance.

The TAMIS parameters serve both as a practical tool for guiding clinical decision-making and as a standardized framework for comparing outcomes across scientific studies.

Patient assessment must comply with national regulations concerning the preparation and use of autologous blood components (MoH Decree, 2 November 2015; updated 1 August 2019). For instance, local health authorities in Italy (e.g., USL Toscana, Emilia-Romagna, Veneto, Lazio) have established eligibility criteria, including:

- platelet count >100×10³/µL in prior 3 months (Toscana, EmiliaRomagna, Veneto);
- exclusion if platelet count <120×10³/µL (Lazio);
- must avoid platelet-interfering medications 5 days before sampling (EmiliaRomagna, Lazio);
- exclude poorly controlled diabetes, active chemotherapy, coagulopathies, immunodeficiencies, immunomodulatory treatment (Lazio).

It should be noticed that the total number of blood components remains constant in a closed system, regardless of processing. Therefore, while plasma volume may be reduced during PRP preparation, the absolute number of platelets remains dependent on the initial volume of whole blood drawn.

To standardize platelet evaluation, the efficiency of recovery should be calculated for each device:

$$Recovery\ efficiency\ \% = \frac{Vol.PRP \times PLT_{PRP}}{Vol.Blood \times PLT_{blood}}$$

An efficiency of 50% (0.5) is generally considered acceptable.

To obtain a desired quantity of platelets (Desired Platelet Quantity, DPQ), the following equation can be applied:

$$Volume\ to\ draw = \frac{DPQ}{PLT_{blood} \times Recovery\ efficiency}$$

Example:
To obtain 3.2×10⁹ platelets in a patient with 300×10³ platelets/µL (0.3×10⁹/mL) and assuming a 60% efficiency, the required blood volume is:

$$Volume\ to\ draw = \frac{3.2}{0.3 \times 0.6} = 17.77\ mL$$

This example, along with others, is outlined in *Table 1*.

Treatment area, application site, and method (topical *vs* injectable) should be considered when determining the desired platelet load, in accordance with the TAMIS protocol. For instance, 25 cm² HA sheets soaked with

Table 1
Practical example of calculation for whole blood volume to be drawn

Patient PLT count (PLT/µL)	Recovery efficiency (%)	Target PLT quantity ($\times 10^9$)	Required blood volume (mL)
150,000	60	3.2	35
200,000	70	3.2	18
300,000	60	3.2	18

1.8 mL of PRP have demonstrated therapeutic efficacy in ulcer treatment [8].

It should be noted, however that a desirable platelet content has to reach a concentration factor of 4-5x, in order to minimize the volumes, particularly for injective procedures in musculoskeletal disorders.

When using devices that employ thixotropic gel, attention must be paid to the gravitational weight and composition of the gel, which may influence the final PRP volume and concentration [97].

It is essential to promote a culture of regenerative medicine that encourages researchers to report all parameters potentially influencing treatment outcomes. Scientific journals should sensitize their peer reviewers to demand comprehensive reporting of platelet concentrate preparation protocols. Researchers must be encouraged to conduct randomized, multicentre, double-blinded trials capable of generating robust scientific evidence.

To this end, scientific publications should ideally include the following information:

1. device used, centrifugation time and temperature, and centrifugal force (g);
2. platelet concentration in the patient's baseline whole blood;
3. platelet concentration in the final product;
4. volume administered, including:
   – injectable form: volume injected in peri- or intra-lesional locations;
   – topical form (dressing): volume applied topically;
5. type of dressing used; for topical application, details of any secondary dressing;
6. additional devices applied (e.g., orthoses, low/high-stiffness bandaging, compression stockings with specified compression level).

Below are reported specific recommendations for PRP use in selected pathologies (schematically illustrated in *Figure 1*):

- the use of PRP for the treatment of diabetic foot ulcers is a safe procedure. For non-primarily ischemic diabetic ulcers without active infection and without bone or tendon exposure (Wagner grades 1-2), PRP treatment is recommended with a relatively high level of evidence. For more severe non-primarily ischemic diabetic ulcers (Wagner grades 3-4), the literature is scarce; however, the available evidence suggests potential efficacy of the treatment, so PRP use is not discouraged;
- the correct approach to treating venous ulcers is based on hemodynamic correction of venous insufficiency, both deep and superficial, typically via elastic compression (which applies counterpressure against transmural pressure) or varicose vein treatments in various forms. If the lesion fails to respond satisfactorily to these treatments, regenerative medicine techniques such as PRP become relevant. The use of PRP for venous ulcer treatment is a safe procedure. The predominant literature supports topical (dressing) use on lesions, while data on injectable treatment are currently too limited to establish comparative efficacy. Therefore, topical PRP use is recommended for venous ulcers, but injectable intra- or peri-lesional PRP is not contraindicated;
- a large body of scientific literature, supported by international consensus, currently supports PRP as a consolidated therapeutic option for various musculoskeletal conditions. Comparisons with other injectable therapies (corticosteroids and HA) do not disadvantage PRP. Its use is therefore recommended, particularly for mild to moderate osteoarthritis and various tendinopathies;

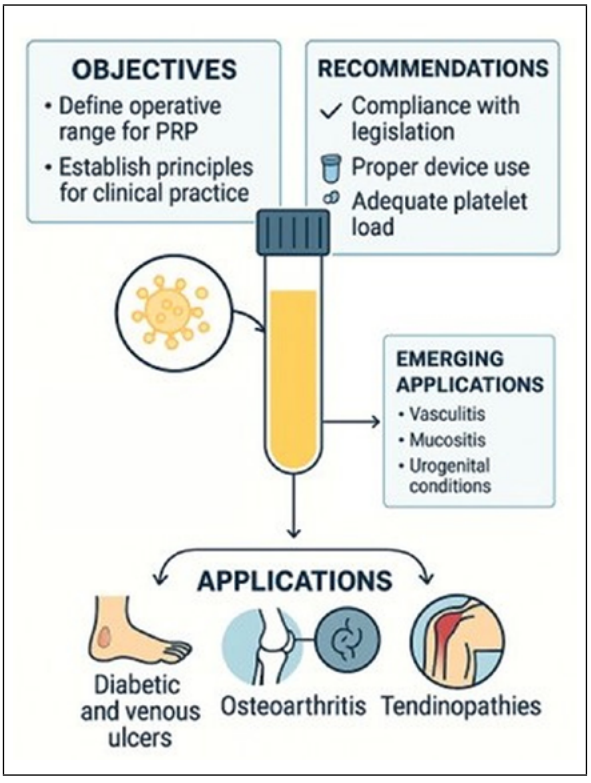

Figure 1
Platelet-rich plasma (PRP) in regenerative medicine. Schematic representation of objectives, recommendations and clinical applications. Image design was created with Artificial Intelligence support (ChatGPT, OpenAI).

- few studies in the scientific literature describe evidence of PRP use in problematic conditions such as various mucositis, all reporting satisfactory results. However, randomized controlled trials are lacking. Given the nature of lesions and the lack of definitive alternative therapies, PRP use is not discouraged if patient conditions permit;
- regarding andrological disorders, PRP use for ED and PD appears safe. It is not discouraged, especially for vasculogenic ED unresponsive to PDE5 inhibitors. Evidence for PD treatment is less clear; injection site, number of injections, and intervals are yet to be standardized. PRP use is not discouraged for stabilized PD without pain and/or ED;
- for some gynaecological disorders (chronic pelvic pain, stress urinary incontinence, ovarian insufficiency, endometrial pathologies, unsuccessful assisted reproduction or recurrent miscarriages), although randomized controlled trials are absent, evidence does not discourage PRP use.

CONCLUSIONS

Ethical considerations

The use of PRP within the context of regenerative medicine raises important ethical questions that require thorough reflection. First and foremost, it is essential to ensure that this therapy is applied in full respect of the principles of autonomy and informed consent, guaranteeing that patients receive clear and comprehensible information about the benefits, risks, and available alternatives. Furthermore, the standardization of procedures and the quality of PRP must be strictly monitored to avoid disparities in treatment and to ensure equity in access to care. Transparency in communicating clinical results and trial outcomes is also crucial, promoting rigorous research free from conflicts of interest and placing patient well-being at the center. Finally, the continuous evaluation of PRP efficacy and safety must be accompanied by ethical attention in clinical application, always considering the cost-benefit ratio and the appropriateness of therapeutic indications.

Limitations and areas for future research

This document, aimed at establishing a consensus on PRP use, originates from a critical review of recent scientific literature and the experience of the participants in the EC. It is a concise text that does not solve all the issues in an ever-expanding field and, therefore, has several limitations. The main limitation concerns the restricted scope of medical areas considered, since PRP is also widely used in dentistry, aesthetic medicine, and dermatology. Moreover, PRP can be combined with other regenerative medicine tools, such as natural or synthetic scaffolds, ozone therapy, photobiomodulation, stem cells, and leukocytes. These are all fundamental aspects requiring further investigation and may be addressed in future studies. The evidence and recommendations presented in this EC may be strengthened by future research based on collaborative and multicentre studies in the field of platelet-rich therapies.

Noteworthy, the implementation of SoHo EU regulation 2024/1938 and the adoption of good clinical practice will significantly impact the field of blood components for non-transfusion use, including PRP.

Acknowledgments

SIMCRI (Società Italiana di Medicina e Chirurgia Rigenerativa Polispecialistica) Expert Consensus Group members served as collaborators and approved the final version of the paper: Alberto Alexandre, Bruno Amato, Andrea Ascoli Marchetti, Antonio Aversa, Alessio Borean, Velia Bruno, Gaetano Caloprisco, Eugenio Caradonna, Francesco Casabona, Valter Cassutti, Rocco Colasuonno, Stefano Cristofori, Marina D' Alagni, Massimo Danese, Giovanni D'Avola, Valentina Del Greco, Marcello Hortencio de Medeiros, Vittoria D'Esposito, Vincenzo Di Donna, Vincenza Dolo, Atanassios Dovas, Michele Angelo Farina, Stefano Fiorentino, Pietro Formisano, Gianfranco Francioni, Ilaria Giusti, Alfonso Maria Irollo, Marco Liccardo, Giorgio Lorenzon, Giulio Maccauro, Rosario Mancusi, Francesca Masiello, Laura Mazzucco, Rosario Miranda, Saverio Misso, Ennio Montonati, Eugenio Peres, Paolo Piccolino, Simonetta Pupella, Angela Rainaldi, Donato Rosa, Anna Rughetti, Raoul Saggini, Lanfranco Scaramuzzino, Carlo Setacci, Maria Alba Stigliano, Massimo Tatafiore, Fabrizia Toscanella, Diletta Trojan.

The SIMCRI Expert Consensus Group wishes to thank Istituto Superiore di Sanità (ISS) and the Centro Nazionale Sangue (CNS) for the continuous support.

Conflict of interest statement

The Authors declare that there are no conflicts of interest.

Received on 3 October 2025.
Accepted on 17 November 2025.

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