CASE REPORT

Platelet, fibrin and leukocyte- rich clot (PFLRC) clot for diabetic foot ulcer healing - Cases report

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ABSTRACT

Diabetic foot ulcers (DFUs) are common and serious complications of diabetes, associated with a high risk of infection, amputation, and reduced quality of life. Conventional therapies, such as biocompatible dressings, have limited regenerative capacity and are costly, especially in developing countries. Orthobiological agents such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in gel form have shown potential for healing, but their preparation is complex. The study presents the efficacy of a new regenerative therapy protocol for diabetic foot using a low-cost, easily obtainable autologous three-dimensional orthobiological agent or clot rich in rplatelets, fibrin and leukocytes (PFLRC). Three clinical cases of patients with DPF treated with four sessions of PFLRC are reported. Complete closure of the lesions was observed, with no recurrence for at least three months. Preliminary results suggest that RF-LR could be a safe, effective, and affordable alternative to conventional treatments and more complex orthobiological therapies. However, randomised controlled clinical trials are needed to validate its efficacy and establish its application in standardised therapeutic protocols. (www.actabiomedica.it)

Key words: fibrin rich in platelets, foot ulcer, diabetic foot, therapy biological

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Introduction

Diabetic foot syndrome is a chronic complication of diabetes, occurring in 25% of cases of diabetes mellitus, and 85% leading to amputation (1). 70% of diabetic foot ulcers (DFU) remain open after 20 weeks of treatment and their prognosis is seriously affected by the presence of ischemia or infection (2). A systematic review concludes that every 30 seconds, a lower limb is amputated due to diabetes, and the average annual cost of the diabetic foot is $8,659 per patient (3). The pathophysiology of diabetic foot ulcers is caused by the triad of peripheral neuropathy, trauma with secondary infection and occlusive arterial disease that causes opening of the skin causing infections (4,5). The infection of the foot ulcer manifests itself as superficial cellulitis to septic shock (6). Occlusive arterial disease is related to atherosclerosis, which causes hypoperfusion of distal tissues and less regenerative capacity in the face of an ulcerous process (7). Ulcer healing is a dynamic and complex process characterized by physiological processes such as hemostasis, inflammation, proliferation and remodeling (8). Diabetic ulcers are those that do not heal after 12 weeks due to an increase in inflammation and a deficit in dermal and epithelial remodeling caused by alterations in neutrophils, macrophages, fibroblasts and colonizing bacteria (9). Treatment of diabetic ulcers is typically based on pain relief, debridement, infection management, and topical dressings (10). Available adjuvant therapies include local negative pressure, hyperbaric oxygen therapy, bioengineered skin substitutes, platelet-derived growth factors (PDGF), PRP, stem cell therapies, extracorporeal shock waves, wireless microcurrent, and PRF (11). These therapies may have some limitations: high costs, required staff training, and infrastructure (12). PRP are blood derivatives obtained by centrifugation without the use of anticoagulants, which allows for faster healing. This is a promising, safe, and probably better option than platelet-rich plasma; its varieties depend on centrifugation, tube technology, and the addition of other components (13,14). A systematic review has concluded that PRF reduces ulcer healing time and increases wound healing rate in 7 studies published from 2007 to 2019 (15). Considering the need for an accessible, low-cost, safe biological product capable of promoting tissue regeneration, the three-dimensional orthobiological PFLRC offers simple preparation and less technological dependence, making it a valid and innovative therapeutic option. The general objective of this article is to present three cases of patients with non-infected diabetic foot ulcers who were treated with a new three-dimensional orthobiologic, PFLRC.

Case report

Three patients with difficult-to-heal diabetic foot ulcers (DFUs) were evaluated, treated between November 2023 and September 2024 in the outpatient clinic of the Bellavista Secondary Hospital in Peru. Two patients were women and one was men, ranging in age from 50 to 67 years (mean: 59 years). All had type 2 diabetes mellitus diagnosed 10 to 15 years ago, and each had a single ulcerous lesion. 2 according to the Meggitt -Wagner classification, with progressive evolution towards exudative lesions with necrotic edges, and with surgical indication for distal amputation by other centers. After specialized evaluation, treatment was proposed with a three-dimensional autologous orthobiological agent rich in fibrin, platelets, leukocytes and erythrocytes, called PFLRC, characterized by its low cost and simple preparation. The patients and their families, not agreeing with the amputation indicated in private centers, opted to accept the proposed regenerative therapy with the described clot, as an alternative for the healing of their wounds and injuries. It is worth mentioning that each patient was informed that the therapy would be autologous and that there would be no risk of adverse reaction to the graft. All patients gave their informed consent prior to the procedure. In each case, the wounds were antisepticized with corhexidine and saline solution. The wounds were then carefully debrided and excised with a scalpel and scissors on an outpatient basis. The wounds were thoroughly washed with saline solution, followed by conventional planimetry measurements using a millimeter ruler and temporary gauze coverage. The alternative orthobiological PFLRC was prepared by collecting peripheral blood from patients using a number 21 x 1.5 inch vacuum extraction needle into yellow tubes containing SST separator gel (approximately 1

yellow tube per centimeter of lesion width), the blood was then mixed by inversion 8 to 10 times and the tubes were left to stand for 10 minutes. Two yellow tubes containing separator gel were used per patient. The clot was then centrifuged at 4,000 revolutions per minute (RPM) for 10 minutes (Boeco 880D centrifuge). The supernatant was then decanted, and the separating gel (aseptic and biocompatible) was removed with sterile forceps, and the sedimented clot was then extracted. Finally, the PFLRC was poured into a sterile kidney bag for application as a membrane orthobiological to cover the lesions (See Figures 1 and 2). Two PFLRC pads were applied to the wound bed to cover the affected area; it was then covered with 2% Mupirocin cream (Peruvian laboratory IQFARMA). Finally, the wound was covered with an adhesive dressing Tegaderm (American laboratory 3M) and bandaged. This procedure was repeated once a week for 4 weeks. Clinical progress was documented by photographic monitoring and periodic check-ups during and after treatment, with a follow-up period of six to twelve months.

Case 1

A 59-year-old woman with type 2 diabetes mellitus diagnosed 12 years earlier presented with a violaceous lesion and paresthesia on her left big toe, measuring 16 cm². She was diagnosed with grade 2 DFU. After four sessions of PFLRC, the wound closed completely. The wound remained stable at 12 months of follow-up, without requiring amputation (See Figure 3 for details).

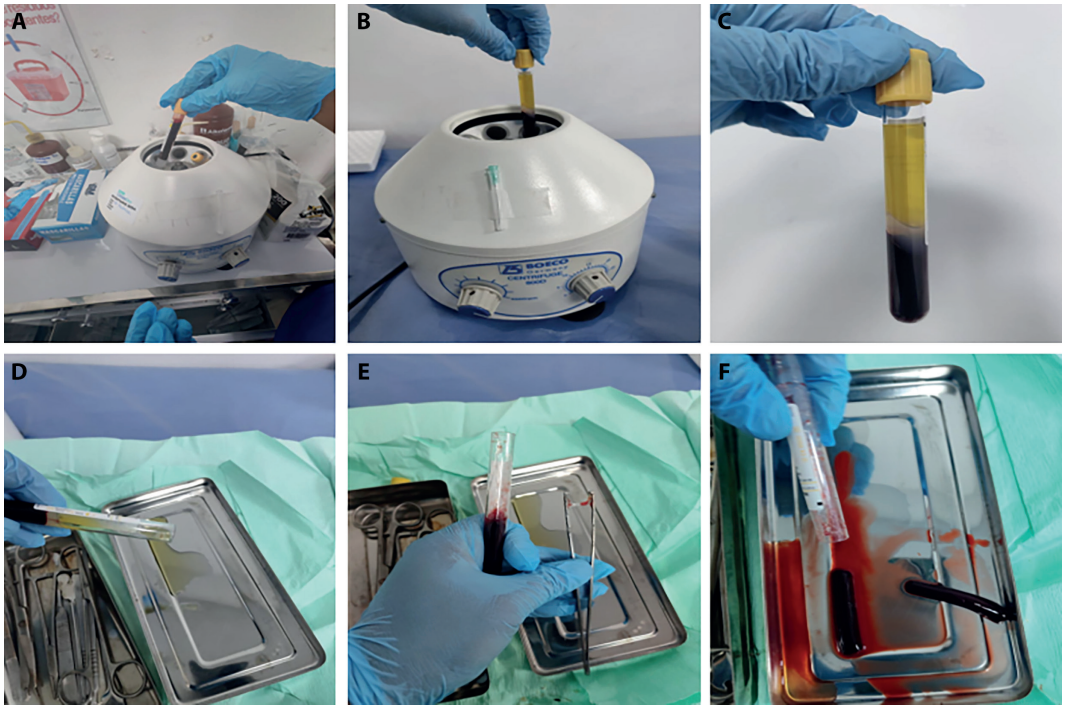

Figure 1. Steps in the preparation of CRPF-L. A) Centrifugation of the yellow tube SST with peripheral blood B) Removal of the SST tube after centrifugation. C) Obtaining 3 phases (globular package, separating gel and serum). D) Discarding the supernatant (serum). E) Removal of the separating gel. F) Obtaining PFLRC "Pedraza Regenerative Clot", ready for use.

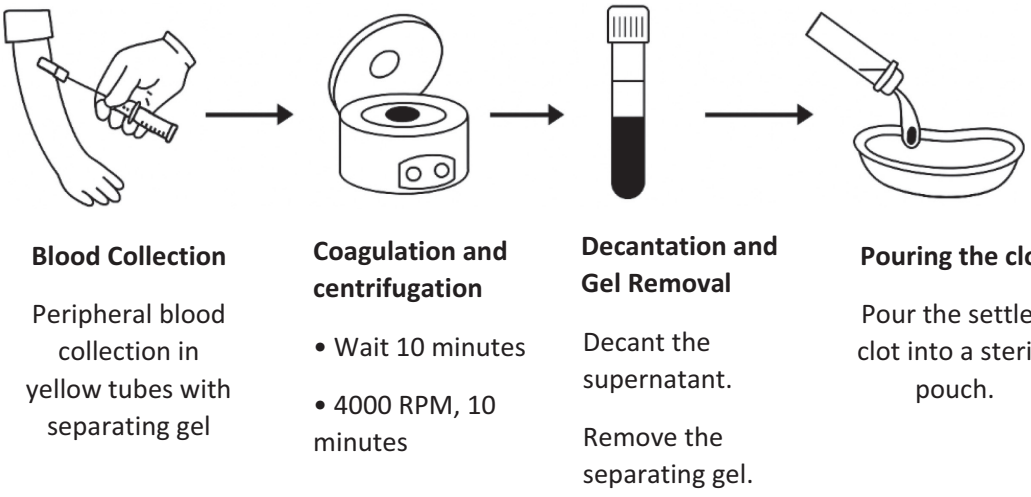

Figure 2. Summary diagram of the preparation of the Pedraza Regenerative Clot.

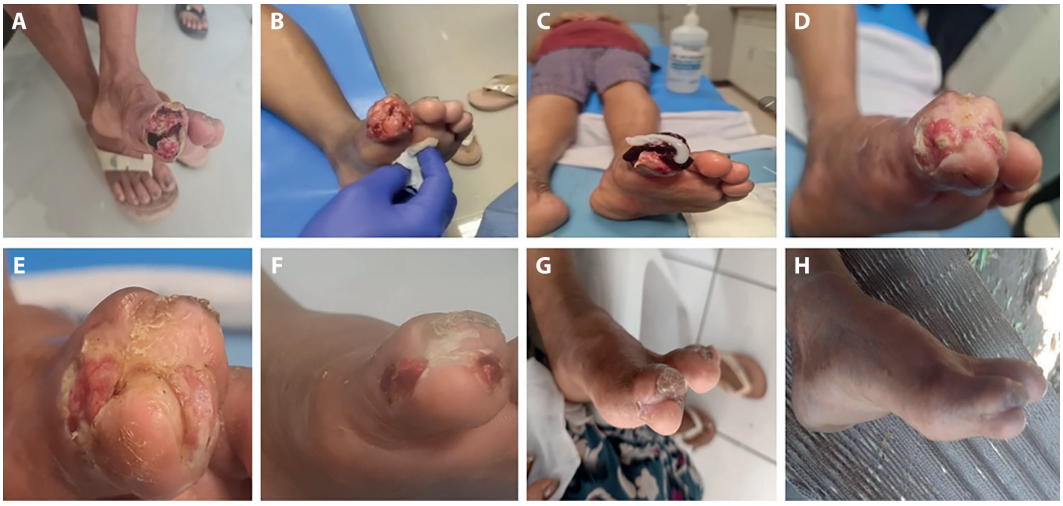

Figure 3. A) Ulcerative lesion on the first toe of the left foot. B) Cleaning, escharectomy, and debridement of debris. C) Application of Pedraza's orthobiological dressing. D) 1 week and second session. E) 2 weeks and 3rd session. F) 3 weeks and 4th session. G) 4th week with complete wound closure. H) 12 months later, the wound remains closed.

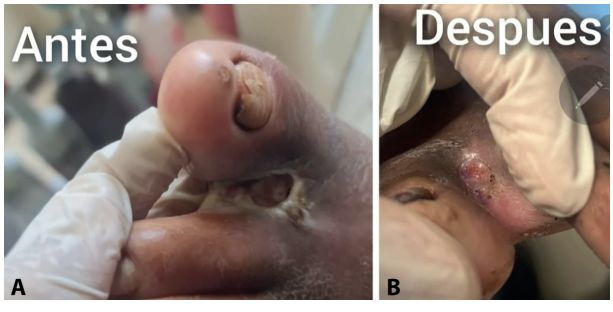

Figure 4. A) Ulcerative lesion between the 1st and 2nd toe of the left foot. B) 4 weeks after 4 sessions with Pedraza regenerative clot.

Case 2

A 50-year-old male, diabetic for the past 10 years, with a history of supracondylar amputation of the right lower limb. He presented with a 4 cm² ulcer on the big toe of his left foot. The same protocol described for PFLRC was applied, achieving complete closure in four weeks, with satisfactory outcome at 12 months (See Figure 4 for details).

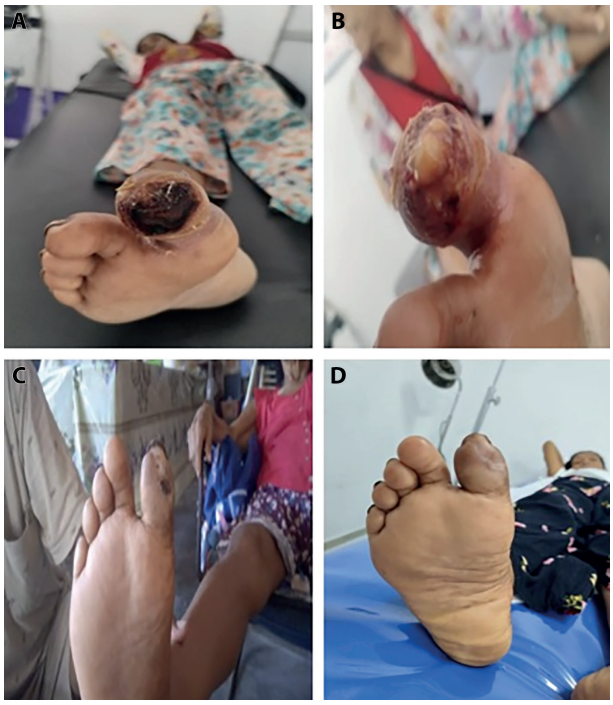

Figure 5. Monitoring the evolution of the wound in case 3. A) Ulcerative lesion on the first toe of the right foot. B) Cleaning, escharectomy, and debridement of debris. C) Four weeks after four sessions of PFLRC, complete wound closure is observed. D) Six months later, the wound remains closed.

Case 3

A 67-year-old woman with type 2 diabetes of 15 years' duration presented with a 4 cm2 necrotic lesion on her right big toe. Four sessions of PFLRC were administered, with complete closure at four weeks and clinical stability at six months (See Figure 5 for details).

Discussion

DFUs continue to be one of the most severe and costly complications of type II diabetes mellitus and in most cases lead to lower limb amputation, especially when there is no early approach. Their torpid evolution, the high rate of associated infections and the risk of amputations make their management still a challenge, especially in settings with limited resources. Despite advances in adjuvant therapies such as platelet concentrates (PRP, PRF, CGF), PRF derivatives (L-PRF, A-PRF, PRO-PRF), hydrogel dressings, biomaterials, Leucopatch systems, hematogels, and even enriched combination therapies (PRP, Growth Factors, MSc, exosomes, hyaluronic acid, negative pressure, photobiomodulation, double-joint hydrogels, among others); these are not always accessible, and some of them are expensive and complex to perform. Ulcers in patients had a median surface area of 4 to 16 cm2, were treated with one session per week, and had a complete healing time of 4 weeks, with no complications or recurrences reported. This result is similar to research in which platelet concentrates were used for the treatment of DFUs (16-21). Several studies have evaluated the efficacy of therapies based on PRP, PRF, CGF, etc.; in the treatment of DFUs. Two systematic reviews and meta-analyses (19,20) found that the use of autologous PRP significantly increased the complete healing rate and reduced the healing time compared to conventional treatment for DFUs. Also, in a randomized clinical trial, Hossam et al. (21) evaluated the use of PRP in 80 patients with non-ischemic DFUs. Their results showed that the PRP-treated group achieved a complete healing rate of 95% within 6 weeks, compared to 77.8% within 9 weeks in the conventional treatment group ($p < 0.001$). They also demonstrated that PRP gel resulted in a greater reduction in ulcer size and shorter healing time compared to conventional treatment. Furthermore, a significant reduction in infection and amputation rates was observed in the PRP group (21). On the other hand, a meta-analysis by Chen et al. (17) determined that PRF is safe and promising in promoting the healing of chronic, difficult-to-heal skin ulcers, compared with standard wound treatment. There are also studies that evaluated the effect of L-PRF, a PRF derivative, on DFU healing (16,22). In a retrospective study by Wang et al. (2024), 42 patients with diabetic foot ulcers were evaluated. The patients were treated with L-PRF for 5 weeks. Their results were that during the initial stage of treatment (1st and 2nd week), the healing rate was significantly better with L-PRF than with conventional treatment. In the later stages of treatment (3rd to 5th week), the overall healing rate was higher with L-PRF than with the traditional treatment method. They concluded that L -PRF can effectively promote the healing of

diabetic foot ulcers (16). Helal et al. (2024) found a similar result. They measured changes in wound area to evaluate the efficacy of L-PRF administration in the treatment of DFUs. For 6 weeks, 20 patients applied L-PRF topically; each patient was administered it once every five to seven days, either as an injectable or in the form of a membrane. As a result, they found that after 6 weeks, a significant decrease was observed in all three ulcer dimensions (length, width, and depth) and the wound surface area. They concluded that the use of L-PRF can reduce disease burden and greatly accelerate the healing of chronic diabetic foot ulcers. Furthermore, they considered it to be a rapid and affordable modality (22). On the other hand, it is worth mentioning a study by Yang et al. (2025) in which they performed a comparative analysis of the preparation methods, biological mechanisms, and clinical efficacy of three generations of platelet concentrates: PRP, PRF, and CGF (23). This study reveals that PRP, the first generation, provides abundant growth factors but depends on anticoagulants, which can hinder fibrin formation and tissue adhesion. Although PRP significantly accelerates DFU healing and reduces the risk of infection, it also has some limitations such as the use of additives, such as thrombin; its preparation is relatively complex and usually requires two centrifugation steps. Furthermore, the fibrin mesh structure of PRP is less developed than that of PRF or CGF, which reduces the duration of growth factor release. (23) PRF, the second generation, eliminates anticoagulants, forming a fibrin matrix that promotes the release of growth factors and improves cell migration. It is obtained by low-speed centrifugation without anticoagulants and is able to slowly release growth factors, promoting wound healing over a longer period. Its preparation is simple and safe. However, its healing efficacy may be lower than that of PRP due to its lower concentration of growth factors, and clinical studies investigating it remain limited (23). CGF employs continuous variable-speed centrifugation to achieve higher concentrations of growth factors and a denser fibrin matrix, thus accelerating tissue regeneration. It also exhibits slow-release properties comparable to PRF, allowing it to deliver pro-healing factors over an extended period, thus accelerating DFU healing. Furthermore, they concluded that the CGF preparation process is simpler and does not require the addition of anticoagulants, thereby reducing the complexity and potential associated risks. Their results demonstrated superior wound healing outcomes with CGF, including faster epithelialization and shorter healing time compared to PRP and PRF (23). Regarding the mechanism by which PRF acts in the healing of DFUs by releasing cytokines and growth factors involved in tissue regeneration, angiogenesis and inflammation. Thus achieving the reduction of inflammation, accelerating closure and relieving pain in diabetic ulcers. The main growth factors involved are PDGF, VEGF and TGF-β, which stimulate cell recruitment, extracellular matrix synthesis, angiogenesis and accelerate collagen production (24). In addition, fibrin plays a role as a three-dimensional matrix that facilitates cell migration towards the wound bed, while leukocytes contribute to modulating inflammation and controlling bacterial colonization. (16,17). In the present study, we applied a novel three-dimensional autologous orthobiological product, called the "Pedraza Regenerative Clot" (PFLRC), which is rich in platelets, fibrin, and leukocytes, in addition to red blood cells; its composition and structure could explain its remarkable clinical efficacy observed in the three cases reported in this study. Our study still includes a small number of clinical cases, but is similar to the study conducted by Saboia-Dantas et al. (18). Tissue regeneration matrix derived from FRP, called PRO-PRF (Progressive Platelet Rich Fibrin) in Giant Pro PRF membranes (GMPro) for the treatment of chronic wounds of diabetic etiology, with an average of weekly sessions of 2 to 4 weeks and wound closure at 12 weeks. However, the total cost of regenerative treatment with said orthobiological ranged from $ 200 to $ 800 (18). Other studies, such as that of Snyder et al. (2023), analyzed the cost-effectiveness of five advanced skin substitutes for the treatment of DFU. They concluded that 12 weeks of treatment were required to treat DFU and the total cost ranged from $1245 to $7647 (25). Our clot, PFLRC, is different from other regenerative matrices and concentrates platelet aggregation, due to its simple preparation, accessibility and

low cost. The variations made to the standard FRP technique have been the following: they do not require chemical activators or additional materials, in this case, yellow-capped SST tubes, a simple conventional centrifuge and the procedure under aseptic conditions are enough; it is also performed in less time. A fundamental advantage of PFLRC is its simplicity compared to FRP. This has allowed costs and time of implementation (approximately 20 minutes) to be significantly reduced, and the cost of our regenerative treatment for diabetic foot ulcers has a total cost of approximately 12 to 16 dollars (3 to 4 dollars per session), a low cost, simple and accessible compared to other regeneration matrices or dressings published by other authors (16-23,25-28). The limitations of our study were that peripheral vascular disease was not assessed in patients (29); the recommended glycemic control (29) was not performed, nor was the platelet count prior to regenerative therapy. Regarding its strengths, our protocol is easy to perform by trained personnel. Also, the clinical implications of using the "Pedraza Regenerative Clot" as a cost-effective alternative for low-income populations are highlighted, in addition to its easy preparation in an outpatient clinic. Because our study involved three cases, with no control group, these findings need to be validated through prospective, randomized studies with a larger number of patients.

Conclusions

Preliminary results from the use of the Pedraza Regenerative Clot (PFLRC) demonstrate high potential for regenerating diabetic foot ulcers, thus potentially reducing the need for amputations due to DFU. The total cost of our regenerative treatment for diabetic foot ulcers ranged from $12 to $16 ($3 to $4 per session), making it cost-effective, accessible, and readily available compared to other published regenerative matrices or dressings. The clinical results obtained in the three treated patients show that this autologous orthobiological product was able to induce complete wound closure in just four weekly sessions, with no adverse events and a favorable 12-month follow-up.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interests, patent/licensing, arrangement etc-) that might pose a conflict of interest in connection with the submitted article.

Ethical Approval: This case was reviewed and approved by the institutional research ethics committee of the Lambayeque ESSALUD-Peru service network, with resolution number 067-GRPL-ESSALUD-2025, dated November 21, 2025, in addition to having signed informed consent forms.

Financing: The procedure described was carried out with institutional resources. No external sponsorship or funding was received for this study.

Collaborations: The authors declare that they did not receive external collaboration for the completion of this study.

Patient Perspective: The patients and their families, not agreeing to the hospital's proposal for amputation or surgical wound cleansing, agreed to the use of "PFLRC" or " *Pedraza regenerative clot"* as an alternative to promote healing of their foot injuries. They were explained in detail that this was an autologous treatment, with no risk of rejection or adverse reactions associated with grafts.

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Authors' Contribution: JPLB contributed to the conception, design, and manuscript drafting; MLS, DRA, DRG, JRO, LBG Y STV were involved in data collection, analysis data interpretation, and critical. Revisions for important intellectual content. All authors reviewed and approved the final version of the manuscript.

Declaration on the Use of AI: The authors declare that no AI was used in the writing of this manuscript.

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