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Effect of homologous platelet rich fibrin matrix and injectable platelet rich fibrin on full thickness skin autograft healing in dogs

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Abstract

Autologous platelet-rich fibrin matrix PRF-m and injectable platelet-rich fibrin i-PRF are hemocomponents that have a crucial role in tissue healing and facilitate improved graft take since they are sources for different growth elements and cytokines. However, the homologous head of platelet derivatives is effective, safe, and unlike their autologous source. This study determined whether homologous PRF-m and i-PRF affect autologous total thickness skin graft survival and healing. Our experiment comprised 18 dogs from the local breed in which autologous grafts were performed and then divided into three groups, designated as control, autologous graft only without any treatment; PRF-m group, graft treated with homologous PRF-m and i-PRF group, graft treated with homologous i-PRP. Animals were followed macroscopically for 30 days after the operation. The histopathological and immunohistochemical assessment for tumor-necrosis factor-α TNF-α and vascular endothelial growth factor VEGF was accomplished on the 7th, 15th, and 30th days after the grafting operation. Results indicated that homologous PRF-m and i-PRF display potential benefits on the healing and acceptance of graft during all stages of the tissue healing process, characterized by 100% uptake of the graft, the cosmetic appearance of the graft with a color similar to recipient skin, enhancement of collagen formation, re-epithelization and better level of TNF-α and VEGF comparison with the control group, which displayed a partial separation of graft. Also, the effect of PRF-m was better than i-PRF in accelerating and improving skin graft healing. In conclusion, the homologous PRF-m and i-PRF were effective in total thickness skin autograft healing.

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Introduction

A full-thickness Skin graft is a piece of skin, including the dermis and epidermis, entirely removed from the donor site and transported to a recipient site. It has been used for over a century to treat defects that cannot be reconstructed by direct apposition or skin flaps. It indicates when there has been a significant loss of skin from trauma or other reasons, such as burns and tumor removal (1,2). Skin grafts provide a suitable option for skin wound cover and provide the supporting bed for earlier tissue regeneration. The transplanted skin also creates a barrier for outside microbes and waste products (1,3). Generally, the best choice for grafting is autografts because they are non-immunogenic, and the rate of take is affected by various factors, including contact between the graft and recipient wound bed (4). To improve the graft take, the graft must be sutured perfectly with the wound bed to ensure stability and nutrition from the wound edges (5). Failure of tissue covering skin wounds may cause re-grafting operation and hence expand the length of hospital remains, increasing the time of reconstructive surgery and medical expenses. Therefore, several approved medications have been used to improve skin graft acceptance, like lowering hematoma formation, advocating

instantaneous skin graft adhesion, increasing and enhancing vascularization, and hindering infection. (5,6). Recently, medical therapies have emerged as a new approach, resulting in the development of many biological and chemical active factors for improving survival and acceptance of grafts for the reconstruction of different tissues in the body (6-8). One such natural product is platelet concentrates or derivatives like platelet-rich plasma (PRP) and PRF, which have been utilized in dermatology and plastic reconstructive surgery as a regenerative tool because they are easily obtainable, capable of releasing growth factors, immune system mediators, enzymes, and bioactive compounds. Also, it has antimicrobial properties, promotes wound healing, and improves scar tissue outcomes (9,10). Generally, it has been confirmed that activated fibrin gel from these compounds plays a vital role in the adherence of grafts and dressings from biological sources to wound beds. In addition to that, fibrin gel presence has been connected with a high rate of graft success, inducing a vascularized matrix for skin grafting, stimulating dermal regeneration and re-epithelialization (11,12). In earlier periods, local therapy by platelet-rich concentrates was accomplished with the restricted use of products from autologous sources because of ethical and legal considerations correlated to the hazard of homogeneous hemocomponents (13). Presently, autologous blood product applications are stressed by controversial outcomes due to highly variable platelet-rich derivatives quality among patients, being influenced by comorbidities, modality of preparation, and age. For these reasons, an allogeneic platelet-rich derivative was used as an alternative source for autogenous products. It offers novel therapeutic options from well-characterized donors for patients who cannot fit for blood donation, such as patients diseased with septicemia or blood disorders, infants and aging patients, or emergency patients who could be subjected to additional health burdens if we withdraw blood from it as in emergency orthopedic surgery (14-16). Soares *et al*., (17) reported that xenologous sources of PRF stimulated the formation of vascularized granulation tissue and significantly prompted the epithelization in lesions with soft tissue deficit. Also, neither immune rejection nor infection signs were observed. Moreover, PRF therapy was shown to be a biological, economical treatment, accelerating the wound-repairing process (17). Of note, a study conducted by Abegão *et al*., (18) comparing heterologous and homologous PRP gel on skin wound healing in animals found that both therapies produced similar outcomes in skin healing and regeneration (19). Homologous source of platelet rich fibrin has been used for skin wounds and resulted in acceleration of epithelization and better scar formation (18,19).

However, according to recent evidence, there are few reports on using homologous PRF for skin wounds. Also, no study was reported on the homologous use of these products on skin graft healing. We hypothesize that homologous PRF can aid in the recovery of skin-grafted wounds. Therefore, the overall goal of this research was to clarify the influences of homologous PRF, either injectable or matrix, as an assistant to improving total thickness skin autograft takes.

Materials and methods

Homologous i-PRF and PRF-m Preparation

For i-PRF preparation, 10 ml of whole donor blood was collected without the addition of anticoagulant and centrifuged at room temperature for 3 min, at 700 rpm. The blood separates into an upper fluid coat, which was collected as i-PRF (Figure 1), (20). Homologous PRF-m was prepared through a procedure as clarified previously (8,21). 10 ml of donor blood was collected and centrifuged at 3000 rpm for 10 min. The resultant product in the tube consisted of the following three layers: PRF clot in the middle layer between the topmost layer consisting of platelet-poor plasma and red blood cells (RBC) layer at the lowermost of the tube. The fibrin clot in the middle layer is withdrawn from the line; the attached RBC is then scraped off and discarded. The fibrin layer was placed on a sterile piece of gauze to squeeze it to obtain a PRF matrix (Figure 1).

Figure 1: (A): Describe the withdrawal of PRF-m from the tube after preparation. (B): describe the withdrawal of i-PRF from the line by syringe after practice.

Animals

Eighteen local breed dogs from both sexes weighing approximately 15-25 kg were used. The animals were housed in cages individually. All animals were allowed to adapt for two weeks before the beginning of the experiment. The dogs were divided into three groups randomly: control, PRF-m, and i-PRF. The Animal Care and the Ethics Committee of the University of Mosul, Iraq, approved all procedures for the animal UM.VET. 2022.016.

Surgical procedure

The animal was anesthetized by administration of 10 mg /kg of ketamine and 3 mg /kg of xylazine intramuscularly. The paravertebral area's left and right sides were prepared under aseptic conditions. Approximately 2*3 cm^2 total

thickness skin grafts were harvested from both sites. After harvesting, extracted grafts were replanted at their original situation. The skin grafts were sutured by a simple interrupted suture technique using silk suture material No.1. After that, the animal was divided into three groups (6 / each). In the control group, the grafted site was left without any treatment. In the PRF-m group, the fibrin matrix was introduced beneath the graft before suturing the two last stitches, and then the suture technique was completed (Figure 2). While in the i-PRF group, i-PRF was injected beneath the skin graft (Figure 2). A non-adhesive pressure bandage covered the grafts in all animals for five days. All dogs received an I/M injection of penicillin-streptomycin for five days postoperatively.

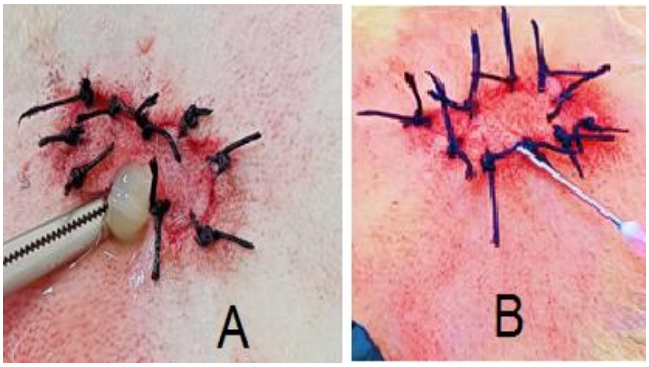

Figure 2: (A): Explain the insertion of PRF-m under the skin graft. (B): Show subcutaneous i-PRF injections.

Macroscopic examination

Macroscopic examination was made daily to monitor the autograft take, hematoma, infection, edema, and scar tissue formation. Survival skin graft rate was also evaluated at the 7^{th}, 15^{th}, and 30^{th} macroscopically via the estimation of color changes for the skin graft.

Histological preparations

The skin grafts were assessed histopathologically at 7, 15, and 30 days after surgery. The skin samples were enucleated and then fixed in the 10% neutral buffered formalin until a histological preparation was done. Following the routine procedures, 5 mm thick paraffin slices of each tissue were sectioned and stained with hematoxylin and eosin. Using a light microscope, investigate the pathological changes, then photograph by a microscope camera (USB 2.0 digital image camera (Omax ToupView 9.0-Megapexil China).

Immunohistochemistry

Paraffin-embedded skin sections were deparaffinized on charged slides, dehydrated by graded alcohols, and washed in PBS. Incubation of the slides in the 0.3% hydrogen peroxide for 30 minutes was done to block endogenous peroxidase. Then, it is covered with a blocking solution for 1 hour. Then, the slides were overnight incubated at four °C with primary antibodies. The primary antibody was a Rabbit polyclonal VEGF Ab-3 (dilution 1:200 clone JH121, NeoMarkers) and TNF-α Rabbit Polyclonal (dilution 1:100 Elabscience). The secondary antibodies were anti-goat, anti-rabbit, and Biotinylated anti-mouse immunoglobulins (LSAB Kit; Dako) diluted in PBS for 30 minutes. The negative control sections were incubated in PBS without primary antibodies. Then, the slides were set in the conjugation of streptavidin with horseradish peroxidase in the buffer of Tris-HCl consisting of 0.015% sodium azide for 30 minutes (LSAB Kit; Dako). Slides were treated with immunolabeling, 3,3′-diaminobenzidine DAB chromogenic substrate, and were counterstained with hematoxylin (22).

Statistical analysis

Collected data was expressed as the mean ± SE. for skin graft survival by one-way ANOVA with the Dunchun used. The chi-square test was used to differentiate between the groups for skin graft, take, and Weeping occurrence of the graft. Statistical significance was considered at $P<0.05$. The data was illustrated as a graph by using the Microsoft Excel application.

Results

Macroscopic assessment

Macroscopic results showed that the percentage of partial loss of skin graft was higher in the control group 25%, while in the treatment groups G2 and G3, the percentage of graft uptake was 100% at the first seven days post grafting (Figure 3). Skin graft survival was significantly higher in groups treated with PRF-m and i-PRF than in the control group on the 7^{th} days 83.3.0, 66.6, and 50.0%, respectively, 15^{th} days 87.5, 75.0 and 62.5% respectively, and 30^{th} days 100.0, 93.7 and 75.0% respectively. On the other hand, the PRF-m treatment group showed a greater survival rate than the i-PRF group, but the difference was not significant at all periods (Figure 4).

During the first 7^{th} days after the operation, in the control group, the hematoma formation was observed in 2(16.6%) cases, and edema was seen in 5 (41.6%) cases for 3-7 days. Neither hematoma formation nor edema formation was observed in patients treated with PRF-m and i-PRF, except 2 (16.6%) cases in the group treated with i-PRF showed the presence of edema in the first three days after the operation, and one point in the group treated with PRF at the first day after treatment. However, weeping in skin grafts was more prominent in the control group than in other groups, especially at the 7^{th} and 15^{th} days post-grafting operation. The weeping event in group control was significantly higher than in 2^{nd} and 3^{rd} groups; it was noticed in 5 cases (41.6%). In the group treated with PRF-m, it was (0%) and in the group treated with i-PRF was observed in 2 (16.6%) cases

(Figure 5). The grafted area treated with either PRF-m or i-PRF showed a lower scar tissue formation after healing compared with the control group (Figure 6).

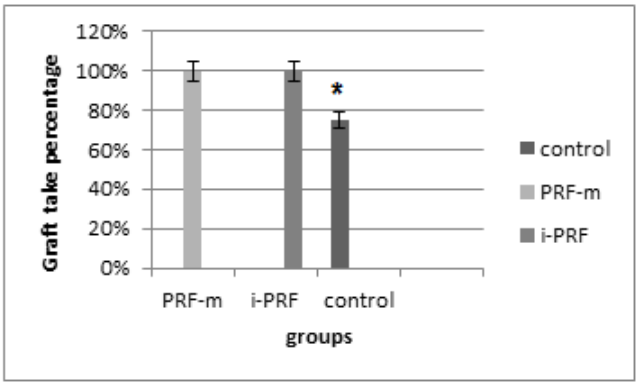

Figure 3: Graphic shows the skin graft takes percentage of all groups. *: significant at P<0.05.

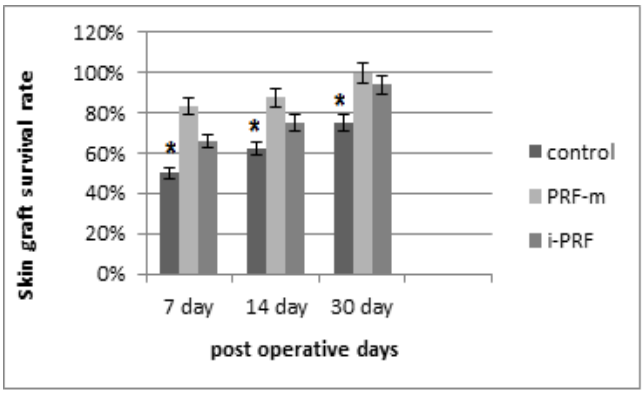

Figure 4: Graphic compares a percentage for skin graft survival between the three groups according to the treatment.. *: significant at P<0.05.

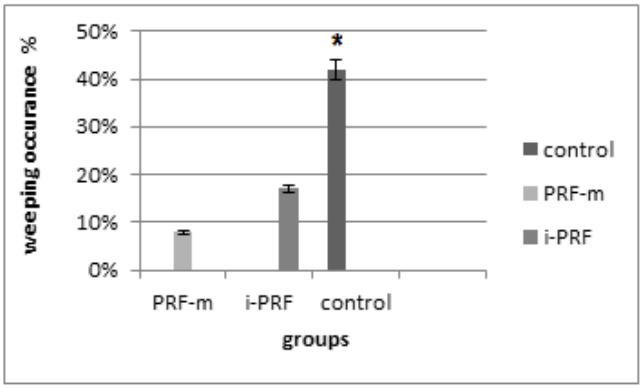

Figure 5: Graphic compares the percentage of skin graft weeping occurrence between the study groups. *: significant at P<0.05.

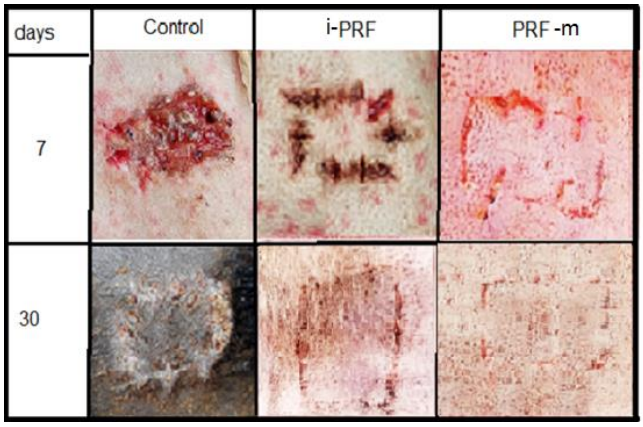

Figure 6: Macroscopic image for a grafted area in all treatment groups at 7 and 30 days post grafting. In the control group on the 7th day: Note the partial loss of graft comparison with other groups. Also, at 30 days, Note higher scar tissue formation in control groups than in the treatment groups. At 30 days: show the cosmetic appearance of graft in groups (PRF-m and i- PRF).

Histopathological assessment

The histopathological evaluations of the skin auto-graft of the control group at 7th days post grafting operation revealed the presence of a severe inflammatory response as an abscess with infiltration of exudative polymorphonuclear and mononuclear inflammatory cells, liquefactive necrosis, hyperkeratosis. The lesions persisted to 15 days post-grafting-operation as inflammatory exudative cells and hair follicle degeneration, with the granulation tissue including angiogenesis and the graft attached to adjacent skin with re-epithelialization. At 30 days post-grafting- operation, the result showed granulation tissue formation with angiogenesis and inflammation attached to adjacent skin with re-epithelialization and hyperkeratosis surrounded by epithelial cells as cell nests (Figure 7).

Generally, compared with control and i-PRF groups, the PRF-m group revealed the best results of skin auto-graft healing. The 7th-day post-operation showed a mild inflammatory response with infiltration of inflammatory exudative cells and the presence of granulation tissue with well angiogenesis re-epithelialization, proliferative hair follicles, and the graft attached to the adjacent skin tissue. At 15 days post-operation, there was no inflammatory response with few inflammatory cells, well-developed granulation tissue with high angiogenesis and re-epithelialization, and the graft attached very well to the adjacent skin tissue. The histopathological changes showed good improvement in skin graft healing at 30 days post grafting operation as the graft merged very well with the adjoining skin tissue with very well-developed granulation tissue with angiogenesis, complete re-epithelialization, proliferative apocrine glands without inflammation (Figure 8).

The histopathological result in i-PRF at the 7th-day post-grafting-operation showed infiltration of exudative inflammatory cells, granulation tissue with angiogenesis, re-epithelialization, and proliferative apocrine glands. A persistent inflammatory response with infiltration of the inflammatory cells was conducted at 15 days with well-developed granulation tissue and high angiogenesis. The graft attached very well to the adjacent skin tissue. Also, at 30 days post grafting operation, the auto-graft merges very well with the adjoining skin tissue with well-developed granulation tissue with many proliferative blood vessels, complete re-epithelialization, and without inflammation (Figure 9).

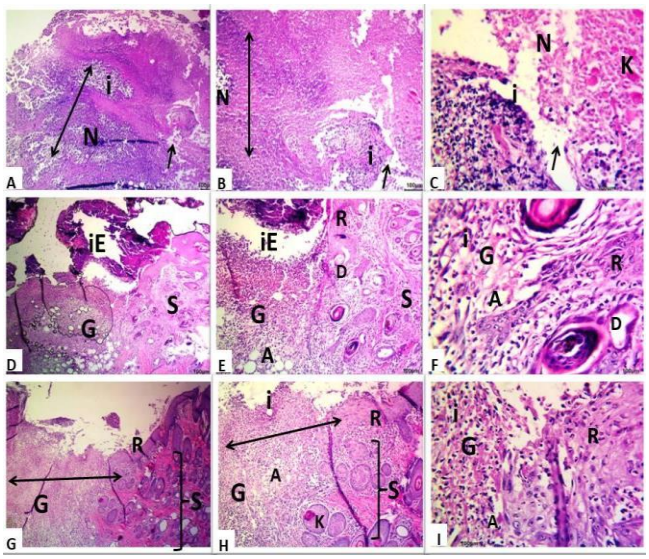

Figure 7: Photomicrographs of the dog skin auto-graft for the control group [A-C] at seven days, [D-F] at 15 days, and [G-I]: 30 days post-operation showing [A&B]: the site of grafting with a severe inflammatory response as abscess (↔), infiltration of inflammatory cells (i), liquefactive necrosis (N) and the graft separated from adjacent skin tissue during microtomy (→).[C]: Necrosis (N), infiltration of polymorph and mononuclear inflammatory cells (i), hyperkeratosis (K), and the graft separated from adjacent skin tissue (→). [D, E, F]: inflammatory exudate (iE), inflammatory cells (i), hair follicle degeneration (D), granulation tissue (G) with angiogenesis (A), and the graft attached to adjacent skin (S) with re-epithelialization (R). [G, H, I]: the auto-graft as granulation tissue (G) with angiogenesis (A) and inflammation (i) attached to adjacent skin (S) with re-epithelialization (R) and hyperkeratosis surrounding by epithelial cells as cell nests (K). H&E stain, [A, D, G: 40X], [B, E, H: 100X], [C, F, I: 400X].

Immunohistochemical evaluations of the VEGF expression in the cytoplasmic patterns in the dog skin auto-graft of the control group revealed a weak positive VEGF expression at whole periods 7, 15, and 30 days post-grafting-operation. The PRF-m group showed strong positive VEGF expressions at seven days and moderate presentations at 15 and 30 days. At the same time, the iPRF group revealed mild positive VEGF expressions at 7,15, and 30 days post-operation (Figure 10). The VEGF assessment result was clarified in table 1.

Immunohistochemical assessments of the TNF-α expressions in the cytoplasmic patterns in the dog skin auto-graft of the control group showed a strong positive TNF-α expression at 7th and 15th days with moderate face at 30 days, while the PRF-m group revealed a mild positive TNF-α expression at seven days, weak expression at 15 days and negative expression at 30 days. In contrast, the i-PRF group showed an intermediate expression at 7 and 15 days and negative presentation at 30 days post-operation (Figure 11). The TNF-α assessment result was clarified in table 2.

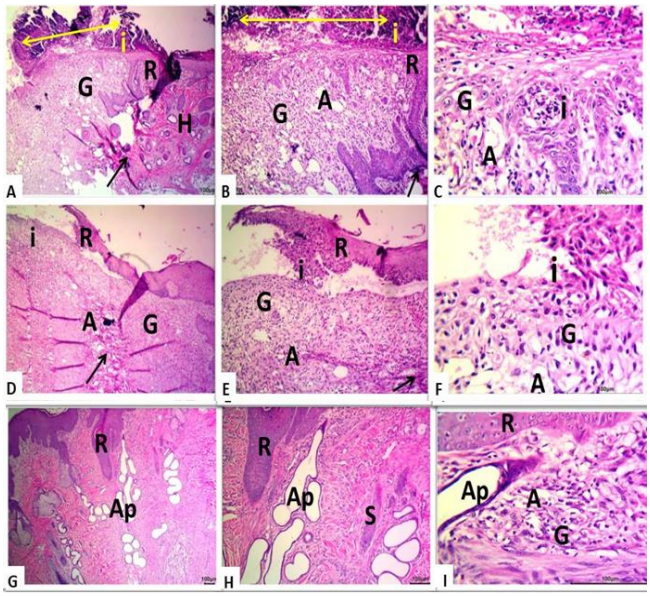

Figure 8: Photomicrographs of the dog skin auto-graft for the PRF-m treated group [A-C]: at seven days, [D-F]: 15 days and [G-I]: 30 days post-operation showing [A, B, C]: the site of grafting with a mild inflammatory response (↔), infiltration of inflammatory exudative cells (i), granulation tissue (G) with good angiogenesis (A) re-epithelialization (R), proliferative hair follicles (H) and the graft attached to the adjacent skin tissue (→). [D, E, F]: absence of inflammatory response with few inflammatory cells (i), well-developed granulation tissue (G) with high angiogenesis (A), well-epithelialization (R), and the graft attached very well to the adjacent skin tissue. [G, H, I]: the auto-graft merges very well with the adjoining skin tissue with very well-developed granulation tissue (G) with angiogenesis (A), complete re-epithelialization (R), proliferative apocrine glands (Ap) and without inflammation. H&E stain, [A, D, G: 40X], [B, E, H: 100X], [C, F, I: 400X].

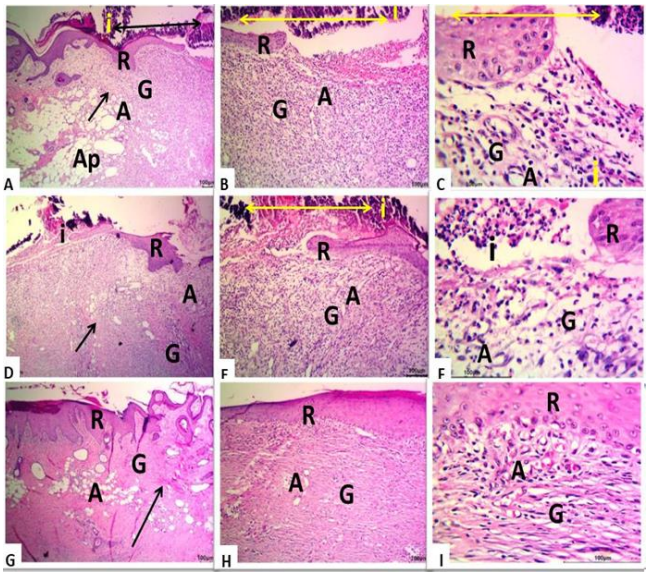

Figure 9: Photomicrographs of the dog skin auto-graft for the i-PRF treated group [A-C]: at seven days, [D-F]: 15 days and [G-I]: 30 days post-operation showing [A, B, C]: the site of grafting with a mild inflammatory response (↔), infiltration of inflammatory exudative cells (i), granulation tissue (G) with angiogenesis (A) re-epithelialization (R), proliferative apocrine glands (Ap) and the graft attached to the adjacent skin tissue (→). [D, E, F]: persisting inflammatory response with infiltration of the inflammatory cells (i), well-developed granulation tissue (G) with high angiogenesis (A), re-epithelialization (R), and the graft attached very well to the adjacent skin tissue. [G, H, I]: the auto-graft merges very well with the adjoining skin tissue with very well-developed granulation tissue (G) angiogenesis (many proliferative blood vessels) (A), complete re-epithelialization (R) and without inflammation. H&E stain, [A, D, G: 40X], [B, E, H: 100X], [C, F, I: 400X].

Table 1: The scores of immunohistochemical expression of the VEGF in the dog skin grafts groups

Groups	7 days	15 days	30 days
Control	1	1	1
PRF-m	3	2	2
if	2	2	2

Table 2: The scores of immunohistochemical expression of the TNFα in the dog skin grafts groups

Groups	7 days	15 days	30 days
Control	3	3	2
PRF-m	2	1	0
if	2	2	0

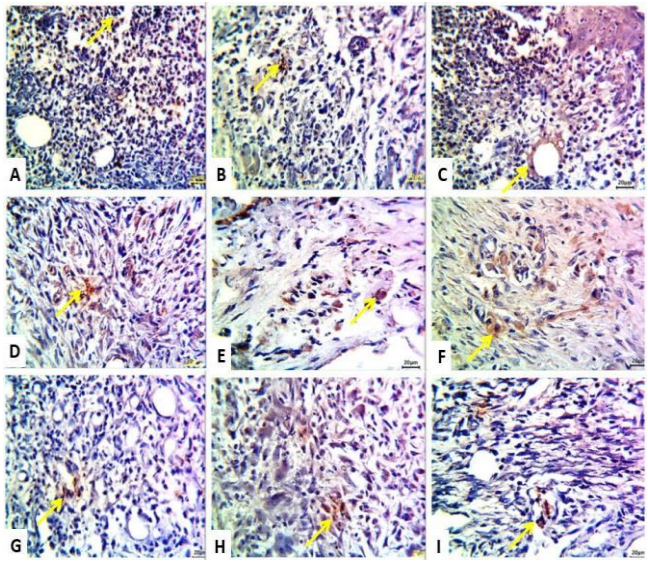

Figure 10: Immunohistochemical features of the VEGF expressions in the cytoplasmic patterns of the dog skin auto-graft for the control group [A, B, C]: weak positive VEGF expressions (→). PRF-m group [D, E, F]: strong positive VEGF expressions at 15 days and moderate presentations at 7 and 30 days. I-PRF group [G, H, I]: mild positive VEGF expressions at 7,15, and 30 days post-operation (Scale-bar=20µm, 400X).

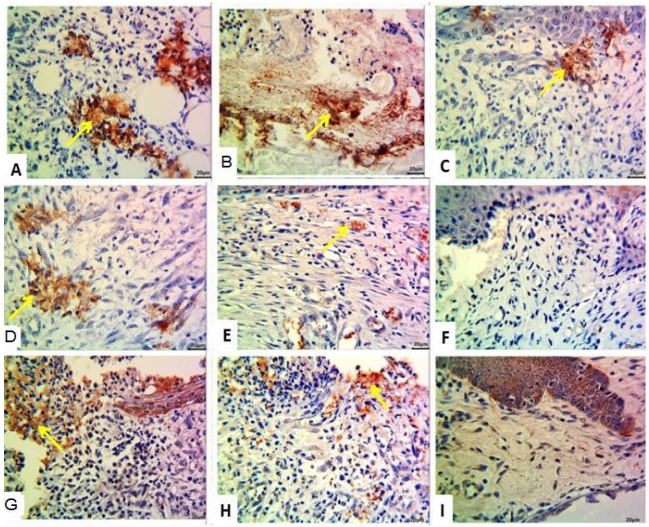

Figure 11: Immunohistochemical features of the TNF-α expressions in the cytoplasmic patterns of the dog skin auto-graft for the control group [A, B, C]: strong positive TNF-α expressions at 7 and 15 days and moderate expression at 30 days (→). PRF-m group [D, E, F]: mild positive TNF-α expressions at seven days, weak indications at 15 days, and negative words at 30 days. I-PRF group [G, H, I]: moderate and negative expression at 7 and 15 days and 30 days post-operation (Scale-bar=20µm, 400X).

Discussion

The extensive loss of skin tissue causes excessive functional loss and cosmetic problems and can result in severe, potentially life-threatening states that demand skin grafts (23). The healing process of skin graft includes a highly complicated interaction of biological and cellular processes that result in angiogenesis, cell proliferation, migration, and differentiation. Cytokines, chemokines, and growth factors are essential for stimulating and modulating these cellular events underlying healing (24). Different efforts have come a long way in utilizing various biological materials to support and upgrade such circumstances, specifically focusing on using natural sources of these elements, such as platelet gel, platelet-rich plasma, and PRF (6,25,26).

Scientifically advanced studies have proved that platelets can release high concentrations of growth factors, immune molecules mediators, enzymes, and bioactive substances that are favorably involved in tissue reconstruction and enhancing healing through the regulation of anti-inflammatory signals, stimulate and activate angiogenesis, cell migration, differentiation and proliferation (6,27,28).

Macropathologecally, in our study, the comparison between all groups showed an apparent difference between control and treated groups (PRF-m and i-PRF) regarding the presence of hematoma, edema, weeping occurrence, skin graft takes, the survival rate of graft, and cosmetic appearance of the grafting area and scar tissue formation with an abettor result in treated groups. Our research result is similar to the findings of previous studies on skin graft healing in terms of the positive healing effects of platelet derivatives such as PRP and PRF. This finding indicates that these derivatives play an influencing role in graft wound regeneration. It acts as a biological filler for tissue. It is an essential catalyst for accelerating skin repair improvement, advancing collagen synthesis, neo-angiogenesis, and tissue remodeling by releasing many cytokine and growth factors (29). PRF, when used with skin grafts, improve vascular in-growth, aid in graft innervation, instant adherence of the graft, accelerate healing, and enhance skin scarring, as well as transplant take and survival. Furthermore, this product's matrix form reduces graft dehiscence and additional problems like infection. PRF preparation is simple, cost-effective, easy to use, and available (25-29). Furthermore, fibrin is one of the components of PRF, which has been used widely as the adhesive substance of skin grafts and biological dressings to a wound associated with a high graft success rate (30,31).

In the current study, using PRF as a liquid or matrix form has reduced hematoma formation, edema, and contamination, which have been recognized as chief reasons for graft loss; these findings agree with others. Nica *et al.* revealed that application of PRF with skin graft at the recipient site diminished hematoma formation and infection, enhanced primary healing, and increased graft take and survival percentage, likely as a result of equipping the graft bed environment with essential growth factors and cytokines that are regulating inflammatory reactions and promoting neovascularization (22). Vaheb *et al.* studied the effects of PRF on the enrichment of skin grafts. The results of this study established a positive impact of PRF in the survival of skin grafts and showed that fibrin clots in PRF can advance blood clotting and faster wound healing. These procedures can diminish hematoma formation on recipient skin graft sites and improve immediate stable skin graft adhesion, which enhances oxygen diffusion to skin graft from the recipient sites and prevents shearing (32). Also, in 2014, Reksodiputro *et al.* proved the effective use of PRF as an additive therapy for skin graft healing in porcine and found that application of PRF-m with skin graft transplants increases the graft take and survival; it has been shown to increase the adherence of skin grafts to wound beds (28). This result agrees with our study, which demonstrated significantly improved skin graft take rates and survival in animals who received platelet-rich fibrin compared to the control group. Graft takes rate in both groups received PRF-m, and i- PRF groups was 100%. This result also mirrors what was reported in the previous studies (25,28,22).

PRF is a blood-derivative product; the benefit of PRF in skin graft survival may be due to many scientific facts. Firstly, PRF is a resource for high kind growth factors, cytokines, and chemokines, which induce and accelerate new blood vessel formation in the skin graft site and improve the budding of new vessels to perfuse the skin graft. Secondly, PRF enhances inflammatory cell migration and fibroblast proliferation, supporting skin wound healing and graft incorporation. Thirdly, PRF contains fibrin, which has been confirmed to play a vital function in biological dressings and graft adherence to wounds that, associated with a high rate of graft, take success and acceptance. Furthermore, PRF diminishes wound infection in skin graft transplantation. Indeed, these benefits are in line with the results reported in our study (8,28,30-33).

In the current research, homologous PRF from the two types was not connected with symptoms indicative of contamination or immune rejection during the study period-similar results were reported by Shan *et al*., who used a homologous platelet gel (34). The absence of infection may be clarified by the presence of leukocytes and antimicrobial molecules in the PRF (8,28,35). A similar result was observed by Marques *et al*. (36) who demonstrated that using homogenous PRF with a skin graft was efficient in treating ulcers for 15 patients? Full healing was accomplished without reporting any adverse reaction or recurrence. Allogeneic PRF was also evaluated in treating Full-thickness skin wounds in the arms of 60 patients. The researchers of this study revealed that the use of homologous PRF resulted in a high rate of wound contraction and complete re-epithelialization without observation of significant

immunological reaction, with a better wound healing rate when compared to the control (16-18).

The histopathological estimations showed an enhanced total thickness skin graft healing process in groups treated with PRF, faster re-epithelialization, and increased granulation tissue formation (22,36,37). However, on the 7th day post-grafting, the micro pathological evaluation of skin graft wound sections in the control animals showed the presence of severe infiltration of inflammatory cells compared with treated groups that showed a less inflammatory reaction. Similarly, Pavlovic *et al*. (28) concluded that PRF types have a potential anti-inflammatory role during regeneration and restoration of tissues. Also, Reksodiputro *et al*. (38) have revealed that PRF decreases the inflammation process like hyperemia, pain, and edema after physiological wound healing and accelerates skin grafting wound healing by increasing the collagen deposition and later accelerating re-epithelialization. We agree with the authors that PRF is anti-inflammatory during total thickness skin graft repair.

The increase of inflammatory reaction in the control group explains why, during the immunohistochemistry assessment, the TNF-a level in this group is higher than that in other groups treated with PRF because many scientific sources indicated that in the case of inflammation, the level of inflammatory factors like TNFa in the diseased tissue rise (39). On the other hand, the immunohistochemistry examination showed an increase in the level of VEGF in the group treated with PRF derivatives compared to the control group; the reason for this may be attributed to the scientific fact that these substances contain a high concentration of this factor, which led to an increase of its level in this groups (40). The current research results showed that compared with the i-PRF group, the PRF -m group has a better effect on skin graft healing based on microscopical, histological, and immunohistochemical examination (39), in the case of using i-PRF, the growth factors are released higher in the early period within seven days, whereas when using PRF, secretion of the growth factor and cytokines continues for a more extended period. Therefore, prolonged treatments require multiple injections of *i*-PRF. According to our information, this is the first research to date about the effects of homologous PRF on the total thickness of skin graft healing and reconstruction.

Conclusion

The outcomes of our study showed that homologous PRF-m and i-PRF had excellent efficacy in total thickness skin autograft healing. It accelerated the reconstruction of the skin grafting wound without infection or immune rejection. More research on homologous PRF for treating different tissue grafts is recommended.

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Conflict of interest

None

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تأثير مصفوفة الليفين الغنية بالصفائح الدموية والليفين الغني بالصفائح الدموية القابل للحقن المتماثلة على التئام رقع الجلد الذاتية بسمك كامل في الكلاب

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الخلاصة

مصفوفة الليفين الغنية بالصفائح الدموية والليفين الغني بالصفائح الدموية القابل للحقن الذاتية هي مكونات دموية لها دور مهم في التئام الأنسجة وتسهيل تحسين أخذ الرقع النسجية لأنها تعد خزانات لأنواع مختلفة من عوامل النمو والسايتوكينات، وهي فعالة وآمنة ولا تختلف عن مصدرها الذاتي، ولهذا تم إجراء هذه الدراسة لمعرفة فيما لو أن مصفوفة الليفين الغنية بالصفائح الدموية والليفين الغني بالصفائح الدموية القابل للحقن لهما تأثير على بقاء وشفاء رقع الجلد الذاتية. شملت دراستنا ١٨ كلبا من السلالة المحلية، تم ترقيع الجلد الذاتي ومن ثم تقسيمها إلى ثلاث مجموعات وهي: مجموعة سيطرة تم فيها ترقيع الجلد برقع ذاتية فقط دون أي علاج، مجموعة مصفوفة الليفين الغنية بالصفائح الدموية وتم فيها ترقيع الجلد برقع ذاتية مع إضافة الليفين الغني بالصفائح الدموية

القابل للحقن المتماثل. تمت متابعة الحيوانات عيانياً لمدة ٣٠ يوما بعد العملية واجري الفحص النسيجي المرضي والفحص الكيميائي المناعي لعامل النمو البطاني الوعائي وعامل نخر الورم الفا في ٧ و١٥ و٣٠ يوما بعد العملية. أشارت النتائج إلى أن مصفوفة الليفين الغنية بالصفائح الدموية والليفين الغني بالصفائح الدموية القابل للحقن المتماثلين كان لهم فائدة كبيرة في شفاء وقبول الرقع الجلدية خلال جميع مراحل عملية الالتئام وتقبل الرقع النسجية بنسبة ١٠٠٪، والمظهر التجميلي للرقع الجلدية إذ ظهرت بلون مشابه للجلد المتلقي، تعزيز تكوين الكولاجين، إعادة التظهر، مع مستويات أفضل لعامل النمو البطاني الوعائي وعامل نخر الورم ألفا مقارنة مع مجموعة السيطرة والتي أظهرت انفصال جزئي للرقع الجلدية، فضلاً عن أن تأثير مصفوفة الليفين الغنية بالصفائح الدموية كان افضل نسبيا من الليفين الغني بالصفائح الدموية القابل للحقن في تحسين والتئام الرقع الجلدية. نستنتج من هذه الدراسة أن مصفوفة الليفين الغنية بالصفائح الدموية والليفين الغني بالصفائح الدموية القابل للحقن كان لهما دور فعال في التئام الرقع الجلدية الذاتية بسمك كامل.