

Original Research Article

Patient perception, satisfaction and cosmetic results of platelet-rich plasma in the treatment of acne scars: a patient-reported outcome of a non-surgical management

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ABSTRACT

Background: Acne is a common skin condition of the pilosebaceous unit that is prevalent up to 80% of the adolescent population. Permanent, disfiguring scar is an unfortunate complication due to abnormal resolution following the damage during acne inflammation. Those troubling noticeable scars may lead to not only cosmetic problems but also psychological and social consequences which could impair the quality of life including diminished self-esteem and disruption of daily activities. We aimed to discuss our results of PRP procedure in the treatment of acne scars using scales based on patient satisfaction, perception and the quality of life.

Methods: This study included 11 patients suffering from post-acne scars who underwent 3 sessions of platelet-rich plasma injection. The outcome was determined by the difference in pre- and post- procedure FACE-Q modules, dermatology life quality index (DLQI) and body image questionnaire (BIQ) which were designed as patient-reported outcome instrument to evaluate the unique outcomes of patients undergoing facial cosmetic procedures.

Results: Overall satisfaction with outcome was 77.18 ± 8.30 (range 63–87). No major complications such as hyper-/hypopigmentation, scar formation, infections, skin necrosis, nodulation, fibrosis, or calcification were recorded. All patients developed ecchymosis and edema in the treated area and all were improved during follow-up. The patient-reported FACE-Q satisfaction, FACE-Q quality of life, DLQI and BIQ scores of pre- and post- procedure showed statistically significant improvement (<0.05).

Conclusions: PRP can increase the quality of life in patients with acne scars in terms of social and psychological function without large damage to the skin.

Keywords: Acne scar, Body image, Face, FACE-Q, Quality of life, Platelet-rich plasma

INTRODUCTION

Acne is a common skin condition of the pilosebaceous unit that is prevalent up to 80% of the adolescent population between the ages of 11–30 years and it may persist into adulthood in approximately 12%–14% of cases.^{1–4} Permanent, disfiguring scar is an unfortunate complication due to abnormal resolution following the

damage that occurs in the sebaceous follicle during acne inflammation. Those troubling noticeable scars may lead to not only cosmetic problems but also psychological and social consequences which could impair the quality of life. The psychosocial effects of unaesthetic scarring include diminished self-esteem, stigmatization, disruption of daily activities, anxiety and depression.⁵

Acne scars can be classified into three different types: atrophic, hypertrophic, or keloidal.¹ Unlike other ordinary scars created by a wound trying to heal itself and the resulting overproduction of collagen, atrophic acne scars are produced by destruction of the dermal matrix, followed by imperfect matrix synthesis or repair.⁶ Therefore, most acne scar treatments work by inducing regeneration and remodelling of the dermal matrix.

There are a variety of treatment modalities for post-acne scars. These include medical, invasive and non-invasive management s including various ablative, non-ablative lasers and light energies. Of these multiple options, treatment has to be tailored to patient's needs, tolerance, and goals along with the physician's assessment, skills, and expectation.² Patient should be informed that the ultimate goal of any intervention is to improve the scars, and no currently available treatment will attain total cure or perfection.² On the other hand, the choice of treatment should be high level in patient satisfaction, less harmful increasing perception and cost effective for the patient. Together with the positive aspects, the negative aspects of each treatment modality should always be considered. In recent studies, fractional CO₂ laser resurfacing was reported as efficient modality in the treatment of acne scars; however, its drawbacks such as long periods of erythema and edema may cause discomfort and hinders patient's daily activities, especially in patients with darker skin phototypes.¹ New biological methods, such as platelet-rich plasma (PRP), may be promising in the treatment of facial scars, as in other facial rejuvenation and aesthetic dermatology particularly in dark-skinned patients.

PRP is an autologous suspension of platelets in a small volume of plasma characterized by a platelet concentration above the basal blood values collected. PRP is used as a growth factor and cytokine pool which contains multiple angiogenic growth factors including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF- β), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and fibroblast growth factor (FGF) for improving tissue regeneration in different fields of surgery and medicine. The growth factors in PRP effect the skin rejuvenation as a chemoattractant for fibroblasts and macrophages, a mitogen for fibroblasts, and catalyser for the synthesis of extracellular matrix components.

Although the current studies in acne scar have positive results, they could not primarily aim to evaluate the change in the quality of life in those patients. In our study, we aimed to discuss our results of PRP procedure in the treatment of acne scars using scales based on patient satisfaction and the quality of life. From this perspective, our study is the first in the literature measuring the effectiveness of the PRP with quality of life scales named FACE-Q in the treatment of acne scars.

METHODS

Between January 2016 and December 2017, 11 patients with unpleasant facial atrophic acne scars treated with PRP injections were recruited from Plastic, Reconstructive and Aesthetic Surgery Clinic in Aydin State Hospital. This procedure was not applied to the patients with concomitant treatments, a propensity for keloids, pregnancy, diabetes, cancer, collagen disorders or immunodeficiency, patients with coagulation defects and/or platelet count <150,000/mm³. Patient demographics were evaluated using patients' medical records. All protocols used in this study were performed according to the recommended International Regulations and Declarations and complied with the Declaration of Helsinki. This study was approved by the Local Medical Ethics Committee. All procedures were performed at outpatient clinics and all patients provided written informed consent.

The treatment course consisted of three sessions of autologous platelet-rich plasma injections into acne scar area with one month apart in between the injections and followed up for additional six months to assess the level of improvement of the scar.

PRP preparation

On the day of the procedure, 11 ml of whole blood was drawn into standard tubes containing anticoagulant citrate dextrose solution-formula A (ACD-A) with a blood to anticoagulant ratio of 9:1. We obtained 4 tubes for each patient (a mean of 44 mL of fresh blood from each patient). The 4 tubes were centrifuged for only 1 spin at a standard relative centrifugal force (RCF) of 1630 g for 5 min using a multipurpose centrifuge device (NF 800®, NUVE Industrial Materials Manufacturing and Trading Co., Turkey). Blood components were separated into the plasma, buffy coat, and erythrocyte layers. In our technique, the plasma layer formed after centrifugation is divided into approximately 3 equal portions, and the uppermost two-thirds is removed.⁸ One-third of the plasma at the bottom and the buffy coat layer were collected without mixing these with the erythrocyte layer. Using this method, we obtained a mean of 1.2 ml of PRP from each tube (we collected approximately 4.8 ml of PRP from all 4 tubes without using any commercial kit systems). As a result of our previous clinical studies, baseline platelet concentrations increased 4-fold in the PRP using this manual technique.⁹ We do not activate PRP with calcium or thrombin since non-activated platelets present in PRP get gradually activated and secrete orchestrated growth factors up to 10 days.¹⁰

Assessment using dermatology life quality index (DLQI)

The DLQI is a validated, simple, compact and uniform measure for the impairment of quality of life through any

skin disease or treatment. The questionnaire consists of 10 questions concerning the 6 dimensions ‘symptoms and feelings’, ‘daily activities’, ‘leisure’, ‘work and school’, ‘personal relationships’ and ‘treatment’.¹¹ A maximum score of 30 represents 100% impairment in the patient’s quality of life and standing for an extremely large effect on the patient’s life. All patients completed a DLQI questionnaire before the procedure and at least 6 months after the last procedure.

Assessment using body image questionnaire (BIQ)

The BIQ was used to evaluate the patients’ perceptions of their bodies and scars. This evaluative tool is a Likert-type instrument which consists of 2 parts. The first 5 questions are related to body image and assess the effect of the disease or scar on the body (the total score varies between 5-20). Higher numbers indicate that body image perception is greater to effect the patient’s life. The second 3 items are the cosmetic subscale questions evaluating self-perceived body-image satisfaction/dissatisfaction by measuring the degree on a cosmetic ruler (the total score is ranging from 3 to 24). A higher score indicates higher cosmetic satisfaction. All patients completed a BIQ questionnaire before the procedure and at least 6 months after the last procedure.

Assessment using FACE-Q scales

The FACE-Q is a revolutionary patient-reported outcome instrument that evaluates specific outcomes in patients undergoing facial cosmetic procedures.¹² It utilizes several assessment scales to evaluate satisfaction with facial appearance, health-related quality of life, and satisfaction with the process of care. The FACE-Q satisfaction scales consist of questions relating to patient satisfaction with regard to facial appearance. Rating is performed based on the following scales: 1=very dissatisfied, 2=somewhat dissatisfied, 3=somewhat satisfied and, 4=very satisfied. Quality of life scales are rated as: “definitely disagree, somewhat disagree, somewhat agree, or definitely agree.”¹²

A pre-procedure FACE-Q was administered including the following modules

- **Satisfaction with facial appearance:** This 10-item scale assesses the overall facial appearance using items including: “How your profile (side view) looks,” “how fresh your face looks, and “how your face looks under bright lights.”¹³
- **Satisfaction with skin:** This 12-item scale assesses facial skin in mind with items such as: “How your facial skin looks when you first wake up,” “how the tone (color) of your facial skin looks.”¹²
- **Psychological function:** This 10-item scale includes a series of positively worded statements that respondents are invited to agree/disagree, for

example, “I feel good about myself,” “I feel confident,” “I feel attractive.”¹³

- **Social function:** This 8-item scale includes a series of positively worded statements that measure social confidence. Respondents are invited to agree/disagree with statements such as: “I make a good first impression,” “I am relaxed around people that I don’t know well.”¹³

All patients included in this study completed a post-procedure FACE-Q at least 6 months after the last procedure. This questionnaire included the same modules as were assessed during pre-surgery evaluation but with the addition of a 6-item “satisfaction with outcome” module. Each FACE-Q scale was scored using a lookup conversion table approach. Scores range from 0–100 with higher scores indicating greater satisfaction and/or quality of life.¹² Results were grouped to obtain the mean pre-and post- procedure results.

Statistical analysis

The SPSS (Statistical Package for Social Sciences, USA) 15.0 Data Analysis System was used for data analysis. Normal distribution and homogeneity tests were performed on all data. Data were expressed as mean±standard deviation (SD). Statistical significance was calculated using the paired t-test if the data was approximately normally distributed and the variance was similar. If not, non-parametric tests were used for calculating statistical significance. Two-sided values of $p < 0.05$ were considered statistically significant.

RESULTS

11 patients were included in the study. The age of patients ranged from 33 to 63 years with a mean of 42.6 ± 9.9 years and all were women. All patients were followed-up over a minimum period of 9 months.

The patient-reported satisfaction and quality of life scores of before the procedure and six months after the last intervention showed a statistically significant improvement in all FACE-Q modules assessed (Figure 1). Satisfaction with overall facial appearance improved from scores of 46.7 ± 10.2 to 68.9 ± 10.9 ($p < 0.05$, paired t-test) whereas satisfaction with the skin improved from scores of 48.1 ± 7.6 to 69.6 ± 10.0 ($p < 0.05$, paired t-test). Social function and physiological function improved from scores of 58.7 ± 6.8 to 82.3 ± 6.3 and 49.9 ± 10.5 to 75.7 ± 9.9 , respectively (for both, $p < 0.05$). Overall satisfaction with outcome was between 63 and 87 (Table 1).

Figure 2 shows the change in DLQI prior to procedure and at least after 6 months of the last application of PRP. The mean $DLQI \pm SD$ prior to PRP procedure was 2.3 ± 1.5 . After the treatment DLQI showed a significantly improvement to 0.9 ± 1.1 ($p < 0.05$, paired t-test).

BIQ scores of prior to procedure and at least after 6 months of the last application of PRP is displayed in Figure 3. BIQ satisfaction scores of image section and

cosmetic section improved from scores of 10.9 ± 2.3 to 7.1 ± 1.1 and 11.9 ± 3.0 to 18.3 ± 3.2 , respectively (for both, $p < 0.05$).

Table 1: Patient overall satisfaction with the outcome of the PRP with FACE-Q at least 6 months after the last procedure.

	N	Minimum	Maximum	Mean	Std. Deviation
Satisfaction with outcome	11	63.00	87.00	77.18	8.30

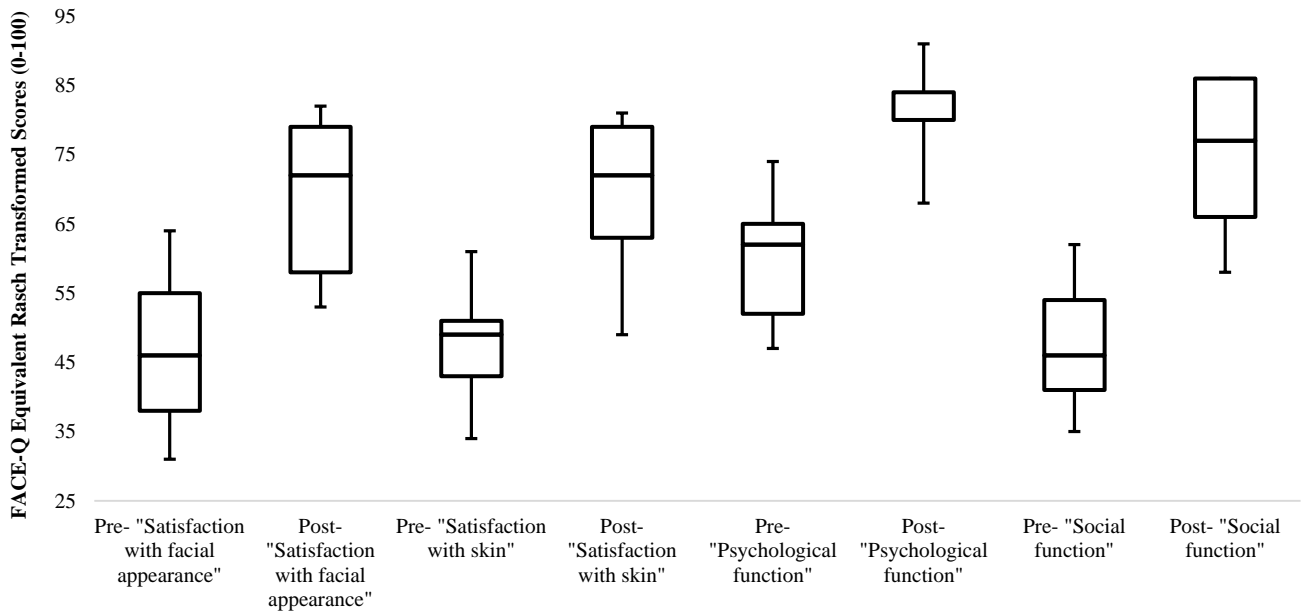


Figure 1: Graphic analysis of FACE-Q scores comparing pre- and post- procedure satisfaction of overall face, skin, psychological function and social function ($p < 0.05$). Data represent group medians and quartiles with minimum and maximum scores. Lower scores represent a less satisfaction in the life with the face and skin, and a less quality of life with facial appearance. Increased scores show the positive effects of the applied procedure on the social and psychological aspects of the patients’ lives as well as facial and skin satisfaction. Changes in grading after the procedure can be seen.

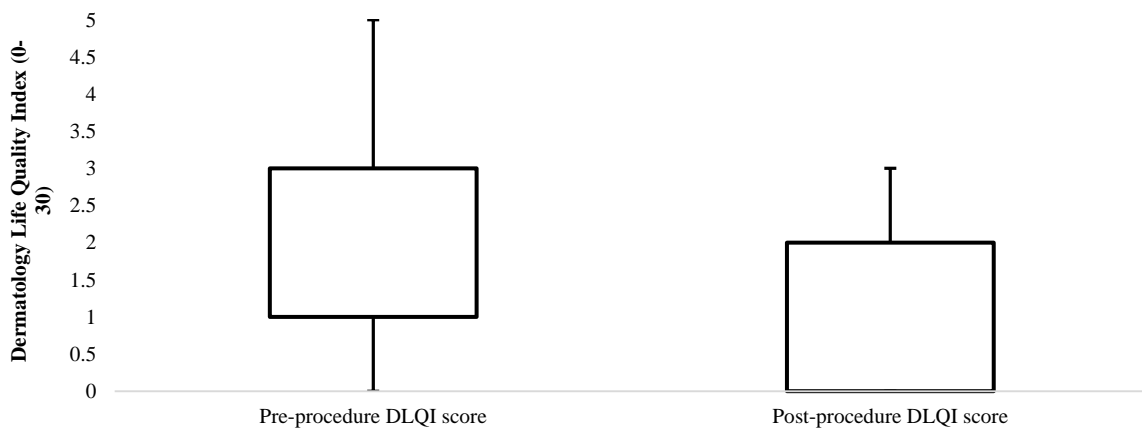


Figure 2: Assessment of the dermatology life quality index (DLQI) between before and after the treatment of acne scar. A higher score represents impairment in the patient’s quality of life and shows the lesion standing for an extremely large effect on the patient’s life. Analysis of DLQI scores improved statistically significant after PRP procedure ($p < 0.05$).

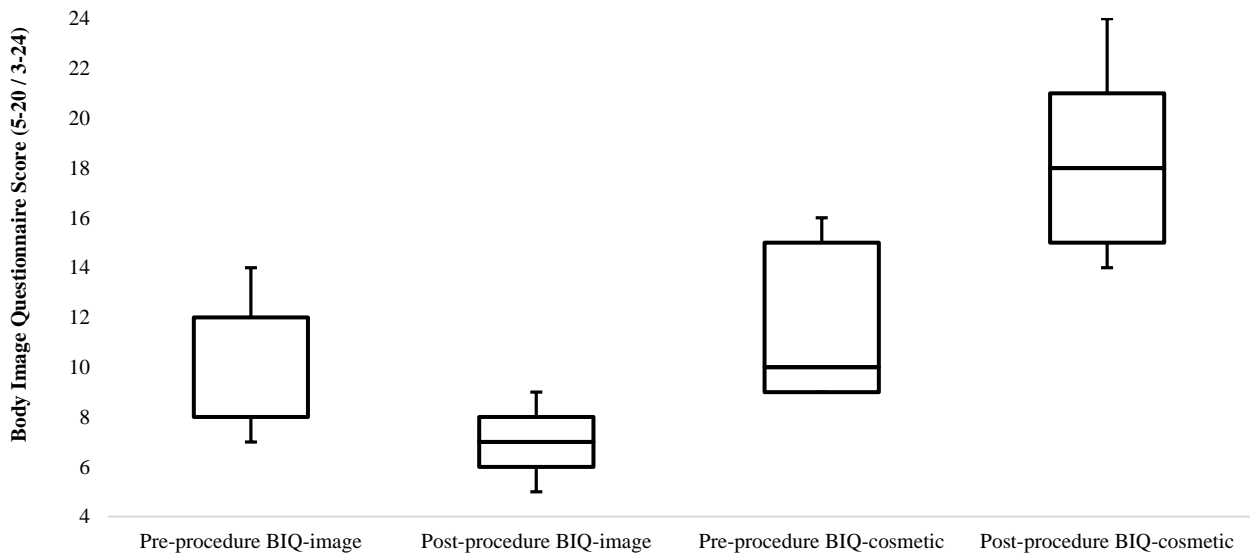


Figure 3: Body image questionnaire (BIQ) scores between before and after the treatment of acne scar. BIQ-image shows the effect of the disease or scar on the body and higher numbers indicate that body image perception is greater to effect the patient's life. Analysis of BIQ-scar scores improved statistically significant after PRP procedure ($p < 0.05$). BIQ-cosmetic evaluates cosmetic outcome and a higher score indicates higher cosmetic satisfaction. Analysis of BIQ-cosmetic scores improved statistically significant after PRP procedure ($p < 0.05$).



Figure 4: (A) A patient with glabellar post-acne scar; (B) 6 months after the last PRP procedure shows us a moderate improvement; (C) 2 years after the last PRP procedure with acceptable improvement.

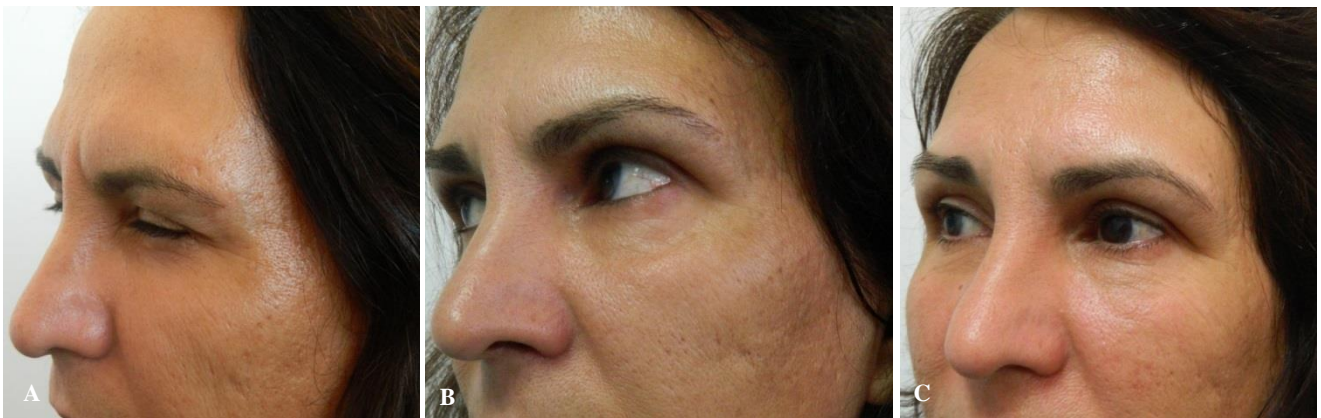


Figure 5: (A) A patient with post-acne scar on left cheek extending to the temporal area. (B) 6 months after the last PRP procedure with a good result. (C) 15 months after the last PRP procedure shows a stable improvement in the left cheek area.

No major complications such as hyper/hypopigmentation, scar formation, infections, skin necrosis, nodulation,

fibrosis, or calcification were recorded. All patients developed ecchymosis and edema in the treated area and

all were improved during follow-up. Some illustrations were given in Figures 4 and 5.

DISCUSSION

Acne is a chronic multifactorial disease of the pilo-sebaceous unit. Despite its common occurrence, the prevalence of acne scarring in the population has not been fully studied. However, according to a study of 2,133 volunteers aged 18-70 from the general population showed that almost 1% of people had acne scars, and only 1 in 7 of these individuals were considered to have 'disfiguring scars'.¹⁴ These unpleasant facial scars may impact the quality of life by affecting physiological, psychological and social functions particularly in adolescents. The inflammatory reactions in acne is formed as a consequence of the development of anaerobic environment and the bacterial growth caused by the hypersecretion of the sebaceous gland and/ or hyperkeratinization of the follicular openings. In some forms of acne such as in nodular cysts, despite various topical and systemic therapies in dermatology, those inflammatory reactions may extend into the deep dermis and result in scar formation.¹⁵ So, that scars may involve textural change in the superficial and deep dermis. Although the pathogenesis of acne scarring is too complex indeed, it is showed that it is more prominent in patients with extensive inflammation associated with severe acne disease. Specifically, the type and timing of the cell-mediated immune response may be associated with the degree of post-acne scarring.¹⁶ Younis et al suggested that in acne lesions, the activated platelets recruit matrix metalloproteinases (MMPs) to the site of initiation and lead to wound healing accompanied with scarring by the activation of toll-like receptor 4 (TLR4).¹⁷ TLR4 acts as a bridge between innate immunity and adaptive antimicrobial immune response and functions as a biosensor of tissue damage and sterile inflammation and it has been shown that TLR4 is overexpressed in pathological fibrotic conditions such as keloids and hypertrophic scars.¹⁸ Human platelets express a range of bacterial recognition receptors and importantly TLR4 is functional in platelets.¹⁷ Activation of TLR4 on platelets surface leads to production of cytokines and chemokines, recruitment of neutrophils, bacterial degradation as well as adaptive immunity activation. The interference of other factors of acne pathogenesis, including immune and inflammatory mediators, may disturb the normal healing process and result in abnormal wound healing leading to scar.¹⁷ In one study, the cellular infiltrate and nonspecific immune response were initially greater but later reduced in patients who did not subsequently develop scars.¹⁶ However, in patients who did develop post-acne scarring, the initially smaller specific immune response later increased.¹⁶ Kang et al showed that transcription factors nuclear factor- κ B and activator protein-1 are activated in acne lesions with consequent elevated expression of their target gene products, inflammatory cytokines and matrix-degrading metalloproteinases, respectively.¹⁹ These elevated gene products are molecular mediators of

inflammation and collagen degradation in acne lesions in vivo.¹⁹ Although a variety of mechanisms and steps as mentioned above have been proposed on the etiopathogenesis of acne scar formation, once formed, pharmacological treatment is no longer available and further procedures are required to improve its appearance.

The number of treatments for acne scarring is obviously too much. In fact, the options are so abundant that even experienced practitioners may have difficulty in making decisions. A customized treatment should be selected for optimal outcomes of these multiple options based on patient's needs and tolerance, invasiveness, risk and effectiveness of the procedure, physician's assessment and skills. The most important point is that patient should be informed that the ultimate goal of any intervention is to improve the scars, and no currently available treatment will attain total cure or perfection.

PRP has been increasingly used blood-derived suspension enriched in fundamental growth factors and cytokines secreted by platelets. PRP thus constitutes a potential to provide growth factors to the target cells and tissues at high concentrations. Receptors for growth factors in PRP are found on adult mesenchymal stem cells, fibroblasts, osteoblasts, endothelial cells, and epidermal cells.²⁰ PRP is more than just a growth factor concentrate; it also contains the 3 proteins in blood known to act as cell adhesion molecules for connective tissue, and epithelial migration.²⁰ As an autologous source of growth factors and cytokines, PRP is completely biocompatible and has therefore gained popularity as a safe and natural healing therapy.

Fibroblasts are the most common cell type in the dermis and the most influential cells in production of collagen and other extracellular components. Fibroblasts are strongly reactive to fibroblast growth factor-beta, platelet derived growth factor and epidermal GF. Cho et al demonstrated that PRP induced increases in cell migration, and proliferation rates, as well as an increase in the expression of G1 cell cycle regulatory proteins, such as cyclin A, Cdk2, and cyclin E in human skin fibroblasts.²¹ In this study, treatment of human skin fibroblasts with PRP resulted in increased expression of type I collagen by matrix metalloproteinases I and II which promote remodelling of extracellular matrix and facilitating cell migration.²¹

PRP can be applied as an isolated therapy or as an adjunct to minimally invasive interventions in acne scar treatment. Nofal et al evaluated the efficacy and safety of intradermal injection of PRP, 100% focal trichloroacetic acid (TCA), and combined skin needling plus topical PRP in the treatment of atrophic acne scars.²² They compared therapeutic response of the groups by using patient satisfaction according to the degree of improvement of acne scars into excellent (>75%), very good (50%–74%), good (25%–49%), and poor (<25%).²² The 3 groups showed highly significant improvement in

the severity of acne scars after treatment but between the three groups, they found no statistically significant difference and concluded that the 3 modalities showed a promising efficacy and safety in the treatment of atrophic acne scars.²²

In a split-face study, Asif et al compared microneedling alone versus microneedling combined with platelet rich plasma in the treatment of post acne scars by patient satisfaction scores calculated for right and left halves of each patient.²³ They showed that PRP side had an improvement of 62.20% contrast to distilled side of 45.84%, and concluded that PRP has efficacy in the management of atrophic acne scars.²³ Chawla performed a study to investigate the efficacy of PRP versus vitamin C as adjuncts to micro needling for the treatment of atrophic post-acne scars as part of a split-face prospective study.²⁴ They reported that patients were more satisfied with PRP as compared to vitamin C.²⁴ Min et al conducted a split-face study applying two sessions of fractional CO₂ laser therapy with and without co-administration of PRP (After each laser treatment, one half of the subject's face was injected intradermally with PRP, and the other half of the face was injected with normal saline) and obtained skin biopsy specimens at baseline, 1, 3, 7, and 28 days.⁶ They reported that no patient had a worse acne score after receiving either type of treatment (combined laser/PRP treatment or combined laser/normal saline treatment).⁶ However, productions of TGF-β1 and TGF-β3 proteins were reported more highly on the PRP-treated side of the face compared to the control side at day 28.⁶

Although the most studies concluded positive results about the use of PRP as adjuvant therapy, the application of PRP to skin traumatized by thermal micro-channels may result in undesired effects. A split-face randomised controlled study was performed by Faghihi et al in which patients with atrophic acne scars received ablative fractional CO₂ laser combined with intradermal PRP treatment on one half of their face and laser with intradermal normal saline on the other half.²⁵ The overall clinical improvement of acne scars was higher on the PRP-laser treated side, but the difference was not statistically significant at four months following the final session. Moreover, the adverse effects including erythema and oedema were more severe and of longer duration in the PRP-laser treated side in a statistically significant manner.^{15,25} In this work, PRP addition to the laser modality appears to produce more severe side effects and longer downtime.^{15,25} So, we agree to speculate that overall, PRP alone may be an effective means of enhancing wound healing, stimulating cellular regeneration, improving skin tightening, remodelling scar and delivering greater patient satisfaction as greater as adjuvant to the traditional modalities.

As seen, a few studies were reported the use of PRP alone in acne scar treatment.^{15,22,26} In addition, the methodology of evaluating patient satisfaction in existing studies of

comparing the modalities in the treatment of acne scar remains quite weak. We used FACE-Q, DLQI and BIQ assessments in our patients before and after the applications. The FACE-Q is a patient-reported outcome instrument that measures the experience and outcomes of aesthetic facial procedures from the patient's perspective giving unprecedented insight into their satisfaction and health-related quality of life.¹² In procedures aiming the aesthetic improvement, patient perception of the treatment outcome appears to be most important because it has a direct impact on patients' body image and self-esteem.²⁷ Anaba and Adebola showed that treatment of facial acne leads to improvement of quality of life with improvement in all components of QOL assessed especially on the component of how the adolescents thought their acne was now irrespective of the severity of the acne.²⁸

Some aspects of our study may be seen as remarkable. The evaluation of satisfaction with facial appearance and skin before and after the procedure makes it clearer how much the acne scars affect the facial appearance and skin satisfaction in patients, in addition to quality of life and body image perception. While those assessments were examined, it was observed that the quality of life of the patients had changed after the treatment with PRP alone. It may be added that treatment of acne scars with PRP even contributes to the increased quality of patient-perceived age feeling. When the satisfaction with outcome is examined, the satisfaction of the patients from the PRP procedure for the treatment of the acne scars was observed to be a mean score of 77 as well as cosmetic scale improvement and could be interpreted as a good satisfaction level. Besides that, dermatology quality of life index and body image perception was improved after PRP treatment.

As a conclusion, our study demonstrated the patient-based outcomes of PRP in the treatment of acne scar. Our study is different from other studies in that aspect and it may be classified as the first study that evaluates the effectiveness of PRP in acne scar by evaluating and comparing the patient's quality of life using FACE-Q and other some scales as before and after. PRP as a potent source of growth factors, can be seen as a safe, biocompatible, relatively long-lasting, autologous and appropriate treatment modality without large damage to the skin for acne scarring that can increase the quality of life in patients in terms of social and psychological function.

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Ethical approval: The study was approved by the institutional ethics committee

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