Current Evidence for Clinical Efficacy of Platelet Rich Plasma in Aesthetic Surgery: A Systematic Review

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Abstract

Background: Platelet rich plasma (PRP) has attracted attention in a number of surgical fields due to a wide variety of potential clinical benefits. Yet PRP has not gained wide popularity in aesthetic surgery as a result of uncertainty surrounding objective clinical evidence.

Objectives: We aim to describe the current applications, define preparation and activation, explore effectiveness, and propose a classification system to facilitate comparisons across studies.

Methods: A comprehensive review of the literature regarding the use of platelet rich plasma in aesthetic surgery was performed. Data gathered included: PRP application, study type, subject number, centrifugation, anticoagulation, activation, PRP composition, and outcomes.

Results: Thirty-eight reports were identified. Applications included injection into aging skin (29%), scalp alopecia (26%), lipofilling (21%), fractional laser (13%), and facial surgery (11%). The majority of studies (53%) were case series without controls. Leucocytes were sparsely defined (32%). The concentration of injected and/or baseline platelets was rarely clarified (18%). The mechanism of activation was described in 27 studies (71%), while anticoagulation was uncommonly elucidated (47%). While most studies (95%) claim effectiveness, objective measures were only utilized in 17 studies (47%).

Conclusions: Current studies produce context-dependent results with a lack of consistent reporting of PRP preparation, composition, and activation in aesthetic applications, making meaningful meta-analysis unrealistic. Thus the method of PRP preparation warrants increased attention. We recommend a set of descriptors, FIT PAAW (described below), to produce scientifically grounded conclusions, facilitating a clearer understanding of the situations in which PRP is effective.

Level of Evidence: 4

Platelet rich plasma (PRP) has been utilized in a variety of fields for over four decades. Despite the premise of improved wound healing, secondary to growth factor release, PRP has not witnessed widespread popularity in aesthetic practice. This is most likely due to the lack of demonstrable objective evidence regarding its efficacy. While primarily anecdotal reports in plastic surgery,1,2 dermatology,3 oral and maxillofacial surgery,4,5 orthopedics,6 sports medicine,7 gynecology,8,9 cardiology,10 ophthalmology,11 dentistry,12 and veterinary medicine13 abound, its effectiveness remains controversial.

Theoretically, the potential benefits of PRP in aesthetic surgery are significant. The concept of generating

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growth factors that can positively modify healing using the patient’s own platelet bank, at an economic price, is extremely attractive.

The aim of this study, therefore, is to: (1) describe the current uses of PRP in aesthetic surgery; (2) identify reported techniques of preparation and mechanisms of activation; (3) explore the evidence of effectiveness; and (4) propose a classification system to facilitate meaningful comparisons across clinical studies.

**METHODS**

A systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. A comprehensive review of the literature regarding the utilization of platelet rich plasma in aesthetic surgery was performed using the PubMed/ Medline and Cochrane databases in September of 2015. The following search terms were utilized to identify articles: platelet-rich plasma [MeSH Terms] OR (platelet-rich [All Fields] AND plasma [All Fields]) OR platelet-rich plasma [All Fields] OR (platelet [All Fields] AND rich [All Fields] AND plasma [All Fields]) OR platelet rich plasma [All Fields]. Studies in English were included if they were published between 1950 and 2015. The abstracts and titles were reviewed to identify studies involving aesthetic applications and human subjects only (inclusion criteria). Animal studies were excluded. An in depth analysis was performed on eligible studies to assess study design, technique of PRP preparation, and mechanism of activation. Reported outcomes were also evaluated. To avoid bias in selection of studies and data collection, dual review—having two reviewers (R.F., B.H.) independently assess citations for inclusion and collect data—was utilized, consulting the third reviewer (C.C.) when needed, as recommended in the Institute of Medicine’s “What works in healthcare: standards for systematic reviews.” The following data for each individual study was collected: (1) the reported PRP application; (2) study type; (3) number of patients; (4) outcome measures utilized; (5) force and time of centrifugation; (6) baseline and final platelet concentration; (7) use of anticoagulation; (8) mechanism of platelet activation; and (9) white blood cell composition. A flow diagram outlining article selection is provided in Figure 1.

**RESULTS**

The initial database search yielded 8688 studies using the keywords listed previously. Title and abstract review resulted in exclusion of 8554 total articles. One hundred and thirty-four articles were read thoroughly. Ninety-six were excluded from the final selection and analysis due to: (1) the PRP was applied to areas other than the face and scalp, (2) they were animal studies, (3) they were review articles, (4) they were non-clinical articles, and (5) they were repeats. This resulted in the final selection of 38 studies (Appendix A). In these reports, PRP was injected to rejuvenate aging skin in 11 (29%), to treat scalp alopecia in 10 (26%), to increase retention of fat grafts in 8 (21%), to enhance the effect of fractional laser resurfacing in 5 (13%), and as an adjunct to facial cosmetic surgery to reduce ecchymoses and the incidence of hematomas in 4 (11%). The majority of studies were case series (Level IV Evidence, 53%), with only 18 studies (47%) designed with randomization and/or controls (Level II or III Evidence). The most convincing and scientifically rigorous published work (randomized double-blind controlled) was limited to only 2 studies. These two studies indicated contrasting outcomes, with Fontdevila et al noting no significant difference between PRP included in fat grafting and fat grafting alone, and Trink et al concluding that PRP significantly improved hair regrowth, decreased hair dystrophy, and increased Ki-67 levels compared to the control. Trink et al had the patients serve as their own controls to eliminate allocation bias, and this is an aspect that Fontdevila et al could have added to eliminate that bias as well. There was no other risk of bias assessments mentioned in these two studies, which presents a possible limitation.

Of the 38 studies we reviewed, the platelet concentrate was classified generally as PRP in 32 (84%), platelet rich fibrin matrix (PRFM) in 4 (11%), leukocyte-platelet rich plasma (L-PRP) in 1 (3%), and plasma rich in growth factors (PRGF) in 1 (3%). The baseline platelet concentration of the patients’ whole blood was not documented in any of the reports and the final platelet concentration of the PRP injected was documented in only 7 studies (18%). The time and force of centrifugation was reported in 76% of studies, with 52% using only one centrifugation and the other 48% using two. The
PRP was activated with a calcium-based activator in 21 studies (55%), a mixture of calcium and thrombin in 4 (11%), thrombin only in 1 (3%), “PRGF Activator” in 1 (3%), and no activation was specified or reported in 11 (29%). Of the 38 studies, 20 reported specific anticoagulant usage (53%), with 10 using sodium citrate, 6 using acid citrate dextrose, 1 using trisodium citrate, 1 using trisodium phosphate, 1 using citrate, and 1 using citrate phosphate dextrose adenine. The white blood cell (WBC) composition was reported in only 12 studies (32%). WBCs formed a component of the PRP preparation in 9 (75%) of these reports, and was excluded in 3 (25%).

All but two studies reported a positive effect from PRP application, including improved healing, correction of wrinkles, increased hair growth/graft survival, and patient satisfaction. However, 53% of the studies did not employ any objective measures to assess the outcome. Assumptions were generally based on patient and physician satisfaction surveys, and occasional photographic comparisons. The forty-seven percent of studies that did use objective measures included histological analysis, computed tomography imaging, magnetic resonance imaging, trans-epidermal water loss, and hair follicle count.

**DISCUSSION**

Physiologically, platelets function as hemostatic agents, adhering to areas devoid of endothelium to form a platelet plug that seals the vessel wall. Platelet adhesion triggers their activation, with subsequent degranulation, and release of granule content. The basic quality for which platelet injections are used in clinical medicine is this well-known release reaction that follows their activation. In this reaction, large quantities of bioactive molecules are released, and are capable of modifying cellular proliferation, differentiation, matrix remodeling, and angiogenesis, enhancing wound healing, and tissue regeneration. The key component of the platelet that is thought to be particularly influential in this regard, is the α-granule, which contains prepackaged growth factors. Thus PRP applications attempt to profit from this large milieu of growth factors and chemokines, including transforming growth factor (TGF-β1), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and fibroblast growth factor 2 (FGF-2), among others (Table 1).

The impact of many of these growth factors has been established in vitro and in animal models, supporting their role in angiogenesis, homing, cell migration, cell proliferation, and collagen deposition. In addition, there are other molecules both in the platelet dense granules, lysosomes, and other plasma constituents that may also prove useful in tissue repair. The exploration of PRP applications in aesthetic surgery is based on these physiologic principles.

**Applications in Aesthetic Surgery**

Due to the anticipated benefits of platelet-rich plasma (PRP), many modes of PRP clinical applications in facial aesthetic surgery include: topical, injection, facelift, blepharoplasty, fractional carbon dioxide laser, fat grafting, hair transplantation, and hemostasis (Appendix A).

**Topical and Injection Applications**

Patients with facial wrinkles, atrophic acne scars, photodamaged skin, or depressed skin areas who received topical applications, skin injections, or a combination of both therapies generally report improvement of the affected areas within weeks of preliminary treatment. However, the presence of uniform and objective clinical outcome measures makes scientifically valid conclusions hard to come by. In a study using both topical application to the forehead, malar area, and lower face injections into the wrinkle’s of crow’s feet, all of the 10 patients saw statistically significant differences regarding the general appearance, skin firmness-sagging, and wrinkles according to the grading scale of the patients before and after three PRP applications. However based on dermatologist assessment, only skin firmness-sagging differences were considered to be statistically significant. In a larger study involving 2005 patients receiving PRP and basic fibroblast growth factor (FGF) therapy injections for the treatment of nasolabial folds, marionette lines, nasojugal grooves, supraorbital grooves, mid-cheek grooves, forehead, temple, and glabellae depressions, the reported patient satisfaction was 97.3% and investigator satisfaction was 98.4%. The authors found that PRP alone was often ineffective and failed to treat deep facial wrinkles, thus they chose to include FGF. The longevity of this treatment was reported to be three or more years, with the primary complication being overcorrection. This is one of very few clinical protocols that has trialed the PRP + FGF combination, and based solely on satisfaction results it is difficult to fully assess the outcome of this treatment. Notably, one study that utilized three treatments of both intradermal and deep dermal injections of activated PRP included histological analysis. There was a significant increase in epidermal and papillary dermal thickness, and the volume of collagen and number of fibroblasts were also increased.

**Facelift Applications**

There are three reported clinical studies that utilize PRP in conjunction with facelift procedures. The most recent study retrospectively reviewed facelift patients either receiving PRP (n = 587) or undergoing the superwet technique (n = 926). Ten hematomas were recorded, six in the group receiving the superwet technique compared to four hematomas in the PRP group. While no significant difference was noted, the authors still advocated for the use of PRP to potentially reduce ecchymosis and edema.
In another study, patients receiving a facelift had autologous platelet gel applied unilaterally and postoperative ecchymosis and edema were graded and compared to the contralateral side. Results showed that of the 19 observations regarding the PRP side, 15 were positive, 3 were indifferent, and 1 was negative. They concluded that PRP may reduce edema and ecchymosis following facelift, but again no statistically significant difference between sides was noted. In a similar study observing the effects of autologous fibrin glue and platelet gel in cosmetic surgical procedures involving the creation of flaps, such as facelifts, the proposed advantages included quicker operating times, reduced need for drains, reduced need for compressive dressings, decreased pain and postoperative swelling, and enhanced wound healing followed by a shorter recovery time. Other than showing its potential effectiveness in sealing facial capillary beds, no comparative assessment was carried out.

**Fractional Laser Applications**

By combining the laser treatment with PRP application, a number of studies propose that the healing results are superior. A report using topical autologous activated PRP with erbium fractional laser therapy for 16 patients with facial acne scars and 6 patients with acne scars concomitant with acne found that after receiving three treatments, 90.9% of the patients showed greater than 50% improvement and 91% of the patients were satisfied. The only outcome measure in this study was subjective photographic grading by evaluators, with no comparative analysis. In another study involving 22 women, half received only fractional laser therapy and the other half received topical PRP application in conjunction with fractional laser therapy. Objective skin elasticity and erythema index at 1-month post-treatment assessments were statistically significant. Clinical assessment, skin roughness, hydration, pain score, melanin index, and immediate erythema comparisons were not significantly different. Histologically, PRP improved the length of the dermoepidermal junction, the number of fibroblasts in their skin, and the volume of collagen. The significance of this study is the utilization of several objective and histological outcome measures, which highlight the potential for study objective repeatability and technique comparison.

**Fat Grafting Applications**

It has been suggested that fat grafts combined with PRP enhance volume maintenance and facial scarring. Autologous facial fat grafting with the addition of PRP has been hypothesized to be beneficial in graft longevity and in a reduction of recovery days. One study, which used fat grafting to reduce the appearance of facial scarring, included 10 patients undergoing stromal vascular fraction enhanced autologous fat grafts and another 10 patients undergoing fat grafting mixed with activated PRP (2:1 ratio). The former group observed 63% improvement of contour restoration after 1 year compared to patients treated with fat grafting and PRP who observed 69% enhancement of contour restoration after 1 year. Both were compared to a control group that only saw 39% maintenance. Therefore, it was concluded that fat grafting with PRP produced a superior result than fat grafting alone. The maintenance percentage was calculated using magnetic resonance imaging-ultrasound imaging, with which comparisons produced a statistically significant difference. In contrast to this study, Fontdevila et al concluded that the addition of PRP to fat grafts does enhance results. Forty-nine patients were included in this study.

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**Table 1. A Selection of Growth Factors Found in Platelet Rich Plasma and Their Actions**

<table>
<thead>
<tr>
<th>Growth Factor</th>
<th>Biological Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet derived growth factor (PDGF)</td>
<td>Mitogenetic for fibroblasts, smooth muscle cells, mesenchymal stem cells, and osteoblasts</td>
</tr>
<tr>
<td></td>
<td>Stimulation of macrophage and neutrophil chemotaxis; activation of macrophages</td>
</tr>
<tr>
<td>Transforming growth factor (TGF-α/β)</td>
<td>Extracellular matrix synthesis</td>
</tr>
<tr>
<td></td>
<td>Keratinocyte regulation in reepithelization</td>
</tr>
<tr>
<td></td>
<td>Stimulation of angiogenesis; Stimulation of type I and type III collagen production</td>
</tr>
<tr>
<td></td>
<td>Stimulation fibroblasts and mesenchymal stem cells proliferation</td>
</tr>
<tr>
<td>Vascular endothelial growth factor (VEGF)</td>
<td>Stimulation of angiogenesis; Chemotactic for endothelial cells</td>
</tr>
<tr>
<td></td>
<td>Mitogenic for endothelial cells and keratinocytes</td>
</tr>
<tr>
<td>Epidermal growth factor (EGF)</td>
<td>Stimulation of epithelial/mesenchymal mitogenesis</td>
</tr>
<tr>
<td></td>
<td>Stimulation of chemotaxis of keratinocytes</td>
</tr>
<tr>
<td></td>
<td>Stimulation of endothelial chemotaxis, mitogenesis and angiogenesis</td>
</tr>
<tr>
<td></td>
<td>Regulation of the secretion of collagenase</td>
</tr>
<tr>
<td>Fibroblast growth factor (FGF)</td>
<td>Promotion of angiogenesis, endothelial and fibroblast proliferation and migration, fibronectin synthesis and secretion</td>
</tr>
<tr>
<td>Connective tissue growth factor (CTGF)</td>
<td>Regulation of collagen synthesis</td>
</tr>
<tr>
<td></td>
<td>Enhancement of platelet adhesion</td>
</tr>
<tr>
<td></td>
<td>Stimulation of white blood cell migration</td>
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<tr>
<td></td>
<td>Promotion of angiogenesis</td>
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</table>
randomized double-blind study, which were either treated with autologous fat injection alone or autologous fat injection with PRP (4:1 ratio). The primary outcome measure consisted of computed tomography volume evaluation pre-, 2-months post-, and 12-months post-treatment. No significant differences were noted between the two groups. However, the study did not report the platelet concentration or the composition of white blood cells, making future comparisons to this well-designed study difficult. Although there is a wide range of variables to consider between these two studies, of note is the difference in PRP concentration, which could potentially have a significant impact on the outcome.

Hair Loss Applications
When PRP has been reported to be an effective treatment in promoting hair regrowth. In a study by Khatu et al., patients with male pattern baldness were injected with PRP resulting in an increased hair count. On average, hair follicles increased from 71 follicular units to 93 follicular units, with a mean gain of 22.09 follicular units per centimeter. In a similar randomized double-blind placebo-controlled study involving 45 patients with alopecia areata, one half of the scalp received intralesional injections of PRP, trimcineolone acetonide, or placebo. All patients were evaluated at four time points: pre-, 2-months post-, 6-months post-, and 12-months post-treatment. Each patch was digitally macrophotographed, measured, and evaluated by videodermoscopy for the detection of dystrophic forms and possible skin-associated manifestations. Additionally, levels of Ki-67, a marker for cellular proliferation, were assessed from 20 hairs that were removed from the active margins of patches at each time point. Ki-67 levels were measured by immunohistochemical staining. Trink et al concluded that PRP significantly increased hair growth, increased Ki-67 levels, and decreased hair dystrophy compared with placebo. Yet, this study neglected to report the concentration of platelets, inclusion or exclusion of WBCs, and anticoagulant usage.

Uebel et al. carried out a study assessing the effectiveness of PRP in increasing the follicular unit yield in hair loss surgery. The study included 20 male patients, where follicular units embedded with platelet plasma growth factors were implanted on one side of the scalp and on the contralateral side untreated follicular units were implanted as controls. There was a statistically significant difference observed in the yield of follicular units, with a 15.1 percent increase in the yield of follicular unit density in the PRP embedded group. Moreover as opposed to many of the other applications of PRP, there are straightforward, objective, and quantifiable measures in terms of hair growth outcomes, making scientifically grounded conclusions increasingly possible in this PRP application.

Further reported clinical applications of PRP in aesthetic surgery are summarized in Appendix A.

Preparation and Terminology
There are numerous steps in PRP preparation, including: (1) blood collection; (2) centrifugation; (3) plasma aspiration; (4) potential second centrifugation; (5) selected supernatant removal; (6) mixing/resuspension of platelets; (7) activation; and (8) application. These processes are usually conducted in a variety of custom made (50%) or commercial systems. Appendix A highlights and details many of these variations in the current clinical applications, which include force of centrifugation, time of centrifugation, sequence and number of centrifugations, temperature, use of anticoagulation, and mechanism of activation. All of which are variables that may yield different platelet concentrations and hence produce variable clinical outcomes in a host of application settings. Based on these variations vaguely applied terminologies are often given to the resulting platelet concentrates. The common step that unites all methods is the use of differential centrifugation to separate the patient’s whole blood into three layers based on density (plasma,uffy coat, red blood cells). However, the force, time, and iteration are usually variable. Longer/more forceful centrifugation cycles may push platelets further down in the sediment layer, be a stimulus for growth factor discharge, and can potentially interrupt the cellular integrity. While the bottom layer of RBCs is discarded in all preparations, variable proportions of plasma anduffy coat can generate different platelet preparations. The resulting preparation has been classified according to the extent ofuffy coat inclusion (specifically the presence of leucocytes) and the use of anticoagulation (specifically the formation of fibrin matrix) into four main categories: (1) pure platelet rich plasma (P-PRP); (2) leucocyte-rich platelet rich plasma (L-PRP); (3) pure platelet-rich fibrin (P-PRF); and (4) leucocyte platelet-rich fibrin (L-PRF). Among these preparations, PRF is an activated fibrin-based biomaterial/gel, not a liquid platelet suspension. Precise determination, in practice, of the exact resultant platelet preparation, as delineated above, however is not so simple. Accurate terminology has thus been frequently avoided in many studies. As a result, the majority of aesthetic reports (82%) only use the broad PRP term.

While this initial classification is useful in dividing the PRP variants, there are many important additional factors that complicate PRP studies, since they affect the final platelet product. This makes even intra-group comparisons difficult.

Notably, the vast majority of studies do not document the baseline concentration of platelets within the patient’s whole blood (0%) nor the final concentration in the prepared PRP (16%). This aspect is vital for comparative evaluations since final platelet concentration dictates the dosage of bioactive molecules available
to the tissues. The normal human platelet levels range from 150,000 to 450,000/μL, a 3-fold difference that clearly impacts the resulting PRP concentration independent of preparation technique. Moreover, simply reporting that the PRP is concentrated 4× does not provide accurate dosage information. Like many pharmaceutical drugs, a dose response relationship is mandatory to establish clinical indications, treatment guidelines, adverse events, side effects, and to titrate the therapeutic dose. In PRP, a dose-dependent relationship has been previously reported. There is a linear correlation between the platelet concentration and proliferation of mesenchymal stem cells, fibroblasts, and in the formation of type I collagen.65,68 Thus in order for any scientifically grounded conclusions to be made, the concentration of platelets in the applied product is fundamental to establish clinical effectiveness, guide treatment, and grade outcomes. Without these two values, the baseline and final platelet concentrate, PRP administration becomes a blind process where unknown levels of bioactive molecules are utilized. Therefore, future reporting of platelet concentrations in both whole blood and PRP should be a requisite for all clinical studies.

Not to be disregarded are the variety of drugs that can affect platelet function, including aspirin, statins, antibiotics, and serotonin reuptake inhibitors.69 Even small amounts of aspirin (30 mg) can irreversibly inhibit the cyclooxygenase-1 pathway by blocking the release of thromboxane A₂, which is involved in the platelet activation pathway, and potentially decreasing the effect of applied PRP. Thus, particularly in this initial phase of PRP investigation, patient medications should be considered a noteworthy variable in examining PRP efficacy.

Anticoagulation is a further element of PRP preparation that must be consistently reported. Utilization of sodium citrate, trisodium citrate, acid citrate dextrose, trisodium phosphate, ethylenediaminetetraacetic acid, and heparin have all been described. Not only could the choice of anticoagulant impact the platelet yield, but it could also potentially impact platelet function through alterations in pH.65,66,70 Specific documentation of anticoagulation use is overlooked in almost half of the studies (53%), representing another significant deficiency. While the majority of studies that report the anticoagulation use sodium citrate (50%) or acid citrate dextrose (30%), it is difficult to deduce any superiority of one over the other, due to the host of confounding variables.16,20,23,26,30,33,36,38,40,41,44,45,47

A point that appears to have been overlooked in the majority of reports is the use of a consistent platelet aggregation inhibitor. It has been suggested that prostaglandin E₁ (PGE₁) be added in addition to one of the above anticoagulants to ensure proper dispersion of the platelets within the platelet concentrate to minimize degranulation.66

The step in which anticoagulation is utilized or reversed dictates whether the platelet concentrate is considered to be activated at the time of application. In order for growth factors to be released, the platelet must become activated exogenously and/or endogenously through the interaction with thrombin, thromboxane A₂, adenosine diphosphate, collagen, or platelet activating factor. This process is often carried out exogenously by adding calcium chloride (45%), which counters the anticoagulant sequestration/precipitation of calcium ions, allowing coagulation and platelet activation to proceed. Administration of activated (a developing fibrin clot) vs inactivated PRP, influences the molecular kinetics and the way in which molecules are presented to their receptors.62 There is no clear consensus on the benefits/detriments of exogenous activation, yet the majority of studies activate PRP at the time of application (71%).

Lastly, the impact of PRP leucocyte content has been controversial with inconsistent reporting.52 While some studies suggest a positive effect from the antimicrobial properties and increased VEGF content, other reports associate it with inflammation and tissue damage.71-73 Since only 29% of papers documented this variable, precise determination of leucocyte composition of the final PRP product was not possible in most studies (71%), rendering outcome analysis more complex.

There are various protocols claiming to have the optimal conditions in their methods of anticoagulation, centrifugation, and activation, yielding the highest platelet concentration.4,65,74,86 These studies highlight the fact that the preparation technique can result in significantly different yields, concentrations, and platelet viability. These variables not only influence the eventual concentration of bioactive molecules released from the platelet granules, but they also influence the clinical efficacy of each PRP preparation.87

**Platelet-Rich Plasma Classification**

To date, there have been no recommended PRP descriptors proposed in the field of aesthetic surgery. The inconsistent reporting of significant PRP variables, discussed in our review, warrants attention and clarification. As noted above there are a number of factors that must be precisely documented, to allow proper standardization of the dose response relationship, to establish clinical guidelines, and to titrate accurate PRP dosage. Taking these factors into consideration and building upon previously described classification systems, specifically the orthopedic PAW classification system proposed by DeLong et al.88 we recommend a set of descriptors organized by the FIT PAW acronym (Figure 2). The **FIT PAW** classification is composed of 7 critical components: (1) the Force of centrifugation; (2) the Iteration or sequence of centrifugation; (3) the Time of centrifugation; (4) Platelet concentration (baseline of patients...
whole blood and final PRP product); (5) Anticoagulant use; (6) the utilization of an Activator including the type and amount; and (7) the composition of White blood cells.

We believe that this is the next critical step in determining the utility of PRP in aesthetic surgery, as well as other fields. Like any novel application in medicine, evolution and progress are dependent upon the accurate documentation of research, and the use of consistent parameters and objective outcome measures. Since PRP conceptually achieves its clinical effect through the release of bioactive molecules, like any drug, a dose-response estimation is critical in establishing clinical effectiveness, and titrating therapeutic levels. Thus, the main limitations of current PRP research are the inaccurate description of PRP composition, dosing, activation, and the use of subjective outcome measures. Recently, similar critiques have been emphasized in letters to the editor in response to published PRP studies.89,90 Unless and until standardization of preparation, application, and objective measures are achieved, the efficacy of this promising and inexpensive bioactive agent will continue to be questioned and debated.

Limitations
Spectrum bias, yielding inadequate identification and selection of studies, could limit the universality of these findings. Yet numerous authors remain confident that the vast majority of pertinent clinical articles relating to PRP in aesthetic surgery have been identified between the two databases. Inter-rater reliability was not statistically calculated for the selection of studies and data, thus unquantified variability could be present. The authors did not calculate statistical significance regarding study inclusion and exclusion, because all differences were discussed and resolved. While the authors could not control for publication bias, this remains an underlying factor in systematic reviews that could attest to the overwhelmingly positive outcomes in PRP application.

CONCLUSION
The purpose of this paper is to highlight the lack of reported scientific rigor, which has placed major limitations on the use of PRP. The recruitment of bioactive molecules that can enhance wound healing, and induce tissue regeneration in a cost effective manner has great potential. Nevertheless, the current literature is disappointing given the inconsistent reporting of PRP preparation techniques, precise composition, mechanism of activation, and the paucity of objective outcome measures to prove therapeutic benefit. This renders meaningful meta-analysis of the available reported data, at present, unrealistic. Therefore, the evidence for PRP clinical effectiveness in aesthetic practice remains largely speculative.

To date, there have been no recommended PRP descriptors proposed in the field of aesthetic surgery. We recommend the reporting of a set of PRP criteria to allow for improved comparisons across studies and scientifically grounded conclusions to be made. Building upon the PAW classification described by DeLong et al, we propose a modified FIT PAW classification that contains steps to standardize PRP reporting. Should such steps be taken, it is possible that PRP might find a more significant place in the wound-healing algorithm. Finally, we advocate for the employment of objective parameters and validated patient reported outcome scales in measuring the results in future PRP studies.

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