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CASE REPORT EXPERIMENTAL/SPECIAL TOPICS

The Effects of Platelet-Rich Plasma on Recovery Time and Aesthetic Outcome in Facial Rejuvenation: Preliminary Retrospective Observations

Joep C. N. Willemsen · Berend van der Lei · Karin M. Vermeulen · Hieronymus P. J. D. Stevens

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Abstract

Background This study focused on the possible effect of platelet-rich plasma (PRP) on recovery time and aesthetic outcome after facial rejuvenation. We conducted a retrospective analysis with regard to recovery time and the aesthetic improvement after treatment among four groups of patients: those treated with fat grafting only (Group I), those treated with fat grafting and PRP (Group II), those treated with a minimal access cranial suspension (MACS)-lift and fat grafting (Group III), and those treated with a MACS-lift, fat grafting, and PRP (Group IV).

Methods For the first part of this study, i.e., evaluation of recovery time after surgery, the following selection criteria were used: nonsmoking females, aged 35–65 years, with a complete documented follow-up. In total, 82 patients were included in the evaluation of patient-reported recovery time. For the second part of the study, i.e., evaluation of potential differences in aesthetic outcome, the records of these 82 patients were screened for the presence of pre- and postoperative standardized photographs in three views (AP, lateral, and oblique), leaving 37 patients to evaluate. A questionnaire was developed to evaluate the aesthetic outcome in all four groups of patients. This questionnaire was given to an expert panel that consisted of ten plastic surgeons.

Results The addition of PRP to a lipofilling procedure resulted in a significant drop in the number of days needed to recover before returning to work or to restart social activities [Group I (no PRP) took 18.9 days vs Group II (PRP) took 13.2 days, $p = 0.019$]. There seemed to be no effect when PRP was added to a MACS-lift + lipofilling procedure. Also, the aesthetic outcome of the lipofilling and MACS-lift + lipofilling groups that received PRP (Groups II and IV) was significantly better than the groups without PRP (Groups I and III).

Conclusions Adding PRP to facial lipofilling reduces recovery time and improves the overall aesthetic outcome of a MACS-lift.

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Keywords Facial rejuvenation · Platelet-rich plasma · Lipofilling · MACS-lift · Fat graft survival · Recovery time · Aesthetic outcome · Skin rejuvenation

Introduction

Since the first transfer of autologous fat as a deepithelialized dermofascial graft in the 1890s and as an injectable graft in the 1920s [1], it took more than 80 years before autologous fat grafting techniques were used on a regular base in facial rejuvenation. Now, it is used in addition to lifting procedures to improve the specific signs of facial aging related to loss of volume [2, 3].

J. C. N. Willemsen (✉) · B. van der Lei
Department of Plastic Surgery, University Medical Center Groningen, Groningen, The Netherlands
e-mail: j.c.n.willemsen@umcg.nl

J. C. N. Willemsen · B. van der Lei · H. P. J. D. Stevens
Bergman Clinics The Hague, Binckhortslaan 149, 2516 BA The Hague, The Netherlands
e-mail: stevens.hp@gmail.com

K. M. Vermeulen
Department of Epidemiology, University Medical Center Groningen, Groningen, The Netherlands

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The unpredictability of the amount of fat graft that takes and to a certain degree the limited fat graft survival after lipofilling has been described [4] and is still a subject for debate [4–7]. Several factors may play a role in fat graft take, such as the harvesting technique [8], the method used for processing the harvested fat [9], and the fat injection technique [10]. Also, the vascularization of the receptor area seems to be of significant relevance [11]. Several studies have demonstrated that fat graft take may significantly increase with the use of platelet-rich plasma (PRP) extracted from whole blood [12, 13] and that PRP may enhance wound healing and thereby speed up recovery time [14–16]. Moreover, PRP by itself might also improve the quality of the skin by increasing elasticity [17, 18].

Since 2010 we have routinely used PRP in facial rejuvenation procedures. We have the impression that using PRP significantly reduces recovery time and enhances the aesthetic outcome. To elucidate these effects, this retrospective study of recovery time and aesthetic outcome was undertaken in the following groups of patients: those treated with fat grafting only (Group I), those treated with fat grafting and PRP (Group II), those treated with a minimal access cranial suspension (MACS)-lift and fat grafting (Group III), and those treated with a MACS-lift, fat grafting, and PRP (Group IV).

Materials and Methods

Patient Selection

All cases were operated on between 2008 and 2012 in the Bergman Clinics, The Hague by the senior author (HPJD Stevens). In cases where loss of volume was the major contributing factor to facial aging, lipofilling was performed. In cases where significant ptosis and subsequent descent of tissues also were observed, lipofilling was combined with a MACS-lift. Since the introduction of PRP in 2010, all cases in which lipofilling was used were treated with PRP simultaneously. As a result, a consecutive series of patients could be analyzed without any bias for the use of PRP.

Evaluation of Recovery Time and Aesthetic Outcome

To evaluate recovery time after surgery, the following selection criteria were used: nonsmoking females, aged 35–65 years, who underwent lipofilling of the face with or without a MACS-lift, with or without the addition of PRP, and for whom there was a complete documented follow-up (including a completed standardized survey that was sent to all patients 4 weeks after the procedure and which included questions regarding recovery time). In total, patient-reported recovery time was evaluated for 82 patients. Recovery time was defined as the number of days that passed before patients considered themselves capable to return to work or to restart social activities.

For evaluation of the aesthetic outcome, records of these 82 patients were screened for the presence of pre- and postoperative standardized photographs in three views (anteroposterior, lateral, and oblique); this left 37 patients for evaluation. Photos were taken during their regular 3-month follow-up appointment. All photographs were cropped with the analyzed area placed on a uniform-colored background; obviously, photos were not edited in any way that could interfere with interpretation. The anteroposterior (AP) photographs were taken in the Francoforte plan, mimicking anatomical skull position.

A questionnaire was developed (based on several existing surveys [19–21]) to evaluate the aesthetic outcome in all four groups of patients. It was given to an expert panel that consisted of ten plastic surgeons with experience in the field of facial aesthetic surgery. Members of the expert panel had not operated on any of the included patients. Each page of the questionnaire contained the pre- or postoperative standardized photographs of just one patient in the three views mentioned [anteroposterior, (AP) lateral (Lat), and oblique (Oblq)] and four questions. Questions 1–3 were scored by using a visual analog scale ranging from 0 to 10, with lower scores representing a lower aesthetic result (Table 2). In total there were 74 pages. All photographs and questions were placed in a digital environment. Page order was randomized, mixing groups and pre- and postoperative pages and procedures throughout the survey. No postoperative photo preceded or followed the preoperative photo of the same patient, and no information was given to the panel on whether a photo was pre- or postoperative or what procedure had been used.

MACS-Lift

MACS-lifting was performed as described by Tonnard and Verpaele [22] with some minor modifications. A three-lobbed pretrageal incision was used (instead of a retrotragal incision), subsequently running vertically upward into the sideburn (instead of running in front of the sideburn). Subcutaneous dissection was extended 1–2 cm anterior to the border of the parotid gland and extended 4 cm under the angle of the mandible, revealing the platysma muscle clearly. One centimeter cranial to the helical root, a pretrageal purse-string suture was anchored to the deep temporalis fascia. Incorporating the SMAS overlying the parotid gland, this first purse-string suture runs inferiorly in a narrow U-shape well beyond the angle of the mandible, including the platysma muscle firmly, before returning to the starting point 1 cm anterior to the first leg of the suture.

In this fashion the suture uses the angle of the mandible as a pulley, resulting in a more pronounced effect on the floor of the mouth when tied. The second purse-string suture starts from the same anchoring point and runs anterior to the first loop, making its turn at the level of the retaining ligaments just above the jowls.

Lipofilling or Micro Fat Grafting

The Coleman technique [23, 24] for fat harvesting and injection was used but modified with the use of a smaller custom-made cannula for harvesting (inner diameter 1.3 mm). The donor sites for harvesting were the upper legs in all patients. Approximately three times more fat was harvested than the estimated amount required for the procedure. Fat was centrifuged for 2.5 min at the maximum speed of 3,000 rpm (IEC MediSpin Centrifuge), after which the oily fraction (top layer) and liquid waste (infiltrate, blood in the bottom layer) were drained away, preserving the preadipocyte-rich pellet [9]. Fat injection was performed using a short curved Coleman cannula with which droplets were evenly injected in a 3-dimensional space. Between 13 and 23 cc of fat was injected in the superficial and deeper planes in each side of the face. Superficial injection was performed in the temporal region (above the superficial temporal fascia for reasons of vascularization), crow's feet area, and anterior part of the cheek (to allow for direct support of the skin in the latter two zones). Injection in deeper planes was performed in the malar eminence, suborbicularis oculi fat (SOOF), tear trough, central part of the midface, the nasolabial folds, and the marionette folds. Injection in these areas was performed mainly to recreate curves and or projection in the face. Injection in the lips and upper eyelid was performed on indication only.

PRP Preparation

Whole blood (27 cc) from the patient was introduced into the Biomet GPS-III© device (after adding 3 cc of citrate to prevent clotting). Fifteen minutes of centrifugation at 3,000 rpm allowed for separation of the whole blood into its three fractions: erythrocytes, platelet-poor plasma (PPP), and platelet-rich plasma (PRP). A total of 3 cc of PRP was yielded in this fashion. The PRP was activated by adding 0.45 cc of $CaCl_2$ (10 %, matching 15 vol% Ca^{2+}) 1 min before injection. The same amount of PPP (3 cc) was used as tissue glue in the MACS-lift by irrigating the pocket. In all other cases PPP was not used.

After PRP activation, the 3 cc of PRP + 0.45 cc of $CaCl_2$ was injected into the lipofilling planes, transcutaneously in small aliquots in a standardized fashion: 1.7 cc was used per side of the face. With an average amount of 15 cc of fat per side, the PRP:fat mix ratio was around 1:10.

Table 1 Recovery time

	Group I	Group II	
Lipofilling	No PRP ($n = 25$)	PRP ($n = 18$)	
Return to work/social activities [mean (SD)]	18.9 (8.5)	13.2 (6.4)	*$p = 0.019$
	Group III	Group IV	
MACS + lipofilling	No PRP ($n = 17$)	PRP ($n = 22$)	
Return to work/social activities [mean (SD)]	18.7 (9.2)	17.5 (10.9)	*$p = 0.424$

Patient-reported number of days after surgery before returning to work/social activities

* Independent samples *t*-test

Statistics

All statistical tests were performed under the supervision of a senior statistician. Descriptive statistics were used to evaluate the population's mean (standard deviation [SD]) age at the time of surgery. Recovery time was defined as the number of days required before returning to work or restarting social activities. A mean number of days was calculated for each group and compared using an independent *t* test (Table 1).

To determine aesthetic improvement and gain after the procedure, scores assigned to the preoperative photos were subtracted from those for the postoperative photos (Table 2). A mean and median number of points gained after the procedure assigned by the ten blinded observers were calculated for every group. A Mann–Whitney *U* test (2-tailed exact) was used to test for significant differences. Data from the patients' records and survey were analyzed using SPSS statistical software (IBM, Chicago, IL, USA).

Results

Of the 82 patients enrolled in this study, 25 underwent lipofilling without PRP (Group I), 18 had lipofilling with PRP (Group II), 17 received a MACS-lift with lipofilling without PRP (Group III), and 22 were treated with a MACS-lift with lipofilling and PRP (Group IV). There was no significant difference in patient ages among the groups when evaluating recovery time and aesthetic outcome, and no significant difference between the observer-assigned

Table 2 Aesthetic outcome

Lipofilling	No PRP ($n = 9$)			PRP ($n = 10$)			
	Mean	Median	Mean rank	Mean	Median	Mean rank	Sig.[a]
Q1	1.211	1	87.02	1.580	1	103.14	(0.039)
Q2	1.355	1	92.93	1.910	1	97.82	(0.536)
Q3	1.644	1	83.23	1.740	2	106.55	(0.003)
MACS + lipofilling	No PRP ($n = 8$)			PRP ($n = 10$)			
	Mean	Median	Mean rank	Mean	Median	Mean rank	Sig.[a]
Q1	0.887	1	78.19	1.580	1	100.35	(0.004)
Q2	1.137	1	80.49	1.910	1	98.51	(0.019)
Q3	1.550	1	87.94	1.740	2	92.55	(0.553)

Q1 Taking the patient's age into account, how would you assess the appearance of this face? (on a scale from 1 to 10, with 1 = much older for age, 5 = according to age, and 10 = much younger for age)

Q2 NOT taking age into account, how would you assess the appearance of this face? (on a scale from 1 to 10, with 1 = many signs of aging and 10 = no signs of aging)

Q3 NOT taking age into account, how would you assess the facial volume of the patient? (on a scale from 1 to 10, with 1 = most profound loss of volume and 10 = no loss of volume)

[a] Mann–Whitney *U* test using median, 2-tailed exact

preoperative mean aesthetic scores when comparing Group I versus Group II, and Group III versus Group IV.

Patients who underwent lipofilling with PRP (Group II) reported that it took significantly fewer days to return to work or restart social activities than those who did not have PRP [Group I (no PRP) 18.9 days vs Group II (PRP) 13.2 days, $p = 0.019$; see Table 1)]. In patients who underwent a MACS-lift with lipofilling with or without PRP, the effect was less distinct: return to work or restart social activities took an average of 18.7 days without PRP (Group III) versus 17.5 days when PRP (Group IV) was used ($p = 0.424$).

When PRP was added to a lipofilling procedure, the patient's appearance improved significantly more than those who had a lipofilling procedure without PRP (see Table 2). For Question 1, appearance with respect to the patient's age, the PRP group improved significantly more: no PRP: 1.211 versus PRP: 1.580 points gained ($p = 0.039$). Question 2, appearance without taking the patient's age into account, showed more improvement, but not a significant one: no PRP: 1.355 versus PRP: 1.910 points gained ($p = 0.536$). Question 3, regarding facial volume, again showed a significant difference with respect to the use of PRP: no PRP: 1.644 versus PRP: 1.740 points gained ($p < 0.01$).

The addition of PRP also improved the results after a MACS-lift plus lipofilling. Questions 1 and 2 showed significantly more improvement: Question 1: no PRP: 0.887 versus PRP: 1.580 points gained ($p < 0.01$), and Question 2: no PRP: 1.137 versus PRP: 1.910 points gained ($p = 0.019$). Question 3, regarding facial volume, the PRP group again showed more improvement, but the result was not significant: no PRP: 1.550 versus PRP: 1.740 points gained ($p = 0.553$).

Fig. 1 Average results after a MACS-lift with lipofilling and PRP. A 52-year-old female **a** before and **b** 3 months after surgery

Average results are presented in Figs. 1 and 2.

Discussion

Our retrospective analysis demonstrated that PRP improves the overall outcome of either lipofilling or a MACS-lift combined with lipofilling in facial rejuvenation with respect to recovery time and aesthetic outcome. Whether

Fig. 2 Average results after a lipofilling with PRP procedure. A 48-year-old female **a** before and **b** 3 months after surgery

this is due to improved fat graft take or to an intrinsic rejuvenation effect of the PRP still has to be elucidated.

Thus far, the number of studies that have used quantitative analyses as outcome variables for recovery to assess the effect of PRP is limited. In cases in which the beneficial effect of PRP is mentioned in the literature (in relation to, e.g., tendon repair, fat graft survival, or increased bone density), the author usually refers to the end result after healing is complete, not to recovery time itself. The study of Na et al. [14] demonstrated a significant reduction in postoperative recovery time and improved healing after fractional carbon dioxide laser resurfacing treatment to the inner arms when combined with PRP injection in the laser-treated area. These findings are supported by the study of Lee et al. [15]. They showed in a split-face trial that when using fractional carbon dioxide laser resurfacing for treatment of facial acne scars, a significant reduction in erythema and a faster clinical recovery rate could be achieved when adding PRP to the wound area.

Accelerated wound healing and thus reduced recovery time when PRP is added to the lipograft might be explained by the addition of a significantly increased amount of platelet-derived growth factors. These growth factors trigger homing, migration, proliferation, and differentiation of a wide variety of cells [16, 25]. In tendon repair, it has been demonstrated that the local inflammatory response is significantly increased when PRP is added [26]. In addition, a higher number of local inflammatory cells could speed up clearance of cellular debris, hematoma, and even bacteria, factors that greatly influence the process of wound healing, including its duration.

The addition of PRP made a significant impact on the recovery time of the patients who received lipofilling only. This effect seems to be absent when lipofilling is combined with MACS-lifting. This might be because the PRP was injected only in the areas where lipofilling was performed and not in the areas of dissection involved in the lifting procedure. Also, the extended dissection of the MACS-lift results in a significantly larger traumatized area (and thus variation in recovery) than the lipofilling part of the procedure, possibly masking the effect of the PRP.

Results from this study further show that lipofilling is an effective treatment option in facial rejuvenation, as based on our photographic evaluation. The effect is probably caused by adding volume and reshaping the curves and contour of the face (Question 3, Table 2). Although the follow-up of this study is relatively short, we believe that the change in volume, confirmed to be present by our panel in their subjective evaluation, is relevant. The study of Nishimura et al. [27] showed that fat graft necrosis, when it occurs, will peak around 30 days. Initiation of vascular ingrowth was seen at around 7 days, making further significant resorption unlikely after 60 days of follow-up. Further supporting facts are found in the well-conducted mice study of Thanik et al. [28] that used human fat. They reported that 82 % of graft volume was, as they described, "viable and vascularized" after 8 weeks.

Our results also show that adding PRP improves the outcome of facial rejuvenation, even more than lipofilling alone. This might be due to an improved angiogenesis pathway and formation of new capillaries, enhancing the viability of the injected fat cells, possibly even allowing for better regeneration. This idea is supported by some fundamental animal studies that demonstrated there is improved graft take when using PRP [12, 13, 29, 30]. A greater number of viable adipocytes and infiltrating blood vessels was found in all these studies. Although the exact underlying mechanism of the findings is still unknown, the improved graft take might be due to a greater number of surviving adipose-derived stem cells (ADSCs). The study by Fukaya et al. [31] showed that PRP can inhibit apoptosis of these cells by reducing DAPK1 and BIM mRNA expression. Fat grafts enriched with ADSCs show a higher graft take [32], emphasizing the important role of this cell in graft survival. Also, according to the in vitro study by Rophael et al. [33], the mix of growth factors in PRP changes the late differentiation of the ADSCs, inducing late de novo adipogenesis, which might also contribute to end-graft volume.

Platelet-rich plasma by itself might also be responsible for the effect of facial rejuvenation. Michalevicz et al. [34] found that vascular muscle cells require mitogens such as platelet-derived growth factor (PDGF) to proliferate and they proved that PDGF is one of the most potent mitogenic factors present in human serum [35]. PDGF might not only enhance the process of inflammation and angiogenesis, it might also help improve skin quality and texture through collagen synthesis and formation. Patil et al. [36] found

that collagen synthesis in humans is critically dependent on the extracellular environment and is dose dependent on procollagenase gene expression, especially for the synthesis of type II collagen. Several studies show skin improvement after direct cutaneous injection of PRP [17, 37]. Prospective studies with only PRP, only fat, and a combination of both might further elucidate the underlying mechanism.

In conclusion, this study clearly demonstrates that adding PRP in facial rejuvenation reduces recovery time after lipofilling and improves the overall aesthetic outcome of both lipofilling and MACS-lifting combined with lipofilling. Both effects might be due to either improved fat graft take or to an intrinsic rejuvenation effect of the PRP. However, the influence of different methods of fat harvesting, processing, and injection of the fat; remains uncertain all of these aspects will have their own special effect on fat graft survival [9, 10] and thereby may contribute to the variation in the final result.

Study Limitations

Because this study was performed retrospectively, all subjects appeared for their postoperative evaluation with their normal make-up on and had not been informed before the postoperative appointment that any photographs taken would be used for statistical analysis. For this reason, the authors believe that no bias was introduced by the fact that all included subjects had some makeup on in their postoperative photographs. As the panel members who evaluated the photographs were not informed about this situation, they remained blinded (statistically speaking). The fact that pre- and postoperative photographs were placed randomly throughout the survey should have further dampened any limitation in this respect.

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