Lipofilling and PRP for aesthetic facial rejuvenation
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THE EFFECTS OF PLATELET RICH PLASMA ON RECOVERY TIME AND AESTHETIC OUTCOME IN FACIAL REJUVENATION: PRELIMINARY RETROSPECTIVE OBSERVATIONS

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Chapter 3 - The Effects of Platelet-Rich Plasma on Recovery Time and Aesthetic Outcome

Introduction

This paper focuses on the possible effect of PRP (Platelet Rich Plasma) 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: a group of patients treated with fat grafting only (Group I), a group of patients treated with fat grafting with PRP (Group II), a group of patients treated with MACS lift and fat grafting (Group III) and a group of patients treated with MACS lift, fat grafting and PRP (Group IV).

Material and Methods

For the first part of this study, evaluating recovery time after surgery, the following selection criteria were used: Non-smoking females, aged 35-65 years, with a complete documented follow up. In total, 82 patients were included to evaluate patient reported recovery time.

For the second part of the study, evaluating potential differences in aesthetic outcome, records of these 82 patients were additionally screened for the presence of pre- and postoperative standardized photographs in three views (AP, Lateral, Oblique), leaving 37 patients to evaluate. A questionnaire was developed to evaluate the aesthetic outcome in all four groups of patients. This questionnaire was used in an expert panel that consisted of 10 plastic surgeons.

Results

The addition of PRP resulted in a significant drop in the number of days returning to work/restart of social activities when added to a lipofilling procedure (Group I: no PRP 18.9 days versus Group II: PRP 13.2 days, p=0.019). The effect seemed absent when added to a MACS-lifting 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).

Conclusion

Adding PRP to facial lipofilling reduces recovery time and improves the overall aesthetic outcome in MACS lifting.
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Introduction

Since the first transfer of autologous fat as de-epithelialised dermofascial graft in the 1890s and as injectable graft in the 1920s, it took more than 80 years before autologous fat grafting techniques were used on a regular base in facial rejuvenation: nowadays, it is used in addition to lifting procedures to improve the specific signs of facial aging related to loss of volume. Unpredictability of the amount of fat graft take and to a certain amount limited fat graft survival after lipofilling has been described and is still a subject for debate. Several factors may play a role in fat graft take, such as the harvesting technique, the method used for processing the harvested fat and the technique of fat injection. Also the vascularization of the receptor area seems to be of significant relevance.

Several studies have demonstrated that fat graft take may significantly increase with the additional use of Platelet Rich Plasma (PRP) extracted from whole blood and that PRP may enhance wound healing and thereby speed up recovery time. Moreover, PRP by itself might additional improve the quality of the skin by increasing elasticity.

Since 2010 we routinely use PRP in facial rejuvenation procedures. We clearly had the impression the additional use of PRP significantly reduces recovery time and enhances the aesthetic outcome. In order to elucidate these effects, this retrospective study with regard to recovery time and aesthetic outcome was undertaken in the following groups of patients: a group of patients treated with fat grafting only (Group I), a group of patients treated with fat grafting with PRP (Group II), a group of patients treated with MACS lift and fat grafting (Group III) and a group of patients treated with MACS lift, fat grafting and PRP (Group IV).

Material & methods

Patient selection

All cases have been operated between 2008 and 2012 in Bergman Clinics The Hague by the senior author. In cases where loss of volume was the major contributing factor of facial aging lipofilling was performed. In cases where also significant ptosis and subsequent descent of tissues was observed, lipofilling was combined with MACS-lifting. Since the introduction of PRP in 2010, subsequently all cases where 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

For evaluating recovery time after surgery, the following selection criteria were used: Non-smoking 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 with a complete documented follow up (including a completed standardized survey that was send automatically to all patients 4 week after the procedure including questions regarding recovery time). In total, patient reported recovery time was evaluated in 82 patients. Recovery time was defined by 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 additionally screened for the presence of pre- and postoperative standardized photographs in three views (AP, Lateral, Oblique). Photos were taken during their regular 3-month follow-up appointment, leaving 37 patients for evaluation. All photographs were cropped with the analyzed area.
placed on uniform colored background; obviously photos were not edited in any way that could interfere with interpretation. The anterior-posterior photographs were performed in the Francoforte plan, mimicking anatomical skull position.

A questionnaire was developed (based on several existing surveys\textsuperscript{19-21}) to evaluate the aesthetic outcome in all four groups of patients by an expert panel that consisted of 10 plastic surgeons with experience in the field of facial aesthetic surgery. Members of the expert panel had not operated 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), Oblique (Oblq)) and four questions. Questions one to three were scored by using a visual analogue scale. This scale ranged from 0 to 10 with lower scores representing a lower aesthetic result (Table II). A total of 74 pages were constructed in this fashion. 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 page succeeded or preceded a preoperative page of the same patient and no information was given to the panel whether a page was pre- or postoperative or what procedure had been used

### MACS-lift

MACS lifting was performed as described by Tonnard and Verpaele\textsuperscript{22} with some minor modifications. A 3-lobbed pre-trageal incision was used (instead of a retrotrageal 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 four cm under the angle of the Mandibule, 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 one cm anterior to the first leg of the suture. In this fashion the suture uses the angle of the mandibule as a pulley, resulting in a more pronounced effect on the floor of the mouth when tied. The second purse-string suture started from the same anchoring point running anterior to the first loop making its turn at the level of the retaining ligaments just above the jowling.

### Lipofilling or micro fat grafting

The Coleman technique\textsuperscript{23, 24} for fat harvesting and injection was used but refined by using a smaller custom made canula for harvesting (inner diameter 1.3 mm). The donor sites for harvesting were the upper legs in all patients. Approximately 3 times more fat was harvested than the estimated amount required for the procedure. Fat was centrifuged for 2.5 minutes at the maximum speed of 3000RPM (IEC MediSpin Centrifuge), after which the oily fraction (top layer) and liquid waste (infiltrate, blood: bottom layer) were drained away, preserving the pre-adipocyte-rich pellet\textsuperscript{9}. Fat injection was performed using a short curved Coleman cannula by which droplets were evenly injected in a 3 dimensional space. Between 13 to 23 cc of fat were injected both in superficial as well as 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), crowfeet area, and anterior part of the cheek (to allow for direct support of the skin in the latter two zones mentioned). Injection in deeper planes was performed in the malar eminence, SOOF, tear trough, central part of the mid face, the nasolabial folds and the marionette folds. Injection here was predominantly performed to recreate curves and or
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projection in the face. Injection in the lips and upper eyelid was performed on indication only.

**PRP preparation**

27 cc whole blood of the patient was introduced in the Biomet GPS-III© device (after adding 3cc of citrate to prevent clotting). 15 Minutes of centrifugation at 3000 rpm allowed for gravitational 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 CaCl2 (10%, matching 15-volume % Ca2+), 1 minute prior to injection. 3 cc of PPP were used as tissue glue in MACS-lifting by irrigating the pocket. In all other cases PPP was not used.

After PRP activation, the 3cc of PRP + 0.45 cc of CaCl2 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.

**Statistics**

All statistic tests were preformed under supervision of a senior statistician. Descriptive statistics were used to evaluate the population’s mean age and SD at time of operation. Recovery time was defined as the number of days returning to work or restart the social activities. A mean number of days was calculated for every group and compared using an independent T-test (Table I).

To determine aesthetic improvement and gain after the procedure, scores assigned to the pre-operative pages were subtracted from the post-operative pages (Table II). A mean and median number of points gained after the procedure assigned by the 10-blinded observers was calculated for every group. A Mann-Whitney U (2-tailed exact) was used to test for significant differences. Data from the patients records and survey was analyzed using SPSS (IBM inc, Chicago,IL).

**Results**

Of the 82 patients enrolled in this study, 25 patients underwent lipofilling without PRP (Group I), 18 lipofilling with PRP (Group II). 17 Patients received a MACS-lifting with lipofilling without PRP (Group III) and 22 were treated by MACS-lifting with lipofilling and PRP (Group IV). No significant differences in patients’ age existed among the groups when evaluating recovery as well as aesthetic outcome, and no significant difference existed between the observer assigned pre-operative mean aesthetic scores when comparing group I versus group II, and group III versus group IV.

Patients that underwent lipofilling with PRP reported a significant lower number of days to return to work/restart social activities (Group I: no PRP 18.9 days versus Group II:PRP 13.2 days, p=0.019; see Table I). In patients that underwent a MACS-lifting with lipofilling with or without PRP the effect was less distinct: return to work/restart social activities was 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 patients improved significantly more then from a lipofilling procedure without PRP (see Table II). With the first question, appearance regarding the patients’ age, the PRP group improved significantly more: no PRP: 1.211 vs. PRP: 1.580 points gained (p=0.039). Question 2, appearance disregarding the patients’ age,
showed more improvement, but not a significant one: No PRP: 1.355 vs. PRP: 1.910 points gained (p=0.536). Question 3, regarding facial volume, again showed a significant difference: No PRP: 1.644 vs. PRP: 1.740 points gained (p<0.01).

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

Average results are presented in Figures I and II.

Table I: Recovery time*

<table>
<thead>
<tr>
<th></th>
<th>Group I (PRP-)</th>
<th>Group II (PRP+)</th>
<th>p**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipofilling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-RTW/social activities</td>
<td>18.9 (8.5)</td>
<td>13.2 (6.4)</td>
<td>0.019</td>
</tr>
<tr>
<td>MACS + Lipofilling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-RTW/social activities</td>
<td>18.7 (9.2)</td>
<td>17.5 (10.9)</td>
<td>0.424</td>
</tr>
</tbody>
</table>

*Recovery time was defined as the patient reported number of days after surgery returning to work (RTW)/social activities

**Independent samples t-test

Discussion

Our retrospective analysis demonstrates that PRP improves the overall outcome of either lipofilling or a MACS lift combined with lipofilling in facial rejuvenation, both in recovery time as well as with regard to aesthetic outcome. Whether 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 case any beneficial effect of PRP is mentioned in literature (in relation to e.g. tendon repair, fat graft survival or increased bone density) it 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 post-operative 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 thereby reduced recovery time when adding PRP 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\textsuperscript{26}. In addition, a higher number local inflammatory cell 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 that received lipofilling only. This effect seems to be absent when lipofilling is combined with a MACS-lifting. This finding might be explained by the fact that the PRP was injected only in the areas where lipofilling was performed and not in the areas of the dissection of the lifting procedure. Also the extended dissection of the MACS-lift results in a significantly larger trauma area (thus variation in recovery) then the lipofilling part of the procedure, possibly masking the effect of the PRP.

Results from this study further support 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 of curves and contour of the face (Question 3, Table II).

<table>
<thead>
<tr>
<th>Tabel II: Aesthetic outcome</th>
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<table>
<thead>
<tr>
<th>Lipofilling</th>
<th>No PRP (n=9)</th>
<th>PRP (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Median</td>
<td>Mean Median</td>
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<tr>
<td>-Q1</td>
<td>1.211 1</td>
<td>1.580 1</td>
</tr>
<tr>
<td>-Q2</td>
<td>1.355 1</td>
<td>1.910 1</td>
</tr>
<tr>
<td>-Q3</td>
<td>1.644 1</td>
<td>1.740 2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MACS + Lipofilling</th>
<th>No PRP (n=8)</th>
<th>PRP (n=10)</th>
</tr>
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<tr>
<td></td>
<td>Mean Median</td>
<td>Mean Median</td>
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<tr>
<td>-Q1</td>
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<td>1.580 1</td>
</tr>
<tr>
<td>-Q2</td>
<td>1.37 1</td>
<td>1.910 1</td>
</tr>
<tr>
<td>-Q3</td>
<td>1.550 1</td>
<td>1.740 2</td>
</tr>
</tbody>
</table>

Q1: Taking the patient’s age into account: How would you assess the appearance of this face? (on a scale from 1-10, 1: much older for age -- 5: according to age -- 10: much younger for age)

Q2: NOT taking age into account: How would you assess the appearance of this face? (on a scale from 1-10, 1: very many signs of aging -- 10: no signs of aging)

Q3: NOT taking age into account: How would you assess facial volume of the patient? (on a scale from 1-10, 1: most profound loss of volume -- 10: No loss of volume)

* Mann-Whitney U test using median, 2-tailed exact
Although the follow-up of this study is relatively short, authors believe that the change in volume, as confirmed to be present by our panel members in their subjective evaluation, is of relevance.

The study of Nishimura et al.\textsuperscript{27} showed that in case there is fat graft necrosis, it will peak around 30 days. Initiation of vascular ingrowth was seen 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.\textsuperscript{28} using human fat. They reported that 82\% of graft volume was, as they described ‘viable and vascularized’ after 8 weeks.

Our results in addition show that adding PRP improves the outcome of facial rejuvenation even further than lipofilling does 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 demonstrating improved graft take when using PRP\textsuperscript{12,13,29,30}. A higher number of viable adipocytes and infiltrating blood vessel was found in all these studies. Although the exact underlying mechanism of the findings are still unknown, the improved graft take might be due to a higher number of surviving ADSC’s (Adipose derived stem cell): the study of Fukaya et al. showed that PRP can inhibit apoptosis of these cells by reducing DAPK1 and BIM mRNA expression\textsuperscript{31} . Fat grafts enriched with ADSC’s show a higher graft take\textsuperscript{32}, emphasizing the important role of this cell in graft survival. Also, according to the in vitro study of Rophael et al., the mix of growth factors in PRP changes the late differentiation of the ADSC, inducing late de novo adipogenesis\textsuperscript{33}, 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.\textsuperscript{34}, found that vascular muscle cells require mitogens such as PDGF to proliferate and proved that PDGF is one of the most potent mitogenic factors present in the human serum\textsuperscript{25}. PDGF might not only enhance the process of inflammation and angiogenesis but also helps in improving skin quality and texture through collagen synthesis and formation. Patil et al.\textsuperscript{36} found that collagen synthesis in human is critically dependent on the extracellular environment and is dose dependent on pro-collagenase gene expression especially for the synthesis of type II collagen. Several studies show skin improvement after direct cutaneous injection of PRP\textsuperscript{37,38}. Prospective studies with only PRP, only fat and a combination of both might further elucidate the underlying mechanism.

Figure I and II. Average results after a MACS-lift with lipofilling and PRP. A 52-year old female before (A) and 3 months after (B) surgery, and A 48-year old female after a lipofilling with PRP procedure, before (C) and 3 months after (D) surgery.
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, it remains uncertain what the influence is of different methods of fat harvesting, processing and injection of the fat; 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**

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

Conflict of Interest: None
Funding: None
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References
