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Effect of Platelet-Rich Plasma on Resorption Rate of Large Volume Autologous Fat Transfer as Evaluated by Computed-Tomography Volumetry

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Abstract: Background and objectives: Although fat grafting is a very common procedure that is being practiced among plastic surgeons, serving diverse purposes ranging from post-traumatic reconstruction to mere aesthetic enhancements of body contour, however the level of evidence beyond such practice is still lacking. Despite clinical optimism associated with autologous fat transfer, uncertainty remains among practitioners regarding the viability of transplanted fat. The optimal technique for harvesting, processing, and grafting continues to be debated. Graft resorption remains highly variable, with 40 to 80 percent graft take reported. The aim of this study is to evaluate the resorption rate of large volume of autologous fat transfer using CT volumetry and the effect of platelet-rich plasma on that rate. **Methods:** The study is a prospective randomized clinical trial. Patients included in the study were100 patients seeking breast or buttocks augmentation by autologous fat transfer, in all cases the left side was injected with PRP. CT volumetry was done to evaluate fat desorption. **Results:** we found that the percentage of fat resorption was around (37%). We also found no significant difference in resorption in the PRP injected sides compared to the non-injected side. **Conclusion:** Resorption rate following large volume fat transfer is around 37% and Platelet rich plasma has no effect on resorption rate. Still, most of patient gave very satisfactory outcome, with no complications which reflect superior result of fat injection as an aesthetic procedure.
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Key words: Fat grafting, Platelet rich plasma (PRP), Fat resorption, CT volumetry.

1. Introduction

Autologous fat grafting is a common technique for treating volume and contour abnormalities not only in aesthetic procedures, but also in reconstructive surgery. In 2013, a survey by Kling and colleagues among the American society of plastic surgeons showed that nearly 80% of plastic surgeons have used fat grafting in their practice.[1]

Fat grafting has been used for diverse applications such as facial contouring, breast augmentation, radiation damage, breast capsular contracture, posttraumatic deformities, congenital anomalies, and burn injuries.[2–5]

Autologous fat grafts are easily accessible and considered to be simple, low cost surgical procedure. Additionally, they lack immunogenicity, and can be harvested from a region that is generally more abundant and injected into a secondary site.[5]

Nevertheless, varying levels of failure were reported in the form of asymmetry caused by fat resorption. Such failures have demonstrated the importance of the techniques used to achieve desirable and sustainable long-term outcomes to address multiple aesthetic and reconstructive problems[6,7]

Beginning in the early 1980s, fat grafting regained its popularity once again in response to multiple positive reports of fat grafting were.[8–10]

Currently, no consensus has been reached regarding the optimal technique with a multitude of variables that remain controversial either in the infiltration, harvest, preparation and placement techniques.[11]

Ongoing research on how fat grafts survive has led to the development of two main theories. One, graft survival theory, further advanced the old Peer cell survival theory and another, graft replacement theory, based on new discovery and understanding of adipose-derived stem cells (ADSCs), based on a number of recently well-conducted experimental studies.[12]

Currently, there is no consensus concerning the best way to process the harvested fat before reinjection. Based on recent literature, it is

hypothesized that adding PRP to fat preparation may be a reliable way to bring appropriate nutrient at the early moments of transplantation to improve fat survival and render the result more predictable.

Aim of the Work

The aim of this study is to evaluate the resorption rate of large volume of autologous fat transfer using CT volumetry and the effect of platelet-rich plasma on that rate.

2. Patients and Methods

The study was conducted on patients presenting to Plastic and Reconstructive Surgery Department in Tanta University Hospitals for Fat injection during the period of this study (from March 2016 to March 2018). Patients seeking breast augmentation and buttocks augmentation were included in the study. Ethical committee approval was obtained prior to proceeding with patient recruitment.

The study is a prospective randomized clinical trial. Patients included in the study were30 patients and subjected to large volume fat grafting (more than 100 ml) (in breast and buttocks), in all these cases, the left side will be injected with fat with PRP and right side will be injected without PRP.

All patients will be subjected to the following:

- Preoperative work up
  - **Informed consent before operation**.
  - **Local examination**: aesthetic lines and measurements of target area, skin (quality, texture and pigmentation)
  - **Photographing:** in standard positions for complete evaluation of the technique.
  - **Investigations**:

1. The routine laboratory work-up.
2. Multislice CT with volumetric measurement of region of interest.

- Operative work up:

1. Preoperative marking and photographing in standard position:

2. Harvesting: Area to be suctioned will be first infiltrated with tumescent solution (epinephrine 1:1,000,000 in ringer lactate solution). Liposuction will be performed using a 2 or 3 mm, three holes, blunt cannula.

3. PRP preparation

PRP will be prepared by manual double spin method, at 1500 rpm for 5 min and 3000 rpm for 10 min.

4. Fat injection

For the left side 10c.c PRP will be injected in the recipient area before fat injection while fat will be injected purely in the right side.

Injected volume of fat to reach the planned desired correction will be recorded for each case.

Improvement in right and left side of the two groups will be assessed after 6 months by:

Photographing and Clinical evaluation

- Preoperative and postoperative photographs will be compared and assessed by plastic surgeon, nursing staff and their average outcome will be graded as (Excellent, Good, Fair and Bad).
- Criteria of clinical assessment (skin texture, volume change color change and pigmentation)
- Patient satisfaction will be tabulated as (bad, fair, good and excellent) result.

Radiological evaluation

- Multislice CT was performed for target region before operative intervention and 6 months after. Scanning of the patients was performed using 320 MDCT scanner (Toshiba Aquilion One, Toshiba Medical systems, Japan) installed at our institution. An axial volume acquisition using 0.5 mm slice thickness and 0 mm spacing was used, and dose reduction protocol was activated providing the lowest kV and mAs settings to avoid excessive exposure to radiation.
- The acquired images were transferred to a post processing workstation that had Slicer 3D open source software. Fat was traced using a semi-automatic process in the consecutive axial images, allowing for volume calculation by the software. Volumes were recorded in pre and postoperative scans for comparison and statistical analysis.
- Patient data will be anonymized and stored in secure files for patient confidentiality.

3. Results

Patients were received large volume fat grafting (more than 100 ml) (breast and buttocks)

- **Donor site**: fat aspirated from abdomen and thigh.
- **Harvesting cannula**: 4mm, three holes, blunt cannula in all cases.
- **Injected amount per side:** mean injected amount was 364cc (±SD 109.857) ranging from 200cc to 550cc.

Table (1): Injected amount per side (cc)

Injected amount per side (cc)			
Range	200	-	550
Mean ±SD	364.000	±	109.857

- **Injecting cannula**: 2mm, one hole, blunt cannula in all cases.
- **Operative time:** 2 hours ± 15min in all cases

- **Complication:** no complication reported in all cases

Mean age was 29 years (±7.672 SD) while the mean body mass index (BMI) was 27.867 (±SD 4.454).

As regard volumetric CT in (Group B) (breast) before fat injection the mean volume of fat was 530cc (± SD 266.583) at right side and 533.5cc (± SD 269.875) at left side.

Table (2): preoperative volumetric CT in (breast).

Breast	CT Pre			Differences		Paired Test	
	Right	Left		Mean	SD	t	P-value
Range	220 - 1000	230 - 930		-3.500	29.444	-0.376	0.716
Mean ±SD	530.000 ± 266.583	533.500 ± 260.875					

P>0.05 not significant

This table shows that there is no significant statistical difference between the two sides as regards volume of fat.

As regard volumetric CT in (buttocks) before fat injection the mean volume of fat was 2905cc (± SD 613.739) at right side and 2922cc (± SD 627.033) at left side.

Table (3): preoperative volumetric CT in (buttocks).

Gluteal	CT Pre			Differences		Paired Test	
	Right	Left		Mean	SD	t	P-value
Range	2310 - 3660	2330 - 3710		-17.000	21.679	-1.753	0.154
Mean ±SD	2905.000 ± 613.739	2922.000 ± 627.033					

P>0.05 not significant

This table shows that there is no significant statistical difference between the two sides as regards volume of fat.

In (group B) Resorption volume percentage at right side (without PRP) was averagely 37.3% (±SD 7.045) that was nearly equal at left side (with PRP) which was 36.533% (±SD 8.570).

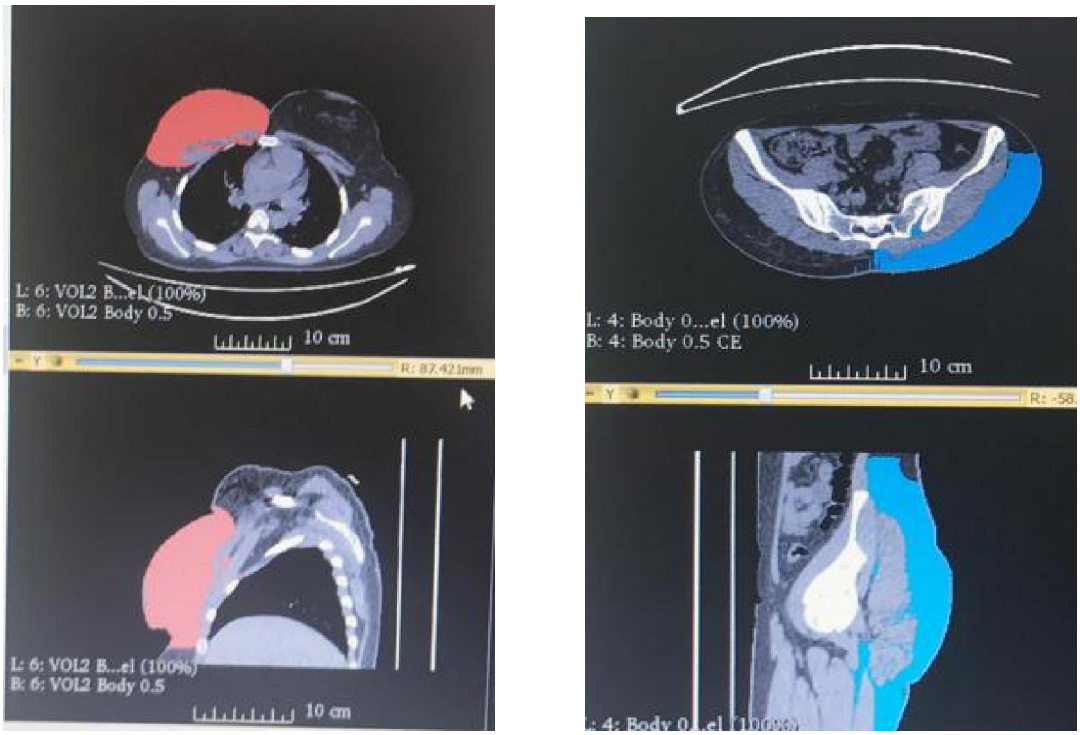


Fig. (1): volumetric CT for fat (breast)

Table (00): Resorption volume % in Group B.

	Resorption volume %						Differences		Paired Test	
	Right			Left			Mean	SD	t	P-value
Range	22.5	-	48.5	22.5	-	52.5	0.767	4.739	0.627	0.541
Mean ±SD	37.300	±	7.045	36.533	±	8.570				

P>0.05 not significant

This table shows that there is no significant statistical difference between the two sides groups as regards the resorption volume of fat.

A, B Axial and sagittal reconstructed CT scan of the chest showing tagging of the right breast for breast volume calculation.

As regard patient satisfaction was very satisfied (8.400±SD 1.882).

Fig. (2) volumetric CT for fat (buttocks)

(A, B) Axial and sagittal reconstructed CT scan of the pelvis showing tagging of the subcutaneous fat of the left gluteal region for volume calculation.

As regard Aesthetic outcome in was excellent (8.200± SD 1.935).

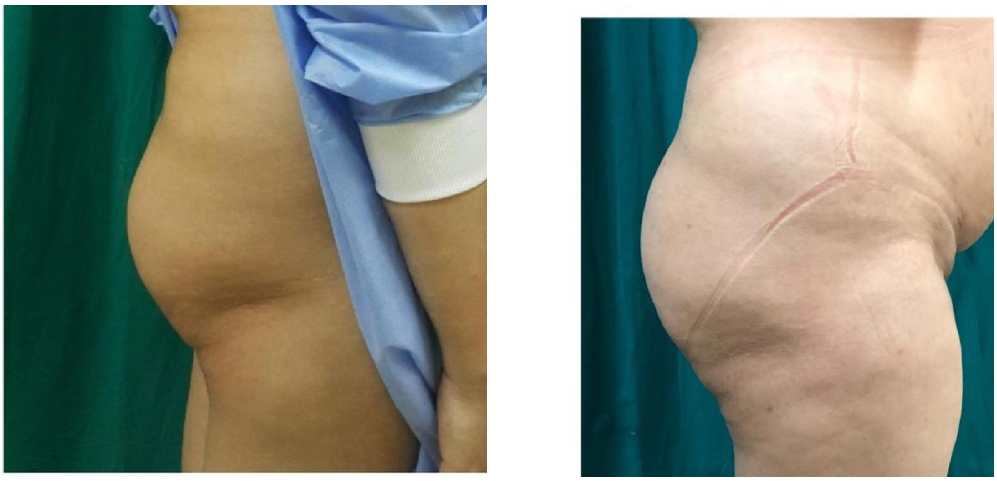
Case Presentations

Preoperative Postoperative

Fig. (3): Injected amount: 270 cc per side.

Preoperative Postoperative

Fig. (4): Injected amount: 400cc per side.



Preoperative Postoperative

Fig. (5): Injected amount: 450cc per side

Preoperative Postoperative

Fig. (6): Injected amount: 400cc per side.

4. Discussion

Although fat grafting is a very common procedure that is being practiced among plastic surgeons [1], serving diverse purposes ranging from post-traumatic reconstruction to mere aesthetic enhancements of body contour, however the level of evidence beyond such practice is still lacking.[13,14]

On experimental levels; two theories have been published with high degree of certainty regarding the way fat grafts survive in recipient site [7,15]. The two theories can be initially perceived as contradicting each other; however they can be also seen as complementary explanation of what is seen in clinical practice.

The clinical research is still struggling to build up the strongest evidence possible with many attempts to standardize the methods of fat harvesting, processing and reinjection. Coleman had laid down the foundation for such techniques [10], however the fact that there are so many variables to be considered adds to the problem of designing a well-controlled comparative study.

Such variables include donor site choice and its preparation [16–18], method of harvest[19,20], liposuction cannula type, size and number of perforations[21,22], processing methods[23,24], reinjection techniques[2,17,19] and recipient site variables [25].

Another problem is encountered when designing a clinical trial is the absence of standardized, measurable and comparable method to evaluate the outcome. Patients and surgeons' satisfaction have been the main outcome measure for many case series. However, other authors have tried to employ the imaging techniques such as high resolution ultrasound, computed tomography or even magnetic resonance imaging. Those methods provide measurable data that can provide better evaluation for the chosen fat graft techniques.

In the current study we tried to find answers to the following questions: what is the percentage of volume loss (or resorption) following fat grafting? Is this percentage different in small injected volumes (less than 100 cc) versus large volumes? Does the PRP enhance the sustainability of transplanted fat grafts in either small or large volumes?

To answer those questions, we utilized the CT volumetry as an objective method to accurately quantify the degree of fat resorption. Computerized tomography is an objective sensitive method to assess fat volumetry. First we measured the fat volume in the sites where we intend to inject the fat preoperatively and another scan was done 6 months postoperatively.

The percentage of fat resorption was calculated as the following: (the six-month postoperative fat

volume – the preoperative fat volume) / amount of fat injected intraoperatively.

Additionally, we investigated our results subjectively by determining the degree of patient's satisfaction and aesthetic outcome on a 4degree scale determined by surgeons.

We included 30 patients seeking for breast or buttock augmentation.

Investigating the fat resorption % in relation to the amount of fat injected; we found that the percentage of fat resorption was around (37%). This was done by comparing the fat resorption% between the sides which didn't receive PRP in both study groups, it was around 37% resorption of the amount injected intraoperatively when measured 6 months postoperatively.

We didn't find any statistically significant correlation between the volume of injected autologous fat and the % of fat resorption in both the study groups.

This simply means that the absolute volume of the transplanted fat is not a determining factor that affects the degree of volume loss following fat grafting; it is rather the amount of the fat in relation to the capacity of the site being injected.

We compared the resorption percentage in small and large volume unlike most of research that study only of those two groups.

Del Vecchio D., and Del Vecchio S., described such principle when they hypothesized that donor fat lobules ought to be embraced on at least four aspects with recipient-site tissue, and hence they supposed that the maximum volume of transplanted fat cannot exceed theoretically a 1:1 ratio. They used terms "the graft-to-capacity ratio" and "percentage volume maintenance" in dealing with large volume fat transplants to augment 30 breasts. They have found a significant inverse relationship between the graft-to-capacity ratio and percentage volume maintenance[26].

Looking at the effect of PRP on the percentage of fat resorption; in the current study; We found that resorption was nearly equal in both sides.

It is noteworthy that the three dimensional CT done preoperatively revealed a degree variability in soft tissue volume between both sides of the patients face (0.26 ± 1.58 cc), breast (3.5± 29.4 cc) and buttocks (17 ± 21.67) denoting that the absolute symmetry between both sides in humans does not exist.

The effect of PRP injection in our patients (receiving large fat volumes) showed no statistically significant difference in the percentage of fat resorption between both sides of the breast or the buttocks.

Those findings can be attributed to the fact that autologous PRP supply is limited by the amount of blood that can be withdrawn from a patient in a single setting. Hence, we can have a mixture of 1:10 (PRP: fat graft volume ratio) only in small volumes. On the other hand, this isn't practical when augmenting the breasts or the buttocks by large volumes more than 100 ml. In such large volumes the PRP will be too diluted by fat to show any noticeable effect under the CT volumetry.

José Maria Serra-Mestre et al 2014, published a systemic review on the effect of PRP on fat graft survival. The review comprised 6 preclinical studies with a control group and 9 clinical studies of humans. It also included comparative studies performed with other prosurvival strategies for fat grafts, such as combination with the stromal vascular fraction and second-generation PRP, also called "platelet-rich fibrin." The results indicated that PRP may have a dose-dependent positive effect on fat grafts and suggest low complication rates.[27]

We noticed that patient satisfaction and aesthetic outcome was excellent although 37% resorption that is attributed to major change in volume, low complication rate and simplicity of procedure.

We also prepared all cases psychologically about sequele of fat injection and explained that immediate result will not be the lasting result and volume will decrease with time as oedema will take about 2 weeks and fat need about 3 months to become stable.

Another observation we came up with in our study; weight must be nearly fixed to avoid high resorption as general body weight for sure will affect the percentage of fat survival.

Our strength point in this research

1. The research in randomized case controlled study in human.
2. We use objective sensitive methods to assess fat volumetry, as CT scan precisely detect fat from other tissue unlike ultrasonography or external advanced method like 3D camera.
3. We compare the resorption percentage in both small and large volume unlike most of other research that study only one of those two group.

Our weaknesses

1. We need further research on bigger sample size.
2. CT scan is expensive tool and we do not recommend usage of CT for patient underwent lipofilling to avoid radiation hazards, and put it only for research purpose.

It is difficult to do any type of histopathological examination of immune-histochemistry study on patient undergo lipofilling for aesthetic purpose.

Conclusion

Resorption rate of fat grafting is a difficult question to answer among plastic surgeons because the

outcome of fat grafting is dependent upon variations in the technique used to harvest, refine and inject the fat.

We used CT volumetry as sensitive objective methods to answer that question and our we find that the resorption rate is about 37% either small or large volume fat grafting after long term follow up.

Platelet rich plasma has practically useful when adding to large volume fat grafting.

Most of patient gave very satisfactory outcome, excellent result with no complications which reflect superior result of fat injection as an aesthetic procedure.

We recommend further research on bigger sample size for more accurate statistical analysis and histopathological examination to clarify the role and benefits of PRP when adding to fat grafting.

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