

# Comparison the Effect of Conventional and Nanofat Injection Methods on Nasolabial Fold Lipofilling: A Case- Control Study

Mina Mamizadeh<sup>1</sup>, Samaneh Tahmasebi Ghorabi<sup>2</sup>, Zahra Mansourinia<sup>3</sup>, Fariba Shadfar<sup>1</sup>, Arian Karimi Rouzbahani<sup>2,4\*</sup>

1. Department of Dermatology, School of Medicine, Emam Khomeini Hospital, Ilam University of Medical sciences, Ilam, Iran
2. USERN Office, Lorestan University of Medical Sciences, Khorramabad, Iran
3. Ilam University of Medical Sciences, Ilam, Iran
4. Student Research Committee, Lorestan University of Medical Sciences, Khorramabad, Iran

**\*Corresponding Author:**

Arian Karimi Rouzbahani

Student Research Committee,  
Lorestan University of Medical  
Sciences, Khorramabad, Iran

Tel.: +98 930 6757977

Email: [ariankarimi1998@gmail.com](mailto:ariankarimi1998@gmail.com)

Received: 1/30/2024

Accepted: 3/30/2024

## ABSTRACT

**Background:** Nasolabial folds are a common sign of aging, accompanied by various manifestations such as skin and tissue loosening, wrinkles, lip corner drooping, mandibular angle loss, platysmal bands, and skin pigmentation changes. Limited research has explored Nanofat injection methods. This study was done with the aim of comparing the effect of fat injection by two methods, conventional and Nanofat, in nasolabial folds.

**Method:** The study conducted in 2020-2021 at the skin clinic in Ilam, western Iran was a case-control study. Participants were divided into two groups, and lipofilling procedures were performed using conventional and nanofat methods with autologous fat. Data collection utilized a researcher-made questionnaire and radiographic results. Follow-up visits occurred on the 30th, 90th, and 180th days to assess complications and recovery rates. After 6 months, participant's photographs were taken and compared with pre-intervention photographs using the GIAS criteria. Data analysis was conducted using SPSS22 version software.

**Results:** The average age of the participants was  $37.80 \pm 8.30$  yr. The treatment response in the conventional fat injection group was significantly better than the nanofat group ( $P < 0.05$ ). Both groups were satisfied with the treatment methods, but high satisfaction was reported in the conventional group, but there was no statistically significant difference between the groups.

**Conclusion:** Both methods of improving wrinkles were effective, but the improvement and response to treatment in the conventional method was better than the Nanofat method, and its effect was felt by the participants for an average period of 3 months.

## KEYWORDS

Fat injection; Conventional; Nanofat; Wrinkles; Nasolabial fold; Lipofilling

## Please cite this paper as:

Mamizadeh M, Tahmasebi Ghorabi S, Mansourinia Z, Shadfar F, Karimi Rouzbahani A. Comparison the Effect of Conventional and Nanofat Injection Methods on Nasolabial Fold Lipofilling: A Case- Control Study. *World J Plast Surg.* 2024;13(1):24-31.

doi: 10.61186/wjps.13.1.24

## INTRODUCTION

The largest and most vital organ for protection, is the skin which covers the entire body's exterior and serves as a first-order physical barrier against the environment. Its responsibilities encompass regulating body temperature as well as protecting against ultraviolet (UV) light, trauma, germs, infections, and toxins. The skin also plays a role in general homeostasis, immunologic monitoring, sensory perception, and the control of insensible fluid loss<sup>1-3</sup>.

Aging skin has a disgusting appearance that can be summed up as follows. - Fine and coarse wrinkles on the frontal, periocular, and nasolabial areas can appear more quickly as a result of photodamage and facial emotions. As people age, more extra epidermal pigmentation accumulates on their skin, leading to skin discolorations like age spots and melasma. Further, the appearance of skin fragility and laxity after bariatric surgery and childbirth is a frustrating issue. People appear considerably older than they actually are due to these skin changes<sup>4</sup>.

This process can be significantly accelerated by a number of variables, such as UV radiation that causes telangiectasias, rhytides, lentigines, uneven pigmentation, coarse texture, laxity, and loss of translucency<sup>5</sup>.

The nasolabial fold begins at the junction of the ala nasi, the cheek, and the upper lip and extends in either a straight, convex, or concave shape or ends below and lateral to the corner of the mouth<sup>6</sup>. Cosmetological care, topical medications, invasive procedures (such as peelings, wrinkle correction, laser, rejuvenation), and systemic medications (antioxidants and hormone replacement therapy) are some of the methods available to prevent and treat premature aging<sup>6,7</sup>. Nonetheless, one of the most popular non-surgical cosmetic procedures worldwide is still the usage of tissue fillers<sup>8</sup>.

The rejuvenating effects of these methods can be seen with things such as protecting the skin against damage caused by external or internal harmful factors, providing nutrients needed by the skin, activating fibroblasts and increasing the synthesis of the extracellular matrix, removing the surface layers of the skin. , protection of the skin against oxidative is related to the removal of free radicals, control of fat secretion, maintaining the integrity and integrity of the skin, moisturizing properties and maintaining

the elasticity of the skin<sup>9</sup>.

In recent decades, a procedure using fat called lipofilling has been used to eliminate wrinkles. The most important advantage of using autologous fat injection is in reducing sensitivity or reaction to foreign body<sup>10</sup>. Fast becoming a popular treatment option for facial rejuvenation, lipofilling helps reduce aging-related changes to the skin (e.g., wrinkles, pigmentation spots, pores, or rosacea) and restore volume lost in the face<sup>11</sup>. The stromal vascular fraction (SVF) of adipose tissue is home to adipose-tissue-derived stromal cells (ASCs), which are primarily responsible for these effects according to the research. The precursors of (cultured) ASCs are attached around vessels as perivascular cells and pericytes<sup>12</sup>. Numerous growth factors, cytokines, and proteins that are secreted by ASCs can promote tissue regeneration through angiogenesis and matrix remodeling. Thus, autologous lipofilling may be able to counteract facial skin elasticity loss<sup>13</sup>.

Fat injection is done in different ways such as conventional, Sharp-Needle Intradermal Fat (SNIF), Nanofat, Emulsion, SNIE, FAMI and SEEFI. The conventional method has been used since the past years and recently the mentioned new methods have also been used and investigated. This progress in new methods for fat processing has made possible the use of small volumes that can be injected using fine needles, which can be effective in improving skin lines and improving tissue quality and remodeling<sup>14</sup>.

Over the past ten years, autologous fat grafting has gained a lot of traction in tissue augmentation and reconstruction. Numerous studies have documented its healing qualities and positive benefits on skin texture<sup>15</sup>. In addition to describing a novel method of applying nanofat, Tonnard et al. also proposed that this technology may be used to treat wrinkles and other skin discolorations<sup>10</sup>. Typically, costly dermatological procedures like "fillers" and erosive chemical peels that need multiple sessions are used to repair wrinkles and skin discolorations. These therapies frequently have no long-term effects. Therefore, the long-term regeneration qualities of nanofat may potentially be beneficial for wrinkles and discolorations<sup>16</sup>. This treatment method, in addition to improving wrinkles, can also be effective in improving skin discoloration, and in addition, it seems to have longer-term effects than methods such as fillers<sup>17</sup>. Several studies have been conducted

on the nasolabial fold using dermal fillers<sup>6,18</sup>. Most of the studies investigated fat injection using the nanofat method in facial rejuvenation<sup>19,20</sup>, so in this study, the effect of conventional fat injection and nanofat in the nasolabial folds was compared.

## MATERIALS AND METHODS

### Study design

This research was approved by Ilam University of Medical Sciences with ID IR.MEDILAM.REC.1400.039. The study was a case-control type and the statistical population consisted of people who visited the skin clinic between April 2020 and April 2021 for nasolabial folds fat injection.

### Sample size

A period of one year (April 2020 and April 2021) was considered for data collection. In this way, the people who applied for nasolabial fat injection were included in the study as they were available. Therefore, the sample size formula was not used. Thirty eight people applied for fat injection, and according to the entry criteria, 30 people entered the study and were randomly divided into two groups. Fifteen people were in the case group (fat injection by Nanofat method) and 15 people were in the control group (fat injection by conventional method).

### Study inclusion and exclusion criteria

- **Inclusion criteria:** Participants were included in the study with the following criteria: consent to participate in the study, candidates for lipofilling due to nasolabial folds, history of no fat injection, no active infection and no history of keloid.

- **Exclusion criteria:** Non-attendance at scheduled visits, patients with severe psychosis, pregnant and lactating mothers, systemic diseases, people with diabetes

### Data collection

The data collection tool included two main parts. The first part of the questionnaire was related to the demographic information of the participants such as (age, gender, education level, marital status), the second part was the questionnaire made by the

researcher and the results of photography.

### Intervention

People were randomly assigned to one of the two groups of conventional and nanofat fat injection. First, the basic information questionnaire and written informed consent were provided to the people to complete it, then the people were photographed before the fat injection using camera canon by a specialist doctor in order to compare and the effectiveness of the methods.

In both methods, fat was taken from the person's side. In the nanofat method, the special set of Nanofat is used to remove fat. After extracting the fat, the fat was digested using different filters, and after obtaining a thick liquid containing digested fat and many stem cells, it was injected. In the old method (conventional), normal sets are used to remove fat. The fat is washed and injected without being eaten and passing through different filters.

Nanofat and conventional were performed by a dermatologist. A total of 2 treatment sessions were performed for each person with a gap of fifteen days between sessions.

### Primary outcomes

The initial results were evaluated by a personal information questionnaire (age, gender, marital status, education level, occupation) and the effect of fat injection by nanofat and conventional methods. The dermatologist used a researcher-made questionnaire with excellent, good, average scales to measure the effectiveness.

The comparison of conventional and nanofat methods was done by global esthetic improvement scale (GIAS) criteria, which was scored from 1 to 5<sup>21</sup>. A score of 1 is if the crease is completely improved, and a score of 5 is if the crease is more than before. 1 – Excellent, 2 – Good, 3 – Moderate, 4 – No change, 5 – Worsening

### Secondary consequences

– Questionnaire designed by the researcher for participants' satisfaction: Participants responded to a researcher-made questionnaire about their satisfaction with the effect of conventional and nanofat fat injection on nasolabial folds based on a

three-level Likert satisfaction scale (low, moderate, high) at the end of the study. Low satisfaction was given a score of 1, moderate satisfaction was given a score of 2, and high satisfaction was given a score of 3.

– Complications checklist: Participants were evaluated based on a researcher-made questionnaire that included mild pain, bruising, swelling, spotting, infection, bleeding, redness, and inflammation.

### Photography results

People were visited on the 30th, 90th, and 180th days after fat injection, and at each visit, people were checked for side effects. Subjects were photographed on the last day of the visit (6 months later) and compared with the photograph taken before the injection based on the GAIS criteria. In this criterion, improvement in nasolabial folds was scored from 1 to 5, where a score of 1 indicated complete improvement, and a score of 5 indicated an increase in folds compared to before.

### Follow up

The general follow-up period of the subjects was visits on the 30th, 90th, and 180th days after fat injection.

### Statistical Analysis

Data analysis was done using SPSS software version 22 (IBM Corp, Armonk, New York) at a significance level of 0.05 (confidence interval was 95%). For quantitative data, descriptive statistics such as the mean and standard deviation were utilized, whereas frequency and percentage were used for qualitative variables. Chi-square test was utilized to evaluate the efficiency of the conventional and nanofat groups.

## RESULTS

The 20 people, including two conventional and nanofat groups, were studied in two groups of 10 people with an average age of  $37.80 \pm 8.30$  in the age range of (22-60) years. 20.3% of the studied subjects were men and 76.7% were women. The majority of people (66.6%) had higher than bachelor's education, 60% were employed and 70% were married. Other details are given in Table 1.

According to the Table 2, based on the physician's opinion, individuals who underwent fat injection using the conventional method reported better therapeutic effects as excellent and good. However, in individuals who received fat injection in the form of nanofat, the therapeutic effects were more commonly reported as good and moderate.

**Table 1:** Determining the demographic characteristics of the studied participants

Variable	Frequency	Percent
Gender	Male	7
	Female	23
Level of education	Diploma and sub-diploma	10
	Bachelor's degree and higher	20
Occupation	Housewife	12
	Employed	18
Marital status	Married	21
	Single	9

**Table 2:** Determining the effect of conventional and nanofat fat injection in the nasolabial fold

Injection method	Effect of injection			P-value
	Excellent number(percentage)	Good number(percentage)	Moderate number(percentage)	
Conventional	8(53.3)	7(46.7)	0(0)	0.003
Nanofat	1(6.7)	8(53.3)	6(40)	

**Table 3:** Comparison of the effect of conventional and nanofat fat injection in nasolabial folds based on GIAS criteria

Injection method	GIAS			P-value
	Excellent Number(percentage)	Good Number(percentage)	Moderate Number(percentage)	
Conventional	8(53.3)	7(46.7)	0(0)	0.020
Nanofat	2(13.3)	9(60)	4(26.7)	

**Table 4:** Comparison of participants' satisfaction with the effect of fat using regular fat and nanofat

Injection method	Satisfaction			P-value
	High Number(percentage)	Moderate Number(percentage)	Low Number(percentage)	
Conventional	11(73.3)	4(26.7)	0(0)	0.690
Nanofat	10(66.7)	5(33.3%)	0(0)	

According to the Chi-square test, there was a statistically significant difference between the two treatment methods ( $P=0.003$ ).

Table 3 shows the comparison results of fat injection based on GIAS criteria in two treatment methods. Using Fisher's exact test, the results showed that the response to treatment in the conventional fat injection group was significantly better than the nanofat group that There was a statistically significant difference between the two groups ( $P=0.020$ ).

Based on people's satisfaction with fat injection methods; People showed high satisfaction from two injection methods, but in the group that had fat injection by conventional method, 73.3% of people showed a high level of satisfaction (Table 4).

In the Nanofat group, one case of bruising and one case of swelling after injection were reported as side effects. Also, in the conventional group, one case of swelling, two cases of pain, and one cases of bruising were reported. Rare side effects were not observed in any of the two injection methods.

## DISCUSSION

In recent years, fat grafting has been widely used in the treatment of aging facial skin to fill surface depressions<sup>14,22,23</sup>. Many doctors have mentioned that the implanted adipose tissue produces rejuvenating effects on the skin around the transplant area<sup>22, 23</sup>. However, the biological mechanism responsible for the rejuvenating and regenerating effects of fat grafting on the skin is still not fully understood<sup>24</sup>. Several studies have evaluated the effect of fat

grafting in facial rejuvenation<sup>25,26</sup>.

The results show that such rejuvenating effects are due to the improvement of deep facial structures. In contrast, others have proposed that ASCs, which are abundant in adipose tissue, contribute to soft tissue regeneration by promoting collagen synthesis, cellular matrix protein synthesis, and dermal revascularization through the production of many cytokines and multipotent proliferation<sup>26, 27</sup>. Various methods are used to rejuvenate and correct deep facial wrinkles. Among the methods used are dermal fillers, which have had satisfactory results based on studies<sup>28</sup>. In recent decades, a procedure using fat called lipofilling has been used to eliminate wrinkles. The most important advantage of using autologous fat injection is in reducing sensitivity or reaction to foreign body<sup>10</sup>.

In this study, the average age of people referred for fat injection was  $37.80 \pm 8.30$  in the age range of 22-60 years. The number of facial rejuvenation requests from people aged 45 to 55 has increased significantly. In this age range, the aging process is mainly loss of volume and aging of the skin, which is probably associated with the decline of tissues in varying degrees<sup>17</sup>.

In the group where fat injection was performed in the conventional way, the treatment effect was reported as excellent in 53.3%, and good in 46.7%. In the group that injected fat in the form of nanofat, the treatment effect was 6.7% excellent, 53.4% good and 40% moderate. There was a statistically significant difference between the two groups ( $P=0.003$ )

The results showed that both methods were effective

in improving wrinkles, but the recovery and response to treatment in the conventional method was better than the Nanofat method, and its effect was felt by the participants for an average period of 3 months. All participants were satisfied.

In Zzam study, the injection of Nanofat caused the disappearance of dark halos around the eyes in 5 cases (50%), showed a significant improvement, in 2 cases (20%) a moderate improvement was observed, in 2 cases (20%) a slight improvement and in one No improvement was observed. In terms of patient satisfaction, 8 (0) were satisfied with the final result, while 2 patients (20) were not satisfied. Postoperative edema and ecchymosis was minimal in 5 cases (50%) and mild in 5 cases (50%)<sup>29</sup>.

In the study of Vavouli et al, 30 patients with dark circles around the eyes and skin type II, III or IV were treated. Almost all patients showed significant cosmetic improvement. The response to treatment was good or excellent in 93.3%. The effect of autologous nanofat injection in the treatment was determined that almost all patients showed significant improvement<sup>30</sup>. Edema and bruising were less in patients injected with Nanofat method. The nanofat grafting procedure may cause swelling for 2-4 days as well as bruising and pain at the donor site for 1 week.

In the study of Baumann et al, all three types of gels containing hyaluronic acid had created a more durable correction in the long term compared to collagen, so that after 24 weeks of the last treatment, 90% of the receiving patients 30HV gel, 88% of patients in 24HV gel group and 81% of patients treated with J30 gel still had significant therapeutic progress. While in the group treated with collagen, the therapeutic effects were much shorter and at the end of 24 weeks, only 36% to 45% of the people had therapeutic effects<sup>31</sup>.

Our results showed that the response to treatment in the conventional fat injection group was significantly better than the nanofat group. Tonnard et al introduced the nanofat transplantation method, in which a mechanical emulsion was used to mechanically break down adipose tissue and preserve the extracellular matrix with all nucleated cells including stem cells present. Then this sample was injected into the fine lines of the face using a 30gram needle<sup>10</sup>.

Fifteen patients including (2 men and 48 women; average age, 35 to 65 years; average follow-up, 9

months) were examined in a study. Clinical results were evident between 2 and 4 weeks after injection, and improvements were consistently observed up to 6 months after surgery. All patients confirmed improvement in skin quality. The lifting effect was also observed. The Nanofat method does not damage the cells, it increases the survival of the cells and the number of fat-derived stem cells. Sampling showed an increase in skin cells, vascular density and density of fibers and collagen. It seems that facial rejuvenation by subcutaneous injection of Nanofat is an effective method that shows the effect of skin rejuvenation by modifying the dermis pattern<sup>32</sup>.

In another study, 20 female patients with wrinkles, hyperpigmentation, erythema and enlarged skin pores were included in the study. Nanofat was injected intradermally in all areas of the face. All patients in the sixth month after treatment, the average time of disappearance was 3.6 weeks. Patients noticed a change about 1-12 months after Nanofat injection. This improvement was observed for skin smoothness (100% of patients), wrinkles (40% of patients), reduction of pore size (15% of patients), improvement of redness (10% of patients). The effect of Nanofat was felt by patients for an average period of 3-8 months. All patients were satisfied<sup>33</sup>. Posttreatment clinical evaluations demonstrated a significant increase in scar quality and excellent patient satisfaction. The outcomes demonstrated that wrinkles seemed less noticeable, discolorations were less noticeable, and scars were smoothed by nanofat grafting<sup>16</sup>.

## CONCLUSION

Both methods were effective in improving wrinkles, but the recovery and response to treatment in the conventional method was better than the Nanofat method, and its effect was felt by the participants for an average period of 3 months. It is suggested that considering that the sample size of our study was small. The study should be conducted in a high sample size to confirm the results of the effectiveness of the methods.

## ACKNOWLEDGEMENTS

We thank all participants in the study and Ilam University of Medical Sciences. The authors also thank the Clinical Research Development Unit

of Emam Khomeini Hospital, Ilam. The principal investigator provided financial support for this study.

## CONFLICT OF INTEREST

There are no conflicts of interest in terms of the present manuscript.

## REFERENCES

1. Maranduca MA, Branisteanu D, Serban DN, et al. Synthesis and physiological implications of melanic pigments. *Oncol Lett* 2019;**17**(5):4183-7.
2. Someya T, Amagai M. Toward a new generation of smart skins. *Nat Biotechnol* 2019;**37**(4):382-8.
3. Yousef H, Alhajj M, Sharma S. Anatomy, skin (integument), epidermis. 2017.
4. Lyu J-J, Liu S-X. Radiofrequency in facial rejuvenation. *International Journal of Dermatology and Venereology* 2022;**5**(02):94-100.
5. Han A, Chien AL, Kang S. Photoaging. *Dermatol Clin* 2014;**32**(3):291-9.
6. Stefura T, Kacprzyk A, Droś J, et al. Tissue Fillers for the Nasolabial Fold Area: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Aesthetic Plast Surg* 2021 2021/10/01;**45**(5):2300-16.
7. Ganceviciene R, Liakou AI, Theodoridis A, Makrantonaki E, Zouboulis CC. Skin anti-aging strategies. *Dermatoendocrinol* 2012;**4**(3):308-19.
8. Arsiwala SZ. Current trends in facial rejuvenation with fillers. *J Cutan Aesthet Surg* 2015;**8**(3):125-6.
9. Campa M, Baron E. Anti-aging effects of select botanicals: Scientific evidence and current trends. *Cosmetics* 2018;**5**(3):1-15.
10. Tonnard P, Verpaele A, Peeters G, Hamdi M, Cornelissen M, Declercq H. Nanofat grafting: basic research and clinical applications. *Plast Reconstr Surg* 2013;**132**(4):1017-26.
11. van Dongen JA, Langeveld M, van de Lande LS, Harmsen MC, Stevens HP, van der Lei B. The effects of facial lipografting on skin quality: a systematic review. *Plast Reconstr Surg* 2019;**144**(5):784e-97e.
12. van Dongen JA, Boxtel JV, Willemsen JC, et al. The Addition of Tissue Stromal Vascular Fraction to Platelet-Rich Plasma Supplemented Lipofilling Does Not Improve Facial Skin Quality: A Prospective Randomized Clinical Trial. *Aesthet Surg J* 2021;**41**(8):NP1000-NP13.
13. Spiekman M, van Dongen JA, Willemsen JC, Hoppe DL, van der Lei B, Harmsen MC. The power of fat and its adipose-derived stromal cells: emerging concepts for fibrotic scar treatment. *J Tissue Eng Regen Med* 2017;**11**(11):3220-35.
14. Charles-de-Sá L, Gontijo-de-Amorim NF, Takiya CM, et al. Antiaging treatment of the facial skin by fat graft and adipose-derived stem cells. *Plast Reconstr Surg* 2015;**135**(4):999-1009.
15. Guisantes E, Fontdevila J, Rodríguez G. Autologous fat grafting for correction of unaesthetic scars. *Ann Plast Surg* 2012;**69**(5):550-4.
16. Uyulmaz S, Sanchez Macedo N, Rezaeian F, Giovanoli P, Lindenblatt N. Nanofat Grafting for Scar Treatment and Skin Quality Improvement. *Aesthet Surg J* 2018;**38**(4):421-8.
17. Bernardini FP, Skippen B, Gennai A, Zambelli A. Minimal Incisions Vertical Endoscopic Lifting (MIVEL) for the management of lateral canthal and lower eyelid malposition. *Aesthet Surg J* 2019;**39**(5):472-80.
18. Monheit G, Beer K, Hardas B, Grimes PE, Weichman BM, Lin V, Murphy DK. Safety and Effectiveness of the Hyaluronic Acid Dermal Filler VYC-17.5L for Nasolabial Folds: Results of a Randomized, Controlled Study. *Dermatol Surg* 2018;**44**(5):670-678.
19. La Padula S, Ponzio M, Lombardi M, et al. Nanofat in Plastic Reconstructive, Regenerative, and Aesthetic Surgery: A Review of Advancements in Face-Focused Applications. *J Clin Med* 2023;**12**(13):1-19.
20. Fakh-Gomez N, Steward E, Orte Aldea M del C. Nanofat in Facial Rejuvenation: Step-by-Step Procedure, Patient Evaluation and Recovery Process. *The American Journal of Cosmetic Surgery* 2021;**38**(1):27-35.
21. Ehlinger-David A, Gorj M, Braccini F, Loreto F, et al. A prospective multicenter clinical trial evaluating the efficacy and safety of a hyaluronic acid-based filler with Tri-Hyal technology in the treatment of lips and the perioral area. *J Cosmet Dermatol* 2023;**22**(2):464-472.
22. Erol OO, Agaoglu G. Facial rejuvenation with staged injections of cryopreserved fat and tissue cocktail: clinical outcomes in the past 10 years. *Aesthet Surg J* 2013;**33**(5):639-53.
23. Chou C, Lee S, Lin T, et al. Micro-autologous fat transplantation (MAFT) for forehead volumizing and contouring. *Aesthetic Plast Surg* 2017;**41**:845-55.
24. Coleman SR, Katzel EB. Fat grafting for facial filling and regeneration. *Clin Plast Surg* 2015;**42**(3):289-300.
25. Sinno S, Wilson S, Brownstone N, Levine SM. Current thoughts on fat grafting: using the evidence to determine fact or fiction. *Plast Reconstr Surg* 2016;**137**(3):818-24.
26. Klar AS, Güven S, Zimoch J, et al. Characterization of vasculogenic potential of human adipose-derived

- endothelial cells in a three-dimensional vascularized skin substitute. *Pediatr Surg Int* 2016;**32**:17-27.
27. Moon KM, Park Y-H, Lee JS, et al. The effect of secretory factors of adipose-derived stem cells on human keratinocytes. *International journal of molecular sciences* 2012;**13**(1):1239-57.
28. Jacovella PF. Use of calcium hydroxylapatite (Radiesse®) for facial augmentation. *Clin Interv Aging* 2008;**3**(1):161-74.
29. Zzam E, Khlosy H, Abouarab M. The Efficacy of Autologous Nanofat Injection in the Treatment of Infraorbital Dark Colouration. *The Egyptian Journal of Plastic and Reconstructive Surgery* 2020; **43**(3): 445-452. doi: 10.21608/ejprs.2020.68188.
30. Vavouli C, Katsambas A, Gregoriou S, et al. Chemical peeling with trichloroacetic acid and lactic acid for infraorbital dark circles. *J Cosmet Dermatol* 2013;**12**(3):204-9.
31. Baumann LS, Shamban AT, Lupo MP, et al. Comparison of smooth-gel hyaluronic acid dermal fillers with cross-linked bovine collagen: a multicenter, double-masked, randomized, within-subject study. *Dermatol Surg* 2007;**33**:S128-S35.
32. Menkes S, Luca M, Soldati G, Polla L. Subcutaneous injections of nanofat adipose-derived stem cell grafting in facial rejuvenation. *Plastic and reconstructive surgery Global open* 2020;**8**(1):1-9.
33. Tonnard P, Verpaele A, Carvas M. Fat grafting for facial rejuvenation with nanofat grafts. *Clin Plast Surg* 2020;**47**(1):53-62.