

Platelet-Rich Fibrin impact on the Diced Cartilage viability in Rhinoplasty

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Abstract

Introduction:

Diced cartilage grafts are well-liked, dependable, and simple-to-use techniques for dorsum camouflage in rhinoplasty. Recent research results demonstrate how effectively PRF increases the survivability of diced cartilage in the nasal dorsum and decreases its absorption. In this study, we intend to investigate the effect of fibrin-rich platelets (PRF) on diced cartilage survival in rhinoplasty surgery.

Materials and Methods:

This clinical trial included people referred to Rasoul Akram Hospital for rhinoplasty between 2020 and 2021. Patients were divided into two groups: Diced Cartilage alone (DC) and Diced Cartilage + PRF (DC+PRF). Cartilage survival was assessed by ultrasound, photography, and nasal examination, and the two groups were compared six months after rhinoplasty. Patients' satisfaction with surgery was also evaluated using the Utrecht questionnaire.

Results:

The mean age of the two groups of 20 patients was 29.05 ± 7.02 and 26.65 ± 8.16 years in the DC and DC + PRF groups, respectively ($P > 0.05$). After treatment, the frequency of irregularity on examination and dissatisfaction score was slightly but insignificantly higher in the DC group compared to the DC + PRF group (25% vs. 15% and 12.25 ± 6.45 vs. 10.45 ± 6.74 , respectively, and P values > 0.05). The total volume decrease, regardless of the injection site, was significant in both groups ($P < 0.05$), but the magnitude of volume reduction was significantly higher in the DC group compared to the DC + PRF group (-0.060 ± 0.087 vs. -0.033 ± 0.017 , respectively, $P < 0.05$).

Conclusion:

PRF may slow down the absorption process of diced cartilage.

Keywords: Diced cartilage, Platelet-rich fibrin, Rhinoplasty.

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Introduction

Nasal structure irregularities, particularly in the dorsum, are a common problem in rhinoplasty surgery. These irregularities may cause post-surgical dissatisfaction, which can lead to complications. It is important to note that several factors, including personal aesthetic preferences and individual perceptions, can affect patient satisfaction. Therefore, addressing these concerns before and after the surgery is crucial to ensure patient satisfaction and a successful outcome. Also, the weakness in the cartilaginous structure of the nose tip, which leads to drooping of the tip of the nose, is one of the reasons for patients to refer for rhinoplasty surgery, and strengthening the cartilage of the tip of the nose is very effective in improving this defect. In rhinoplasty, cartilage grafts are a standard method to cover skin and skeletal defects and irregularities, the advantages of which are cartilage grafts and the variety of graft placement sites (1-3). Dorsal nose camouflage is a method to protect soft skin tissue and correct minor irregularities. It is used for bony and cartilaginous dorsum (4). Diced cartilage is a popular, reliable, and easy-to-use technique for dorsum camouflage in rhinoplasty. When transferred to the recipient site, it is important to use these cartilages to maintain their structure, function, and durability (5,6). Rib cartilages are a rich source for extracting graft parts, but they have some disadvantages, including problems caused by the change in shape and prominence of cartilage edges (7). In one technique,

autogenous cartilage is initially cut into 0.5-1-millimeter pieces. In this method, the temporal fascia is used because of the effect on the reduction of cartilage absorption. The main point of these methods is to worry about the amount of cartilage absorption in the postoperative period (8). As a stabilizing scaffold to prevent these problems, cartilage and other materials have been combined and used (9). Regenerative medicine protocols have recently been used to solve the problems of the DC-based approach. Platelet-rich fibrin-embedded cartilage (PRF) has been described as a reliable alternative to the existing procedure (10). As a bioactive agent, PRF can stimulate tissue regeneration using high concentrations of different growth factors. Various studies have shown the successful role of PRF in reducing the absorption of diced cartilage in the nasal dorsum and increasing its survival (11-14). Considering the high prevalence of nose surgery worldwide, especially in Iran, the importance of improving the results of these surgeries, and their high impact on the patient's quality of life, the present study, due to the lack of sufficient studies on the use of PRF, investigated the effectiveness of platelet-rich fibrin in diced cartilage survival in rhinoplasty surgery.

Materials and Methods

Patients and groups

In this clinical trial survey, the study population was all patients (40 patients) referred for rhinoplasty to the ENT clinic in 2018 and 2019.

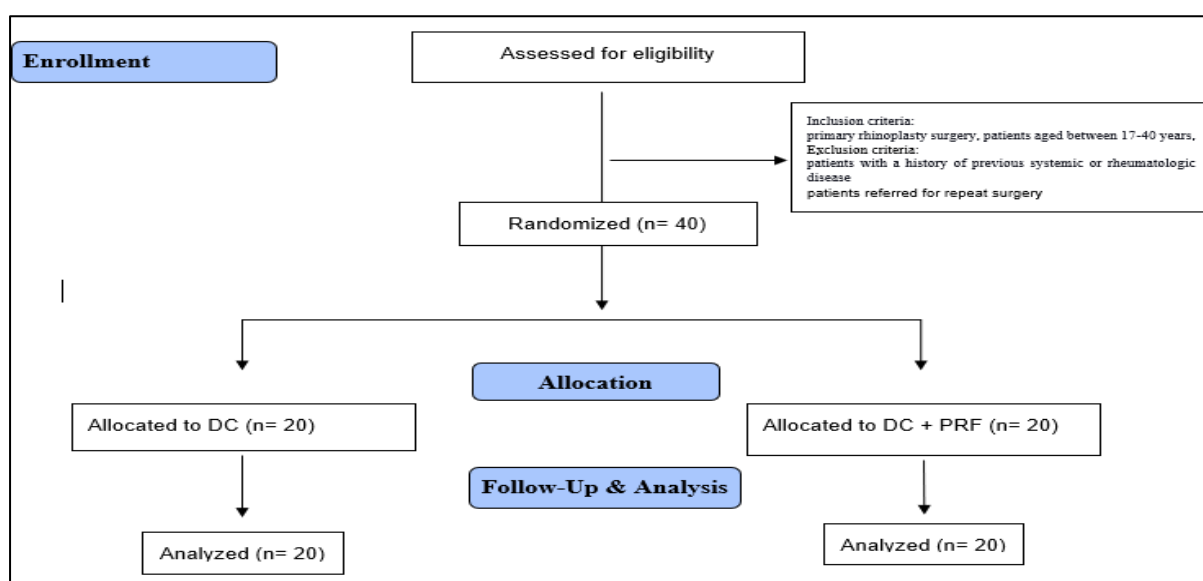


Fig1: Study consort chart

The minimum sample size was calculated based on the formula to be 16 cases for the study and control group. Inclusion criteria were primary rhinoplasty surgery, patients aged between 17-40 years, patients with a history of previous systemic or rheumatologic disease, and patients referred for repeat surgery were excluded from the study.

Demographic data, including gender and age, was collected. Patients' files during hospitalization and examination, ultrasound, and photography were reviewed for data collection, and the following patient satisfaction questionnaire (Utrecht) was filled out after surgery (15).

The information of each patient was recorded in the relevant checklist. Then, using block randomization, the patients were randomly divided into two groups: the first group was those who used Diced cartilage alone at the end of their rhinoplasty surgery, and in the second group, Diced cartilage was combined with Platelet-rich fibrin and then used (Figure 1).



Fig 2: Process of collecting platelet-rich fibrin (PRF) from blood and mixing it with diced cartilage (DC+PRF)

PRF extraction

Twenty ml of blood was taken from the patient's peripheral vein and centrifuged at 1300 rpm for 8 minutes. The top layer, the obtained PRF, was collected. Then, it was combined with diced cartilage large enough to be removed from the insulin syringe head (approximately 0.1 to 0.3 mm) and transferred to the insulin syringe according to the desired group of cartilage combined with PRF or cartilage alone (Figure 2).



Fig 3: Injection of the combination of cartilage and PRF (DC+PRF) in the tip of the nose using an insulin syringe

Surgery method

A surgeon performed all open-method operations. The skin flap was lifted in the subperichondrial plane, Pitanguy's midline ligament was cut in all patients, and the scroll ligaments were preserved.

The cartilage volume or the combination of cartilage with PRF was measured in cc. At the end of surgery and replacement of the rhinoplasty flap to the initial location, diced cartilage alone or the combination of cartilage with PRF, depending on the surgeon's diagnosis, was used by insulin syringe in the tip, supratip, dorsum, or radix (Figure 3).

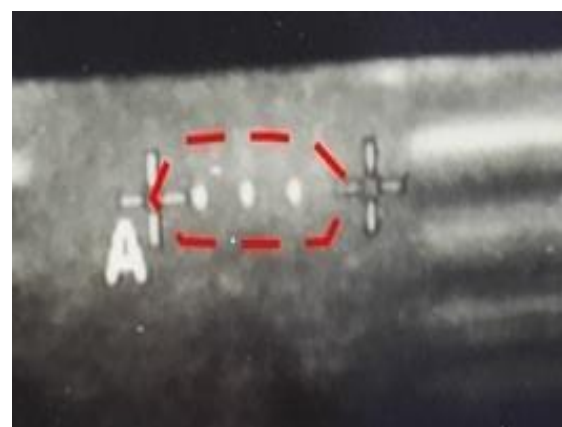


Fig 4: Ultrasound image of cartilage volume 6 months after surgery (Longitudinal dimension of cartilage marked with white dotted line and cartilage border with red dotted line)

Diced cartilage was utilized in primary rhinoplasty surgery to address various nasal

irregularities, such as dorsal irregularities and tip weakness. The specific indication for its usage varied depending on individual patient anatomy and aesthetic goals. The operating surgeon determined the amount of diced cartilage used in each patient intraoperatively based on the extent of correction required and the desired outcome. For this study, cartilage grafts were meticulously harvested from the nasal septum cartilage, following strict criteria to ensure optimal quality and viability for transplantation.

Post-surgery follow-up

Six months after surgery, the cartilage survival rate in two groups was investigated by three methods: 1) Ultrasound, determined by a radiologist measuring its volume on the cc scale. The remaining three dimensions of the cartilage were obtained by placing the ultrasound probe longitudinally and transversely, and the cartilage volume was the result of the product of these three dimensions divided by two. According to Figure 4, which is marked by placing the probe longitudinally on one side of the cartilage with the nasal tip area marked with marker A. 2) Another skilled surgeon evaluated the nasal examination, and the irregularities of all four cartilage injection sites were carefully noted. The means of observation and palpation were recorded. 3) The level of patients' satisfaction with surgery was also evaluated with the Utrecht questionnaire. Standard photography before and after surgery was also performed (Figure 5).



Fig 5: Before (left side) and six months after surgery (right side) photograph in a 19-year-old female participant with the complaint of nose deformity: Open-strategy rhinoplasty surgery with the injection of the combination of Diced cartilage with PRF utilized by insulin syringe within the dorsum.

Statistical analysis

Data were inserted into SPSS, version 22 (SPSS, Inc., Chicago, IL, USA). Mann-Whitney tests were used to analyze data, and $P < 0.05$ was assumed significant. Fisher exact t-test or the Wilcoxon test was used to analyze the variables depending on the data distribution pattern. Data were expressed as mean and standard deviation.

Ethical considerations

Before conducting the research, an introduction letter was obtained from the Research Council and the Ethics Committee of the Iran University of Medical Sciences and Health Services (Ethical Code IR.IUMS.FMD.REC.1399.150), and the necessary coordination with the officials of the ENT clinic was attained. Also, the registration code was obtained after registration in the Iranian Registry of Clinical Trials (IRCT20221011056150N1). Participants were informed about the following, and written/oral informed consent was obtained from them:

- The aims of the research were explained to all the studied patients.
- Had the right to withdraw from the study at any time during the study.
- Participation in this study had no complications or additional patient costs.
- Potential complications observed in previous studies were noted in the patients.
- Non-participation in the study was not an obstacle to patient treatment services.
- The principle of information confidentiality of the research units was respected, and instead of the names of the people in the questionnaire, the code was used.
- The participants were thanked for their participation in the research project implementation.
- In presenting the results of the research project, all material and intellectual rights of the university were considered.

Results

In this research, the subject of investigation is the case of 40 female patients in two groups of 20 people. The average age of patients in the DC and DC +PRF groups was 29.05 ± 7.02 and 26.65 ± 8.16 , respectively ($P=0.163$).

As shown in Table 1, after the treatment, the frequency of irregularities in the examination was higher in the group without PRF injection. Although this difference was not statistically significant, the low sample size may be the reason (Table. 1).

Table 1: Dissatisfaction with appearance, clinical examination status, total graft volume before and after six months of surgery, amount and percentage of reduction in graft volume according to injection site.

Variable	DC	DC+PRF	P-value*
Dissatisfaction (Mean ± SD)	12.25 ± 6.45	10.45 ± 6.74	0.207
Clinical examination status			
Normal	15 (%75)	17 (%85)	0.695***
Irregularity	5 (%25)	3 (%15)	
Total	20 (%100)	20 (%100)	
Total graft volume before and after 6 months of surgery			
Injected volume	0.332 ± 0.288	0.312 ± 0.114	0.577
6-month volume	0.272 ± 0.204	0.295 ± 0.105	0.140
Volume loss	-0.060 ± 0.087	-0.017 ± 0.033	0.008
Percentage of volume loss	14.42	4.75	0.03
P-value**	0.001	0.027	-
Mean volume loss			
Dorsum	-0.022 ± 0.033	-0.002 ± 0.033	0.019
Supra tip	-0.000 ± 0.033	-0.002 ± 0.033	0.317
Tip	-0.038 ± 0.033	-0.006 ± 0.033	0.057
Radix	-0.000 ± 0.033	-0.007 ± 0.033	0.152
Mean volume loss percentage			
Dorsum	18.13 ± 6.32	1.82 ± 4.04	<0.001
Supratip	0 ± 0	10 ± 14.14	0.317
Tip	14.24 ± 13.25	7.22 ± 13.40	0.263

* Mann-Whitney Test ** Mann-Whitney Test *** Fisher's Exact Test

The dissatisfaction score was higher in the group without PRF injection. Although this difference was not statistically significant, the low sample size may be the reason.

The above table also shows that overall graft volume has decreased in both groups, regardless of the injection site. However, the amount and slope of the decrease in the group without PRF were significantly higher. In other words, PRF prevents the reduction of graft volume and has a protective effect.

The maximum volume reduction in the tip and dorsum region was more significant in the group without PRF injection than in the other group. The volume reduction in the Radix and Supratip region was more significant in the group with PRF injection, but these differences were significant only in the dorsum region (Details are shown in Table 1).

Discussion

This study aimed to investigate the effect of fibrin-rich platelets on the survival of diced cartilage in rhinoplasty surgery in patients referred to the otolaryngology clinic. It was accomplished in 2018 and 2019. Two groups of 20 women candidates for primary rhinoplasty surgery were evaluated: the first received DC alone, and the second received DC combined with PRF. There was no significant difference in the ages of the patients in the two groups, indicating that the age parameter (confounding variable) did not affect the results of this study. Although not statistically significant, the PRF group showed a lower rate of irregularities in

the examination and less dissatisfaction with the nose's appearance after six months. The graft volume did not differ significantly between the two groups before and after the operation. Both groups decreased over time, but the graft thickness reduction in the PRF group was significantly lower. The volume reduction in the tip and dorsum area was significantly more significant in the DC group than in the PRF group.

Several studies have been conducted on diced cartilage as a graft since Peer introduced it in the 1940s (16). However, until 2000, grafting with diced cartilage was uncommon in nasal surgery. Although non-coated diced cartilage can be used as a graft, there is a significant risk of deformity, cartilage fragment displacement, and surface roughness, especially in patients with thin skin (17). Some studies on using fiber sealant in conjunction with diced cartilage found that it is effective, providing ease of use, greater flexibility, and increased healing potential of cartilage and surrounding tissues. Bracaglia et al. introduced the so-called "nougat graft" in a 2012 study, combining diced cartilage and fibrin sealant (18). Tasman et al. described a diced cartilage graft and fibrin sealant using "Tasman's technique" a year later. Tasman et al. used this type of graft in 28 nasal dorsum augmentation patients. They were monitored for a period of 4 to 26 months. These researchers assessed early shrinkage after grafts and performed sonography (10 out of 28 patients) and histopathological analysis (2 out of 28 patients). Shrinkage was minimal, and all

grafts were stabilized between the third and fifteenth postoperative months. (19). Stevenson and Hodgkinson employed "cartilage putty" grafts, which included fibrin sealant (Tisseel) and diced cartilage, in 19 rhinoplasty patients. Despite incorporating complicated rhinoplasty patients, these authors did not meet any cases of absorption during the 1-year follow-up (20). However, cartilage and fibrin glue grafts are pricey and need large pockets for graft implantation without compression.

Furthermore, diced cartilage in these transplants may migrate from the graft's edge. (21). Tisseel's maker advises that fibrin sealant may induce sensitivity. Because it is generated from human plasma, it can trigger allergic responses and carry the risk of transferring pathogenic germs (22). Bullocks et al. demonstrated the bonding maintenance of diced cartilage using autologous tissue glue (ATG), which is made by combining platelet-rich plasma (PRP) and platelet-poor plasma (PRP) (23). The fundamental benefit of ATG over commercial fibrin glue is that it is non-infectious. However, bovine thrombin can still cause hypersensitivity responses, and ATG manufacturing requires specialized equipment. Autologous and commercial fibrin glues stabilize but do not cover cartilage transplants. PRF is an autologous substance that fixes and encapsulates diced cartilage without the danger of hypersensitivity or disease transfer. PRF is a second-generation platelet concentrate with growth factors and potent cytokines. PRP is a platelet concentration of the first generation. The preparation of PRF, on the other hand, takes less time and is less expensive than the preparation of PRP. Blood is collected in anticoagulant-containing tubes, doubly centrifuged, and bovine thrombin and calcium chloride are added (24).

Preparing PRF entails collecting blood from the patient in tubes devoid of anticoagulants and centrifuging it in a single-phase centrifuge devoid of chemical additions or bovine thrombin. By binding to particular receptors, growth factors in PRF affect cell proliferation, differentiation, and migration (25). TGF-1 boosts proliferation, PDGF aids mesenchymal cell migration and survival, IGF inhibits cell death, and VEGF initiates and encourages angiogenesis. EGF promotes cell proliferation and differentiation (26,27).

Gradual polymerizations of PRF during centrifugation form a complete and flexible fibrin network (28).

Güler et al. studied the survivability of diced cartilage coated with Alloderm, Surgicel, or PRF. They discovered that the survival of diced cartilage coated with PRF was much higher than that of the other groups. They defined cartilage survival as the loss of chondrocyte nuclei and the proliferation of chondrocytes in the surrounding area. Güler et al. discovered that PRF-covered grafts had reduced inflammation levels and infection incidence (29). The study by Göral et al., which intended to explore the survival rate of diced cartilage in conjunction with PRF on rabbits, found that cartilage grafts containing PRF outlive standard grafts employing oxidized regenerated cellulose. However, no substantial change was seen between diced cartilage with and without PRF (30). These findings contradicted the conclusions of the current investigation. The contradiction of results in the Göral et al. study might be attributed to differences in the study population (rabbits and humans) and the small sample size (9 rabbits in each group). Gode et al. investigated the effect of platelet-rich fibrin (PRF) on the survival rate of diced cartilage in rhinoplasty, as did the current study, which included 40 participants divided into two control and case groups. According to their findings, including PRF decreased graft absorption and boosted survival. According to their results, the average volume reduction in the control group after three months was 0.82 cc and 0.58 cc in the PRF group (31). The current study found similar results, showing the efficacy of adding PRF to diced cartilage to enhance survival. One of the possibly crucial elements in improving cartilage survival may be growth factors in PRF and enhanced stability of diced cartilage by the fibrin matrix.

The study by Santos et al. aims to assess the long-term cosmetic effects of two methods for the dorsum of the nose: diced cartilage vs. shaved cartilage with platelet-rich fibrin (SC PRF). In this prospective interventional trial, 200 patients had surgery using the abovementioned procedures and were assessed three and twelve months later using the Utrecht questionnaire. Furthermore, it was shown that SC PRF delivers better long-term cosmetic effects for most patients (4), similar to our

study's findings. In addition, in a research done by Manoel et al. to evaluate the use of an autologous membrane in rhinoplasty surgery as an alternate way of camouflaging and filling, PRF membrane derived through centrifugation was employed in rhinoplasty surgery of 23 patients. The clinical examination, photographic findings, and the Utrecht questionnaire were assessed. The use of fibrin rich in leukocytes and platelets (L-PRF) for camouflage and filling was determined to be adequate in all patients, and the patients were also satisfied. Furthermore, the PRF membrane is rich in substances that promote and speed tissue regeneration (32). The study by Dong et al., which was done as a systematic review and analyzed the methods of utilizing Diced cartilage technology in rhinoplasty surgery, found that the combination of Diced cartilage with blood products such as PRF or growth factors, cosmetic results are more reliable, and long-term. However, the use of fascia entails issues such as donor site morbidity, inadequate amount, and time-consuming, and in cases of hyaluronic acid (33).

Although the degree of irregularity in the inspection and dissatisfaction with the nose's appearance was reduced in the PRF-treated group after six months, the difference was not statistically significant. Because one of the limitations of this study is the small sample size, these two characteristics may become relevant when the sample size grows larger. PRF had a considerably favorable effect on the survival of cartilage transplants in our investigation. PRF requires a centrifugation stage and is less durable than fascia during preparation. Our findings, however, validated using PRF as a material for supporting diced cartilage. This study was a prospective survey, which is one of its strengths. However, its limitations include single-centeredness and a low sample size, which made some tests non-significant. Until now, studies in this field have been conducted on either animal or human samples with limited sample sizes, so there is a need to conduct studies with a large and multi-center sample size in the future. In addition, a randomized clinical trial (RCT) should be conducted in this field to reduce possible biases as much as possible. Designing and conducting studies comparing PRF's effect with other wrapping materials is also recommended.

Another limitation of this study is the absence of preoperative measurements of skin thickness. Skin thickness is a critical factor influencing the aesthetic outcomes and the technical approach in rhinoplasty. Different skin thicknesses can affect the visibility of irregularities and the integration of the graft material. For patients with thinner skin, for instance, minor graft irregularities or absorptions are more likely to be visible, potentially compromising aesthetic outcomes. Conversely, thicker skin might better disguise such irregularities and mask some subtle enhancements desired from the grafting procedure. Our inability to account for this variable may limit the generalizability of our findings and could represent a confounding factor in the assessment of graft survival and patient satisfaction.

Given this gap, future research should incorporate detailed preoperative assessments of skin thickness using reliable measurement techniques, such as high-resolution ultrasound. This inclusion would enable a more nuanced analysis of how skin characteristics influence the outcomes of diced cartilage grafts with or without PRF, potentially leading to more targeted and effective surgical techniques. Such studies could significantly enhance our understanding of the interplay between biological materials used in rhinoplasty and patient-specific anatomical features.

Conclusion

In conclusion, this study suggests a potential impact of PRF on diced cartilage survival in rhinoplasty surgery. The observed trends indicate promising implications for using PRF in enhancing cartilage graft outcomes. Further research with larger sample sizes and randomized clinical trials is warranted to corroborate these findings and establish the efficacy of PRF in clinical practice.

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