Noncentrifuged Autologous Fat Graft Use On The Treatment Of Lower Extremity Wounds

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Abstract

Background: There is limited number of report related to the direct use of non-centrifuged adipose graft in the literature. This preliminary study aims to present our experience on the efficacy of non-centrifuged autologous fat graft use in the treatment of lower extremity wounds. Methods: 16 wounds treated with non-centrifuged autologous fat grafts were retrospectively analyzed. VAC (vacuum-assisted therapy) or silver-impregnated dressing was used to reduce wound exudation and provide a healthy wound bed before fat grafting. Autologous fat grafts were harvested from abdominal or gluteal regions of the patients and injected into the wound bed and wound environment. Clinical observation and photograph records were used to follow the wounds. Results: 12 wounds needed for covering with skin graft or flap surgery whereas 4 healed without surgery. After debridements, the mean wound surface area was 92.69±62.74 cm2 (125[52-175] cm2 for venous ulcers, 100[25-112] cm2 for diabetic ulcer, and 81[42-120] cm2 for traumatic ulcers). The mean fat injection time was 1.63±0.89, and the mean fat volume was 26.56±15.33 cc. The mean healing time was 32.56±12.03 days. The wounds were uneventful in the average 12 month-following periods. Conclusion: With the results of our study, it can be said that non-centrifuged autologous fat grafts can have beneficial effects on the treatment of chronic challenging wounds when it is present on the wound site during healing.

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healing.

Key words: Diabetic foot, Lower extremity, Fat graft, Needle, Noncentrifuged.

Introduction:

Fat grafting has been a commonly used method in both cosmetic and reconstructive surgery for a long time. Autologous fat graft has an easily accessible donor source, and it is a minimally invasive procedure with low morbidity (1-4). The method has also received a great deal of attention in tissue engineering over the last years due to its stem cell content which has differentiation capability to different tissues under appropriate conditions (5,6).

Diabetic foot ulcer is one of the chronic complications of diabetes and it is the main risk factor leading to non-traumatic amputation in diabetic patients. The prevalence of peripheral vascular disease in diabetic patients is 15-30% (7,8). Diabetes and other chronic conditions negatively affect all wound healing processes and the duration and degree of hyperglycemia play a major role in terms of complications (9,10). The deterioration of the metabolic system leads to reduced resistance to infections, which often result in amputation. A healthy wound healing process needs a well-orchestrated integration of cell migration, cell proliferation, and extracellular matrix deposition. Whereas, chronic conditions such as diabetes, venous and/or arterial insufficiency, lead to dysregulation of the cellular and molecular signals during this process and it can result in inadequate wound healing and chronic ulcers.

In the literature, there have been lots of reports related to the chemical and physical pre-manipulated adipose tissue use and it was generally used in the treatment of chronic scars and burn scars or cosmetic conditions. Besides, there have been a few papers about the direct use of non-centrifuged adipose tissue in the treatment of chronic ulcers in the human subject. In our previous experimental study, adipose tissue was used centrifuging alone in nerve healing with various surgical methods and we obtained considerably beneficial effects of fat grafts when used on nerve healing (5). At this time, autologous adipose tissue was used without centrifuging in the treatment of lower extremity wounds and directly applied to the wound bed and environment after achieved a healthy and suitable wound bed for fat graft take. Thus, the present study aimed to investigate whether non-centrifuged autologous fat graft has efficacy on the treatment in various chronic challenging wounds on the lower extremity.

Patients and methods:

In this preliminary study, 16 lower extremity wounds treated with using non-centrifuged autologous fat graft between 2015-2018 years, were retrospectively reviewed and data were collected from the patient files and photographs (Table 1). The wounds continued for at least three months of high to moderately exudate and required open management to the secondary intervention were included in the study. An informed consent form was taken from all patients. The mean age of the patients was 55.88±9.71 years. The etiologies of the wounds were diabetic, venous or traumatic ulcers. The wounds were debrided and, VAC therapy or silver-impregnated dressing alone (Silverlon; Cura Surgical, Geneva, Illinois) was applied to achieve a healthy wound bed for achieving fat graft take. The wound dressing change was made at 24-48-hour intervals, and VAC therapy was set at intermittent mode at -80mmHg. If the wound was smaller than 10cm2 and/or less exudate at the beginning, the silver-impregnated dressing was used alone to prepare the wound bed for fat grafting. Silver-impregnated dressing was used in 4 cases. When wound exudation was considered to reduce and a healthy granulation tissue started to observe clinically, VAC therapy or silver-impregnated dressing was stopped, and fat grafting was planned.

Autologous fat grafts were harvested from the abdominal or gluteal region. After the infiltration of the standard tumescence solution was performed, tunneling was made with the liposuction cannula (3–5 mm). The cannula was attached to a syringe to harvest the fat grafts from the deep subcutaneous tissue. The volume of fat graft depended on the wound size. An abdominal garment was used for 2 to 4 weeks to minimize swelling and allow for smooth, controlled adaptation of the elevated pockets of subcutaneous tissue to the underlying fascia. The fat grafts were filtered under sterile conditions using a metal sieve and then

washed with 0.9% saline solution to concentrate the fat particles and separate them from fluids and debris. The purified fat was placed in 10 cc syringes using a sterile spoon. Then, the fat grafts were injected around the wound bed and surrounding areas approximately 1cm from the wound edge by 1using 4G blunt single hole cannula or with 2.5cc syringe so as to stay in contact with the wound site (Figure 1,2). It was taken account not to tighten the skin edges so as not to cause any skin necrosis. The amount and frequency of fat graft was determined on clinical observation of the wounds. Ointment dressing and a plaster cast were used for the stabilization of fat graft. The wounds were followed closed for 5-7 days. Patients were received perioperative and postoperative antibiotics guided by positive culture results and sensitivities. Dressing changes were made on 10, 14, 21 days. When the wound shrinkage was observed, the wound was left secondary healing, whereas, the wounds not showing any shrinkage required skin grafting or flap.

Case1: The patient applied to our clinic with signs of diabetic foot ulcers. The wounds were at the left lateral of his left foot, large and highly exudate. It was considered Wagner grade 3-4. The wound debridement was made under general anesthesia (Figure 3). The VAC therapy and debridement period have continued for 13 days (Figure 4). When debridement and VAC therapy was completed, autologous fat grafting was planned. The method was performed under general anesthesia and 19cc fat grafts were injected into the wound site. The wound was followed by closed dressing for 7 days and it was found to be suitable for skin graft in this period (Figure 5). However, the patient didn't accept the operation, so, he was followed by wet-to-dry wound care. In this period, the wound was completely healed at 55 days (Figure 6).

Case 2: A 45-year-male patient was admitted to our clinic because of venous ulcer on his right cruris (Figure 7). First, the wound debridement was made under spinal anesthesia and the silver-coated dressing was started for decreasing exudate and reaching a healthy wound bed. After wound care of 3 days, fat grafting was performed under general anesthesia. 10cc fat graft was transferred to the wound site in this operation. 10 days after the application, considerable wound shrinkage was observed, and this wound was left secondary healing. The total treatment time was 10 days and the wound completely healed in 16 days (Figure 8).

Case 3: The patient had us malodorous, necrotic, and large traumatic foot ulcer (Figure 9). After debridement, the wound has been applied VAC therapy for 7 days. After the VAC therapy, the wound was found suitable for fat grafting and the procedure was performed 2 times (Figure 10). VAC therapy has been continued 12 days more. Then, the wound has become suitable for covering by skin graft. The total treatment period was 53 days (Figure 11).

Case 4: A 55-year-female diabetic patient was admitted to our clinic with signs and symptoms of diabetic foot ulcer on her left foot at the first toe to the level of the metatarsophalangeal joint. The wound debridement was made under spinal anesthesia and VAC therapy was applied (Figure 12). VAC therapy has been continued for 10 days. When the wound exudation was clinically observed get less, fat graft was planned. A single fat application of 10cc was made and then, the wound was covered by skin graft (Figure 13). The total healing time was 28 days.

Statistical analysis

Quantitative data were obtained regarding the arithmetic mean, standard deviation or frequency, percentage. One-way analysis of variance (ANOVA) test was used to compare quantitative variables among groups. A p-value <0.05 was considered significant. Analyses were performed using SPSS 19 (IBM SPSS Statistics 19, SPSS inc., an IBM Co., Somers, NY).

Results:

Tables 2 and 3 show the distribution of quantitative and qualitative variables according to wound etiologies. 4 cases were venous ulcer, 10 cases were diabetic ulcers and 2 were traumatic. All wounds were applied vacuum-assisted therapy or silver-impregnated dressing alone so as to reduce exudation and provide a healthy wound bed before fat grafting. A healthy granulation tissue formation was generally started to observe by day 5. At the commencement, the mean wound surface area was 92.69 ± 62.74 cm2. The measurement for venous ulcers was 125[52-175] cm2, 100[25-112] cm2 for diabetic ulcer and 81[42-120] cm2 for traumatic ulcers. Total healing

time was 23.5[13-31.5] days 34.5[23-35] days and 45.5[38-53] days, respectively. The fat injection was made 1[1-1.5] time for venous ulcers, 1.5[1-2] times for diabetic ulcers and 2[1-3] times for traumatic ulcers. The mean fat volume used was 20[10-30] cc, 20[19-30] cc, and 50[50-50] cc, respectively. Seven wounds required applying fat graft one more time. According to fat injection, mean fat volume and mean treatment time, statistically significant difference was not found between the measurements. 12 wounds required using a skin graft or flap surgery to cover and 4 were left secondary healing. Cross-leg flap was used for one diabetic heel ulcer because these wounds were at the weight-bearing area. The following period was averaged 12 months and the patients were uneventful in this period.

Discussion:

In chronic wounds, the use of adipose tissue has become very popular due to its regenerative capacity and its stem cell content and a great promise in tissue engineering and reconstructive surgery over the last years (5). The stem cells secrete various growth factors and cytokines named paracrine function. Experimental and previous clinical studies have shown that transplantation of autologous mesenchymal stem cells into ischemic limbs could promote collateral vessel formation and angiogenesis (11-16). Stem cells have also enormous potential for skin tissue regeneration, as the cells can both regenerate lost tissue and promote wound repair through paracrine coordination of their actions (5). Thus, the rationale of the present study was to investigate whether adipose tissue could aid the cutaneous wound healing process owing to its rich stem cell content in various acute and chronic wounds. This study describes our clinical outcomes on the treatment of lower extremity wounds with directly using the non-centrifuged fat graft.

In clinical practice, centrifugation is routinely made in 3000 rpm for 3 minutes during various fat grafts uses. Centrifugation is introduced to concentrate adipocytes and separate them from substances that may degrade adipocytes, such as blood cells, proteases, and lipases, and establish a better environment for tissue viability, although there is no consensus on the latter (17). A recent study by Conde-Green et al. compared the influence of the three most used fat-processing techniques (i.e., decantation, washing, and centrifugation) on the viability and number of adipocytes and mesenchymal stem cells in the aspirated fat (18). They conclude that washing is the best processing method for adipose tissue grafting, as it maintains adipocyte integrity and number, clears the fat with most blood contaminations, and has a greater number of endothelial cells and mesenchymal stem cells. Asilian et al, no significant difference was found between the two fat-processing methods (19). Similarly, in a different study, transplantation of non-centrifuged adipose tissue was found to have more active pre-adipocytes which could possibly lead to better potential chances of survival and even de novo development of fat (20). In the present study, the non-centrifuged autologous fat graft was applied to the wound edge, wound bed and environment. And, we observed better results compared to our previous observation and experiments for similarly wounds as it was used without centrifuging.

In our study, before fat grafting, the wound debridement was made, and then, they were treated vacuum-assisted therapy or silver-impregnated dressing to accelerate reducing exudation and providing a healthy wound bed for enhancing the fat graft take. In the majority of the wounds, VAC therapy was preferred, because these wounds were larger and have more exudates than others. In other wounds, silver-impregnated dressing alone was used to prepare them for fat grafting. A healthy granulation tissue formation was generally started to observe by day 5. In a similar study, the authors used autologous fat graft without centrifuging in chronic lower extremity wounds and they obtained completely healing in twenty-two of 25 wounds (9). However, the authors used the fat grafts for relatively smaller sized wounds compared to those of our study, and parallel to that, they transferred a smaller amount of fat grafts. Also, our mean healing time was shorter. VAC therapy was also used after fat grafting in that study. So, it can be speculated that VAC therapy can positively affect their results although they suggest that VAC therapy time of 4-5 days was probably not responsible for the good outcomes. In the present study, VAC therapy was used before applying the fat grafts. However, we also had to use VAC with fat in one case. This was because tissue necrosis was ongoing, and the wound was relatively large and highly exudated than others. We also used silver-impregnated dressing in 4 wounds relatively smaller than others and less exudated. The silver-impregnated dressing or VAC therapy has several theoretical advantages including antimicrobial inhibition and enhancement of soft tissue granulation

(7). So, it can be an explanation of the difference in mean healing time between two comparable studies.

Various intrinsic factors such as microcirculation, and chronic diseases, diabetes, and venous insufficiency determine the wound response to the fat grafts used. After the non-vascularized fat grafting, the connective tissue or extracellular matrix may be preserved as a scaffold, and all differentiated cells usually die and are replaced by those of the next generation derived from tissue-specific stem cells, depending on the microenvironment (5,6). Besides these intrinsic factors, the fat graft volume is mainly determined according to the wound surface area. Therefore, while making a decision about any therapeutic fat grafts dose or frequency of application, it should be taken wound etiology and localization into consideration. Hypoxic or diabetic environment can affect fat graft survival increasing the mesenchymal and endothelial progenitor cell responses and enhancing the formation of blood vessels and (21,22). In our study, we generally observed that the skin surrounding the wounds started to turn into normal color especially in venous ulcers. It is known that these pathologic tissue changes in chronic wounds can arise by the inflammatory process and extensive inflammation plays a major role in the disruption of the normal healing cascade (23,24). So, it can be speculated that our clinical observations can be related to the anti-inflammatory and immunoregulatory function of stem cell content of adipose tissue graft (25,26,27). We can say that it can be one of the clinical signs indicating the efficacy of fat grafts on the treatment of challenging wounds.

Limitation:

In the present study, although traumatic ulcers were relatively smaller than other wounds, total fat volume, application frequency and total healing time were found longer in traumatic ulcers. We think that the number of cases was less to make comparisons and provide a significant conclusion. Also, the reason for longer treatment time and more fat volume need in traumatic ulcers might have been due to these ulcers being complicated wounds. In addition, fat graft volume used in wounds causing by different etiologies was always not correlated with the degree of clinical signs and improvement.

Conclusions:

There are limited numbers of papers with the direct use of adipose tissue grafts in the literature and they are generally related to the burn scars. In the majority of these reports, the centrifuged fat graft was used. In this preliminary study, we found that the presence of non-centrifuged fat graft during wound healing on the wound site could have beneficial effects. However, more clinically and experimental studies are needed to provide more comparable, clarifying and optimal results.

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Figure and table legends:

Figure 1. The fat grafts were filtered under sterile condition using a metal sieve and then washed with 0.9% saline solution to concentrate the fat particles and separate them from fluids and debris. The purified fat was then collected using a sterile spoon and placed in a 10 cc syringe. Various cannulas and syringes were used to inject the fat grafts to the wound site.

Figure 2. After debridement and wound care, autologous fat graft was transferred to the wound bed and environment approximately 1cm from wound edge and site by a sharp cannula or 18G syringe.

Figure 3,4. The diabetic patient with chronic non-healing ulcer for over 3 months. The patient was admitted to our clinic with infected, abscess and highly exudate foot ulcer. The wound was immediately debrided. Meanwhile, VAC therapy was started.

Figure 5. 19cc fat grafts were injected to the wound site. The wound was followed in closed dressing for 7 days and the wound was found to be suitable for skin graft at the end of the period.

Figure 6. The wound was left secondary healing and it was healed by 55 days.

Figure 7. 45-year-male patient applied to our clinic with the venous ulcer on his right cruris.

Figure 8. 10cc fat graft was transferred to the wound site in this operation. 10 days after the application, rapidly wound shrinkage was observed, it was left secondary healing. Total treatment time was 10 days and the wound completely healed in 16 days.

Figure 9. 51-year-male patient was presented with sign of odor, necrotic, moderately exudate and large foot ulcer by trauma. The wound was serially debrided and VAC therapy was applied.

Figure 10. Fat grafts injections were made as exudation was less and necrotic tissues properly cleaned. The method was applied two times. Total volume was 40cc.

Figure 11. As the wound was found to be suitable for skin grafting, it was covered and completely healed in total treatment period of 53 days.

Figure 12. A-55-year-old diabetic patient was presented with sign of odor, necrotic, moderately exudate and large foot ulcer. Debridement and VAC therapy was made for 5 days.

Figure 13. Single fat application of 10cc was made and the wound was covered by skin graft. Total healing time was 28 days.

Table 1. Summary of the patients.

Table 2. Distribution of qualitative variables

Table 3. Distribution of qualitative variables by Wound etiology.

Data are shown as mean±standard deviation or median[interquartile range].

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