

Original Paper

Split-thickness Skin Grafting in the Treatment of Surgically Operated Diabetic Foot. A Retrospective 2-Year Study (2010-2011)

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REZUMAT

Plastia cu piele liberă despicată în tratamentul piciorului diabetic operat. Studiu retrospectiv pe 2 ani (2010-2011)

Plastia cu piele liberă despicată, metodă folosită în chirurgia plastică și reparatorie în tratamentul defectelor tegumentare rezultate în urma intervențiilor chirurgicale, este o tehnică din ce în ce mai utilizată în ultimul timp în tratamentul plăgilor cu lipsă de substanță apărute în cursul evoluției patologiei piciorului diabetic, dar în același timp un subiect extrem de controversat în ceea ce privește eficiența sa pe termen lung la pacientul diabetic.

Material și metodă: Prezentăm un studiu retrospectiv pe un interval de 2 ani (2010-2011), analizând 44 pacienți diabetici cu defecte tegumentare post-operatorii la nivelul membrelor pelvine cărora li s-au aplicat plastii cu piele liberă despicată.

Obiective: Scopul analizei a fost identificarea cauzelor care au influențat eșecul sau succesul grefării la cei 44 de pacienți diabetici, care pe lângă terenul vasculopat sau neuropat diferit, au asociat și comorbidități importante.

Rezultate: Din cei 44 pacienți, 11 femei (25%) și 33 bărbați (75%), 36 au avut succes al grefării (82%) iar în 8 cazuri (18%) s-a constatat eșec. Pacienții au fost urmăriți săptămânal post-operator în prima lună, apoi la 1 lună, 2 luni, până la 2 ani. Timpul mediu de vindecare a fost între 2 și 8 săptămâni. Au fost analizate: distribuția pe sexe și pe medii de proveniență a pacienților, durata de spitalizare în raport cu localizarea defectului, gradul de anemie, valorile hemoglobinei glicozilate, a glicemiei a jeun, suprafața defectului tegumentar, comorbiditățile, fumatul, flora microbiană de la nivelul patului receptor imediat înainte de aplicarea grefei, toate corelate cu rata de eșec respectiv succes a grefării. Au fost comparate costurile spitalizării în cele două loturi.

Concluzii: Rezultatele acestui studiu retrospectiv situează plastia cu piele liberă despicată în categoria metodelor de ales în accelerarea vindecării defectelor tegumentare la pacientul cu picior diabetic operat.

Cuvinte cheie: picior diabetic, plastie cu piele liberă despicată, defect tegumentar, eșecul grefei

ABSTRACT

Split-thickness skin grafting, a method used in plastic surgery in the treatment of skin defects resulting from surgery, has lately been used more and more widely in the treatment of wounds with significant missing tissue occurring in the evolution of diabetic foot pathology; at the same time, it is a highly controversial topic as regards its long-term effectiveness in diabetic patients.

Material and method: This is a presentation of a retrospective 2-year study (2010-2011) involving 44 diabetic patients with post-surgical skin defects in the lower limb who underwent split-thickness skin grafting.

Objectives: The aim of the analysis was to identify the causes influencing the success or failure of the graft in the 44 diabetic patients who, apart from different vasculopathies or neuropathies, also have significant comorbidities.

Outcome: Out of the 44 patients, 11 female (25%) and 33 male (75%), 36 had successful grafts (82%) and in 8 cases (18%) the graft failed. After surgery, the patients were monitored weekly in the first month, then monthly, and then every 2 months up to 2 years. Average healing time was between 2 and 8 weeks. The following aspects were analyzed: breakdown according to gender and patient background, length of hospitalization relative to the defect site, the degree of anemia, the levels of glycated hemoglobin and fasting glucose, the area of the skin defect, comorbidities, smoking, microbial flora in the recipient site right before grafting. All of these aspects were correlated with the rate of success or failure of the graft. The cost of hospitalization was compared between the two groups.

Conclusions: The results of this retrospective study indicate that split-thickness skin grafting should be a method of choice in reducing the healing time for skin defects in patients with surgically operated diabetic foot.

Key words: diabetic foot, split-thickness skin grafting, skin defect, graft failure

INTRODUCTION

Diabetes mellitus is a major health problem with significant impact on the quality of life, due to both its complications and comorbidities and due to the costs it generates. There is widespread agreement that the incidence of the disease has increased over the last years, both due to better population monitoring and improvements in diagnosing methods.

Thus, the number of cases of diabetes mellitus worldwide was 382 million in 2013 and the number is rising; there are 75 million cases of diabetes mellitus which go undiagnosed, as the majority of diabetic patients are discovered only when complications set in. (1)

According to the American Diabetes Association, the prevalence of diabetes mellitus is expected to reach 9% in 2025 (2); according to US estimates, if the current trend continues, one in three adults will have diabetes in 2050.(3)

Out of the numerous complications of diabetes mellitus, the diabetic foot stands out due to the morbidity and mortality its evolution generates; it is defined as the presence of ulceration, infection and/or deep tissue destruction in the lower limb of a

patient diagnosed with diabetes mellitus, in the context of evolving neuropathy and various stages of peripheral vascular disease. (4)

The septic complications of the diabetic foot are noticed late and sometimes neglected by the patient; consequently, they generate lesions that require various types of surgical intervention (from simple debridement – excisions and incisions, to amputation, whether minor – toe or ray amputation – removal of the toe along with a greater or lesser portion of the metatarsal head – or major, below-knee or above-knee amputation). Note that diabetic foot ulceration is the pre-amputation lesion in approximately 80% of cases. (5,6)

Treating the skin defects of the surgically operated diabetic foot is a real challenge for the surgeon and a significant part of the surgical management of this pathology. In order to perform amputation as distally as possible and to preserve locomotion, “conservative” surgery employs focal interventions whose immediate result is often a significant amount of missing tissue, which requires eventual filling up. An intermediate stage in this sequence of surgical events is obtaining the granulation of the wound tissue, with the immediate goal of

speeding up the healing process irrespective of the chosen therapeutic method (surgical or non-surgical). Because there is no “ideal” standard management for such wounds, the therapeutic approach in various stages in the evolution of these wounds relies on a variety of methods, both surgical (debridement, secondary sutures, covering the defect by means of autografts, allografts, xenografts, biomaterials) and non-surgical (from the least costly: application of topical preparations – zinc oxide, carboxymethyl cellulose, alginate hydrogels, sulfadiazine, antibiotics, povidone-iodine etc., to the more costly, such as hyperbaric oxygen therapy or negative pressure).

Covering skin and soft tissue defects by means of autografts is a relatively inexpensive method available to the surgeon involved in the treatment of diabetic foot lesions.

The rationale for the study was based on the different evolution of split-thickness skin grafts and subsequent graft failure in some patients, despite using the same methods for harvesting and grafting. The study aimed to identify the factors which might have a positive or negative influence on the evolution of grafts applied to the skin defects of the operated diabetic foot.

MATERIAL AND METHOD

This retrospective study involved a group of 44 diabetic patients admitted to the Surgical Clinic of Cantacuzino Hospital in 2010-2011 who underwent split-thickness skin grafting for skin defects caused by various lesions related to the diabetic foot. We analyzed the success or failure of grafting by examining certain variables which will be presented in more detail below.

The criteria for inclusion in the study were the following: both male and female patients with a history of diabetes mellitus and age under 18, with

granulating post-operative wounds in the lower limb following the treatment of lesions related to the diabetic foot, irrespective of the location and extent of these skin defects, and irrespective of the patient’s vasculopathies or neuropathies. The criteria for exclusion were the following: non-diabetic patients, patients aged below 18, with lesions caused by other factors than the diabetic foot (venous ulcers, chronic wounds due to trauma or radiation), non-granulating wounds.

We analyzed the distribution according to gender, background, comorbidities, smoking, and complications of diabetes mellitus related to graft success or failure. We correlated the degree of anemia, the levels of glycosylated hemoglobin and glucose, and the area of the skin defect to the outcome of the grafting. We analyzed the microbial flora in the recipient wound bed and the duration of hospitalization correlated with the location and extent of the defect and the cost of hospitalization, both in the success group and in the failure group.

Some further clarification is in order: graft failure means failure of the graft to adhere within 2 months of the grafting, and post-grafting complication means any pathology occurring in the grafted leg within the follow-up period, beyond the first 2 months up to at most 2 years. The patients were monitored weekly after surgery in the first month, then monthly, then every 2 months for a total of 2 years, which corresponds to the recommended follow-up period in the literature. Average healing time was between 2 and 8 weeks.

Outcome

Out of the 44 patients, the sex-ratio M/F was 3/1, most of them - 32 patients – living in urban areas. The average age of the patients was 58.06 years. Therapeutic success was achieved in 36 patients (82%). The length of diabetes mellitus ranged between newly discovered (0 years) to 38 years, the

Table 1.

	Laength of diabetes mellitus (mean)	Age (mean)	Sex ratio (M/F)	Treatment Oral antidiabetic drugs/ Insulin/Diet	HbA1c (mean)
Total 44	10.4	58.06	3/1	16/26/1/1	9.23
Failure (8/44)	8.87	60.63	7/1	2/5/1/0	9.3275
Success (36/44)	10.77	57.5	2. 6/1	14/21/0/1	9.21
p	0.54				

average being 10.4 years. A comparative analysis of the two groups shows a higher mean age in the failure group (60.63 years) compared to the success group (57.5 years). There is also a minimal difference between the mean levels of glycolysed hemoglobin in the failure group (higher) than in the success group.

A comparative analysis of the two groups examined the number and type of comorbidities (arteriopathy, neuropathy, nephropathy, smoking) as well as the presence of anemia and bacterial contamination of the granular wound bed before the application of the graft, in an attempt to identify any generic factors that might influence the evolution of the graft.

There is no difference between the two groups in terms of the (proportionate) number of comorbidities, the presence of arteriopathy, neuropathy and nephropathy, or the presence of germs on the granular wound which might have a negative influence on the evolution of the skin graft. However, there are differences in terms of smoking, as 75% of the patients in the failure group are smokers, compared to 55% in the success group. There are also differences in the number of anemic patients, as well as in the degree of anemia in the two groups. Starting from the fact that there are differences between the normal levels of hemoglobin in males versus females, we tried to compute the actual level of anemia by deducting the actual hemoglobin level of the patient at the time of grafting from the lowest normal hemoglobin level for the patient's

gender (12 g/dl for females and 13 g/dl for males). In the success group there are only 12 (33%) anemic patients, with a mean degree of anemia 1,13 g/dl. In the failure group, 6 out of 8 anemic patients have a degree of anemia of 0.99 g/dl. Finally, we compared the characteristics of the graft surface (area, location) and the consequences of the skin graft failure as regards the extended length of hospitalization and related costs.

An analysis of the location of the defect relative to graft success/failure shows that in 50% of the patients in the failure group (4 out of 8) the defect was located on the sole (3) and the calcaneus (1), unlike the success group, where these locations occurred in a percentage of 13.88%; a tentative conclusion may be that grafting on the sole might contribute to failure.

There are differences (though without statistical significance) ($p = 0.65$) between the mean area of the grafting surface, which is 25.5 cm² in the failure group and 23.3 cm² in the success group, as well as in the length of stay, which is extended by an average 0.5 day for unsuccessful graft patients. Consequently, there will be a difference between the costs of hospitalization for the two groups (treatment failure entails higher costs).

DISCUSSION

Historically, skin grafts were made since 2500-3000 B.C., initially in the reconstruction of facial defects (7). In 1872, Ollier and Tiersh described the

Table 2. Comorbidities

	Number of CMB	A/N/M	Smoking	Nephropathy	Anemia	Degree of anemia	Mono/polymicrobial contamination/ no bact. exam.
Failure (8/44)	5/8	3/2/3	6/8	2/8	6/8	0.99	5/1/2
Success (36/44)	24/36	11/8/17	20/36	7/36	12/36	1.13	17/9/10
p						0.721	

CMB-comorbidities; A/N/M-arteriopathy/neuropathy/mixed; bact. exam. – bacteriological examination

Table 3.

	Defect area (mean)	Defect location calcaneus/sole/TMT/other	Length of stay (hospitalization)	Costs
Failure (8/44)	25.5	1/3/3/1	7.62	2,653
Success (36/44)	23.36	1/4/15/16	7.16	2,188.05
p	0.65		0.7	0.48

TMT-transmetatarsal

method of grafting split-thickness skin (7). Nonetheless, split-thickness skin grafting was not recommended traditionally in the treatment of skin defects associated with the diabetic foot, particularly in the case of sole defects (8). With the accumulation of experience, this method tended to be used more and more frequently in the diabetic population, and is now considered an effective alternative compared to other methods (7,9). The use of autografts in the treatment of post-surgical skin defects of the diabetic foot seems to reduce healing time, as confirmed by recent research. For instance, Mahmoud and colleagues conducted a prospective study comparing the healing time required by diabetic foot wounds after split-thickness skin grafting versus the conservative treatment employing the application of topical products; the mean healing time after grafting was 28 days versus 122 days after conservative treatment (10).

Out of the 44 patients involved in our analysis, grafting was successful in 36 cases (82%) and failed in 8 cases (18%), which is similar to some studies in the literature: Mahmoud (Sudan) claims 86% success rate in patients monitored for 1 year after grafting (10) and Puttirutvong (Thailand) had 82.5% success rate in patients monitored for 6 months after grafting (11).

Given the majority of male patients (3/1 M/F) (75%), the mean age of 58.06 years and the duration of follow-up of up to 2 years, our analysis is consistent with the studies in the literature (72% males in a patient group of 84, a mean age of 61 years and a duration of follow-up of up to 2 years). (8)

In our group of 44 patients, 15 patients (34.09%) had no comorbidities, 12 patients (27.27%) had 1 comorbidity, 9 patients (20.45%) had 2 comorbidities, 7 patients (15.90%) had 3 comorbidities and 1 patient (2.27%) had 4 comorbidities. In the failure group, 3 out of 8 patients (37.5%) had no comorbidities, and in the success group 12 out of 36 had none (33.3%).

In a retrospective study on 107 diabetic patients (12) who had undergone split-thickness skin grafting, 56.1 % of the patients had no comorbidities, 27.1% had 1 comorbidity and 16.8 % had 2 or more comorbidities.

Our criteria for inclusion are similar to the ones used in the study mentioned above, except for the fact that the authors excluded from their study patients with a follow-up time shorter than 6 months and patients with sole ulcerations, which we included

in our study (12). The mean defect area in the same study (12) was 69.3 cm², and approximately one half of the patients (53/107) had a defect area which was smaller than 50 cm². Mean healing time ranged between 3 and 16 weeks, on average 5.1 weeks (12). In our study, the mean surface area of the defect was 23.27 cm² and healing was achieved within 2-8 weeks.

In another study, the mean follow-up duration was 12.6-12.9 months, the mean surface area of the defect was 81.6 - 140.3 cm², and mean healing time was 5.4 - 7.7 weeks. (8)

Mahmoud's article shows that 86% (43 patients) healed completely within 8 weeks, which is similar to the data obtained in our study. (10)

Most of the studies on skin grafting in non-diabetic patients indicate shorter healing times, ranging between 2 and 4 weeks.

The delay in healing in diabetic foot patients has been analyzed and seems to be due to multiple factors, including alterations in micro- and macro-circulation, peripheral neuropathy, epithelium dysfunction and poor control of blood glucose. (13, 14, 15, 16).

Ramanujam and colleagues did not identify statistically significant correlations between the levels of pre-graft HbA1C and healing time, despite the high levels of pre-surgery HbA1C (17), while a study by Marston shows a direct correlation between high blood sugar and delays in healing. (18)

Oyibo and colleagues have concluded that ischemia, the depth of defect, and infection have a negative influence on healing. (19, 20)

Obtaining wound granularity does not always correlate with graft success. In the case of granular wounds with abundant exudate and local signs of infection (purulent discharge, erythema, pain, edema), grafting was postponed until after improvement, which was achieved by using various types of dressings (wet, silver), saline solutions, including negative pressure therapy in selected cases, in order to speed up optimal granulation and to reduce the exudates, in association with surgical debridement (21, 22, 23).

In the absence of local and general signs of infection, the presence of germs in the wound before grafting was not a contraindication for grafting. No grafting was performed in areas with bone, joint, tendon, vessel or nerve exposure in the wound.

Surgery was performed under rachianesthesia. In all cases, the split-thickness skin graft was harvested with a manual knife from the anterior or antero-

lateral aspect of the thigh (ipsilaterally), with no complications (e.g., seroma, hematoma, suppuration). The donor area was covered with tulle-gras and exposed to air on the next day after surgery. Some studies in the literature compare dressings both for the donor area and the recipient site, and according to the most recent studies there is no "ideal" dressing (24). The epithelium in the donor area recovered within 2-3 weeks, but the patients complained of pain in the area (which decreased after the first week). The skin graft was expanded manually. Puttirutvong and colleagues compared the healing rate in patients with expanded grafts compared to patients with unexpanded grafts, and there were no significant differences in a group of 42 patients. (11, 25). Healing time was 19.84 days for patients with expanded grafts and 20.36 days for patients with unexpanded grafts. After degranulation and irrigation of the recipient site with saline solution, the graft was attached to the recipient site with monofilament sutures (3-0 or 4-0) and covered with tulle-gras, and the leg segment was immobilized for up to 5 days after grafting, time during which capillarization and implicitly graft adherence are achieved. (26). Some authors have successfully (97%) used negative pressure in order to immobilize the graft during inosculation. (21, 23, 26, 27).

Hospitalization costs for our two study groups were as follows: 2,653 RON in the failure group versus 2,188 RON in the success group, which indicates a significant cost difference.

In a prospective study conducted by Apelqvist in 1994 on 314 diabetic subjects with lower limb ulcerations, the average cost for patients with per primam healing of ulceration was 6,664 \$, whereas the average cost for patients who required amputation was 44,790 \$. (28, 29)

Stockl conducted a retrospective study (2000-2001) on 2,253 patients with diabetic foot ulcerations, and found that the cost of an episode depends on the stage of ulceration (from 1,892 \$ in grade 1 to 27,721 \$ in grade 4 or 5). (30)

However, it is difficult to compare direct costs, because there is significant variation between countries concerning the cost and availability of investigations, physician's fee, treatment protocols and corresponding costs in each country. What is obvious, though, is that diabetic foot pathology entails high costs (31).

Using grafts to cover skin defects ensures healing in the majority of cases, thus postponing radical

surgery (amputation) and all the associated inconvenience (disability and its social impact, direct and indirect costs, including costs related to prosthetics).

This study is retrospective, descriptive, and small-sized, which rules out the application of statistical methods to gauge the effect of each variable on graft healing time. A larger sample would have allowed for a statistically significant analysis and would have had the added benefit of examining possible interactions between the variables and their effect on graft healing time. In our opinion, a prospective study is required to identify the effects of various risk factors and comorbidities on the healing of split-thickness skin grafts in diabetic foot patients.

CONCLUSIONS

The study shows a low rate of failure (18%), with a mean healing time of the graft ranging between 2 and 8 weeks. No major differences in healing time could be found in patients with comorbidities versus patients without comorbidities. However, failure occurred in a significant percentage of the patients with defects located on the calcaneus and sole. No statistically significant correlations could be found between graft failure and existing vasculopathy, degree of anemia, high blood sugar, glycosylated hemoglobin or microbial flora in the recipient site. However, there is a difference between the mean length of stay and hospitalization costs of the two groups, as patients in the failure group had longer stays and higher costs of hospitalization. The failure group also had a distinctly higher mean surface area of the defect.

It is our opinion that, by contributing to the reduction of healing time in diabetic foot wounds, split-thickness skin grafting remains a useful surgical method available for the treatment of the diabetic foot.

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