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IMPROVEMENT OF SCAR QUALITY IN SPLIT-THICKNESS SKIN GRAFT DONOR SITES: A SINGLE BLIND RANDOMIZED CLINICAL TRIAL COMPARING RIGENASE® AND POLYHEXANIDE VERSUS HYALURONIC ACID AND SILVER SULPHADIAZINE BASED DRESSINGS

Giovanni Papa[1], Francesca Mosella[2], Giorgia Meshini[1], Giulia Benedetta Sidoti[1], Antonio Zaffiro[2], Umberto Rega[2], Grace Marchi[1], Matteo D'Andrea[2], Paolo Turco[2], Giovanni Polverino[2], Vittorio Ramella[1], Luca Spazzapan[1], Francesco D'Andrea[2]

[1] Department of Plastic Surgery, Cattinara Hospital, University of Trieste, Trieste, Italy; [2] Department of Plastic Surgery, "Federico II" University, Naples, Italy

Summary

Skin graft is a reconstructive technique widely used in plastic surgery. A split-thickness skin graft (STSG) donor site represents a partial-thickness wound that is at high risk for infections, which is often underrated by healthcare practitioners. Therefore, the research of new smart dressings to achieve prompt wound healing is becoming highly important. Recently, two advanced dressings for the treatment of STSG donor sites are proposed: dressing A, based on Rigenase® and polyhexanide (Fitostimoline® Plus, Farmaceutici Damor SpA, Naples, Italy) and dressing B, based on hyaluronic acid and silver sulphadiazine (Connettivina® Bio Plus Fidia Farmaceutici SpA, Abano Terme, Italy). They both favor epithelialization, which represents the main characteristic that an ideal donor site dressing should have. However, since in medical literature there is a lack of consensus about the first choice of dressing to use for STSG donor treatment, we designed a single blind randomized trial to compare these two dressings.

The study included a total of 61 adult patients, all were Fitzpatrick skin type II and III. They were 59% males and the mean age was 70.3 ± 16.5 years. Thirty three donor sites were randomized to dressing A and 28 to dressing B. All donor sites were digitally photographed at regular intervals during the wound healing process and then 3 months later.

The primary endpoint was to compare long-term scar outcome of STSG donor sites 3 months after surgery. The quality of the scar was assessed using two different scar scales: the Vancouver Scar Scale (VSS) and the Manchester Scar Scale (MSS). In both scales, a lower score means a better scar result. The average VSS total score was 3.6 for dressing A and 5.5 for dressing B ($p = 0.017$). Similarly, the mean MSS total score were 7.4 for dressing A and 9.2 for dressing B ($p = 0.03$).

Both dressings showed interesting results but dressing A, either as impregnated gauze than as cream, demonstrated significant better scarring of the donor site. Although time to epithelialisation was similar in

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Correspondence

Luca Spazzapan
Department of Plastic Surgery, Cattinara Hospital, Strada di Fiume 447, University of Trieste, Trieste, Italy
E-mail: lucaspazzapan@gmail.com

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both the treatment groups, our results suggest that dressing A is better than dressing B in long-term scar outcome.

Key words: wound healing, Rigenase®, polyhexanide, hyaluronic acid, silver sulphadiazine, speed of closure, quality of the scar

INTRODUCTION

It is fundamental to consider that the harvest of split-thickness skin grafts (STSG) creates a partial-thickness wound that requires special care. Donor sites result in significant scars, which may heal in an aesthetically displeasing way, with noticeable depigmentation and hypertrophy [1]. In contrast to full-thickness skin graft (FTSG), in STSG there is sufficient reticular dermis left after the harvesting to enable the skin to regenerate itself. Therefore, donor sites heal by secondary intention through epithelialization which could take from 1 to 4 weeks or more depending on different factors, such as age and nutritional status of the patient [2,3]. In addition, even when the donor site re-epithelializes quickly, it may induce pain, pruritus, wound exudation as well as contracture over time and poor durability if subject to trauma. Many patients report that their levels of pain and discomfort are more significant at the donor site than at the graft-treated site, because of the presence of exposed dermal nerve endings. Furthermore, since the donor site is often a large wound, the healing process can be complicated by infection [4]. Advances in anatomical understanding and especially in technological innovations have improved the ability to achieve wound closure in a wide range of patients. For a skin graft to adhere successfully, the wound bed must be free of infection and provide adequate blood supply. When the vascularization is inappropriate or critical structures are exposed, dermal substitutes have been lately introduced into clinical practice as a mean of reconstructing the dermal layer prior to skin grafting. They show a perfect integration and persistence of a peculiar three-dimensional structure (neodermis) throughout the years [5].

The risks and burdens of donor-site morbidity are often understated and there are very few published studies and reviews reporting data and recommendations for donor site's management and treatment. Understanding the complications of donor sites may drive innovative treatments, which also take into account its morbidities and long-term outcomes [4]. In medical literature, there is a lack of consensus about the proper kind of dressing to use for the donor site management, which represents a superficial wound and, in the process of epithelializing, needs a moist and microbe-free environment to heal properly [6]. Treatment strategies are still alternated, indicating that existing dressings do not meet all the criteria of an ideal donor site dressing:

- a dressing which contains Rigenase®, a specific aqueous extract from the Triticum vulgare plant, associated to poly-hexanide (PHMB);
- a dressing whose main ingredients are hyaluronic acid and silver sulphadiazine.

Rigenase® is a specific extract of Triticum vulgare (TVE), a plant belonging to the family of Graminaceae, isolated by Farmaceutici Damor. It exhibits hydrating properties. Rigenase® and polyhexanide dressings have been widely used in the treatment of cutaneous lesions, such as decubitus ulcers, sores, burns and scarring delays, in which stimulation of the repairing process is needed. Used as cream or impregnated gauzes they form a protective layer against the external environment, generating favorable conditions for a faster re-epithelialization of the skin and a more effective wound healing. The activity of Rigenase® and PHMB, favors the wound healing process [7] so that it is considered as a very good solution for STSG donor site treatment.

The second dressing derives from the combination of hyaluronic acid and silver sulphadiazine. It is indicated for the treatment of skin lesions, both acute and chronic, especially those with a delayed healing and a high risk of infection. There are different formulations, such as creams and soaked gauzes [8]. Hyaluronic acid is a glycosaminoglycan and a major component of human connective tissue, with important mechanical and structural functions. Moreover, it has remarkable tissue regeneration potential and it can be easily included within gauzes, foams or creams. It provides a moist environment to protect wounded tissue surface from dryness, it promotes wound healing. In fact, it stimulates fibroblasts proliferation and migration through chemotactic factors upregulation and regulates extracellular matrix (ECM) organization and metabolism. In this manner, it leads the development of proper granulation tissue; it also triggers macrophagic responses and stimulates neo-angiogenesis [9].

Silver sulphadiazine (SSD) has well known broad-spectrum antimicrobial properties. Sulphadiazine exerts its bacteriostatic effect by acting on the cell membranes of microorganisms, while silver nitrate has an effect on the endocellular structures. This association strongly prevents the bacterial colonization of the wound, but it has a very important dis-advantage, such as the prolongation of the wound re-epithelialisation process and a delayed wound healing. SSD has been reported to exert cytotoxic effect on dermal cells [10] possibly through an impaired cytokine activities eventually resulting in aberrant recruitment and activation of macrophages [11]. In

order to combine the properties of hyaluronic acid and silver sulphadiazine and overcome the SSD's downsides in wound healing, a new advanced dressing has been developed.
Therefore, we designed a randomized single blind trial to compare the effectiveness of these two different kinds of dressing, both based on natural substances, which have been proposed in the treatment of STSG donor sites.

MATERIALS AND METHODS

Patient population

We designed a single blind randomized clinical trial to be conducted in patients aged 18 to 90 years who required split-thickness skin grafts. All the patients admitted at the Plastic and Reconstructive surgery hospital units between September 2022 and December 2022 were screened. Patients with any of the following conditions were excluded from the study: pregnancy or breastfeeding, current neoplastic disease or other concomitant serious infections, presence of other important medical conditions (e.g. uncontrolled diabetes mellitus, severe hepatic or renal insufficiency, immunodeficiencies, HIV infection, obstructive arteriopathies involving the area of the study lesion, uncontrolled arterial hypertension), treatment with local antiseptics, analgesics or antineoplastics, known allergies or intolerances of any of the substances administered in this trial. Demographic data were recorded and careful medical history was collected from each patient with special focus on the comorbidities that may negatively influence wound healing: diabetes, end-stage renal disease, connective tissue diseases, anticoagulant therapy, immunosuppressive therapy, malnutrition, obesity, hypothyroidism, chronic venous insufficiency, arterial hypertension, heart failure with reduced ejection fraction, chronic obstructive pulmonary disease. Smoking was also considered to be a risk factor for delayed wound healing. Enrolled patients underwent the same pre- and intra-operative treatments. All grafts were harvested with the same thickness.

Study design and treatment

The study protocol was reviewed and approved by the Institutional Ethic Committee.
All patients enrolled in the trial provided written informed consent prior to the start of any study-related procedures. The donor sites were randomly assigned with a 1:1 ratio to receive either Fitostimoline® Plus Fitostimoline® Plus (Farmaceutici Damor SpA, Naples, Italy, hereinafter named "dressing A") or Connettivina® Bio Plus (Fidia Farmaceutici SpA, Abano Terme, Italy, hereinafter named "dressing B") dressings, in the form of soaked gauzes and cream. Randomization was performed by using an excel "random" scale and by dividing the patients in two groups: group A (Fitostimoline® Plus) and group B (Connettivina® Bio Plus). Pre-operative antibiotic prophylaxis consisted of the administration of cefazolin 2g (3g for weight > 120 kg), following the current standard adult surgical prophylaxis guidelines. In patients with beta-lactam allergies, clindamycin or vancomycin were used as alternatives.
All skin grafts (0.3 mm thickness) were removed by a plastic surgeon from the thigh using an electric dermatome. Before the harvest, the suitable donor site area was checked and prepared in a sterile way, using povidone iodine. After measuring the recipient site, the donor site was marked to ensure that the harvest would be of the appropriate size. A sterile lubricant was applied on the donor site to make the harvesting process easier. Immediately after harvesting, the donor site was covered with a calcium sodium alginate wound dressing for haemostasis and exudate control until surgery had been completed. At the end of the operation, the wound was cleaned with saline solution and either Fitostimoline® Plus or Connettivina® Bio Plus impregnated gauzes were applied. Then, an absorbent foam dressing and two layers of cotton gauze pads were placed onto the medicated gauzes. Moreover, in order to provide increased protection to the donor site wound, self-adhesive elastic bandages were applied on top of the primary dressing.
All patients were hospitalized in the plastic surgery unit, with bed rest restriction after skin grafting. Analgesic, antibiotic and low molecular-weight heparin were administrated when necessary. Paracetamol 1000 g was prescribed on demand according to pain intensity. The dressing of the donor site remained intact until postoperative day 5 if no complication arose. Then, the dressing was changed every 3-4 days, depending on the exudate amount. The plastic surgeon removed the top-dressing layer, and either Connettivina® Bio Plus or Fitostimoline® Plus cream were topically spread on the original gauze on the donor site with a sterile spatula, as allocated. If some parts of the gauze were no longer adherent to the wound bed, the surgeon could decide to remove that part in a sterile way. According to the study protocol, treatment was stopped when complete healing of the wound had occurred. If large amounts of secretions or signs of infection were observed, all non-adherent dressings were changed and a swab culture was taken for microbiological analysis.
After discharge, the patients were instructed to return to the outpatient clinic for examination every 3 days. The last follow up visit was performed 3 months after surgery in order to evaluate the long-term quality of the

donor site scar. All donor sites were digitally photographed at regular intervals during the wound healing process and then 3 months later.

Outcomes

Clinical evaluations were performed by suitably trained and qualified staff surgeons and nurses, who were blinded to treatment. During each visit, a physical examination of the donor site wound, wound edges and perilesional area was performed. The primary out-come of the trial was the quality of the scar after 3 months. Secondary outcomes included healing rate, time to re-epithelialization, local pain and discomfort, infection rate and other postoperative complications. Data on all of these items were prospectively collected and assessed.
Wounds were considered to have achieved complete epithelialization when the entire STSG donor site was covered by epithelium and the primary dressing spontaneously separated itself. Healing was expressed as the total time in days required for complete re-epithelialization of the wound. Patients were asked about the level of pain and discomfort at the donor site and the need for pain medications.
Scarring of the donor site was assessed by the plastic surgery team after 3 months from the operation.
We used two different observer dependent scar assessment methods: the Vancouver Scar Scale (VSS) and the Manchester Scar Scale (MSS). The VSS uses a 0-to-13-point scale to assess pigmentation, vascularity, pliability and scar height, with higher scores indicating more severe scarring. The MSS assesses and rates 5 scar parameters: scar colour, skin texture (matte or shiny), contour in relationship to surrounding skin, distortion and scar texture. The score varies from 4 to 18, with higher scores representing clinically worse scars [12].

Statistical analysis

We based our sample size calculation on results of preliminary observations. We previously observed in a small population a difference of VSS an MSS of -20% between treatment with Dressing A *vs* Dressing B and we determined that a sample size of 56 subjects (28 in each group) would provide 80% power (beta 20%). Considering a possible drop out of about 10%, 66 donor sites should be recruited (33 in each group).
For our study we used the software Python. In particular, for data analysis we used the open-source package pandas, for statistical analysis we used SciPy and for the plots we used matplotlib.
We utilized descriptive statistics to analyze our study group. We used both measures of central tendency, such as mean and median, and measures of variability, such as standard deviation, variance, minimum and maximum variables. Descriptive data were provided as mean ± standard deviation (SD) and range, or as median and interquartile range (25-75th).
To detect any significant differences between the composition of our two treatment groups the Mann-Whitney U test was used. The Fisher exact test was also used when needed. Comparison between the two dressings in terms of time to re-epithelialization was performed using the Mann-Whitney U test.
To detect any significant difference in the quality of scarring results between the two dressings, using VSS and MSS scores, the Student's t-test was used. Statistical significance was set at $p \leq 0.05$.

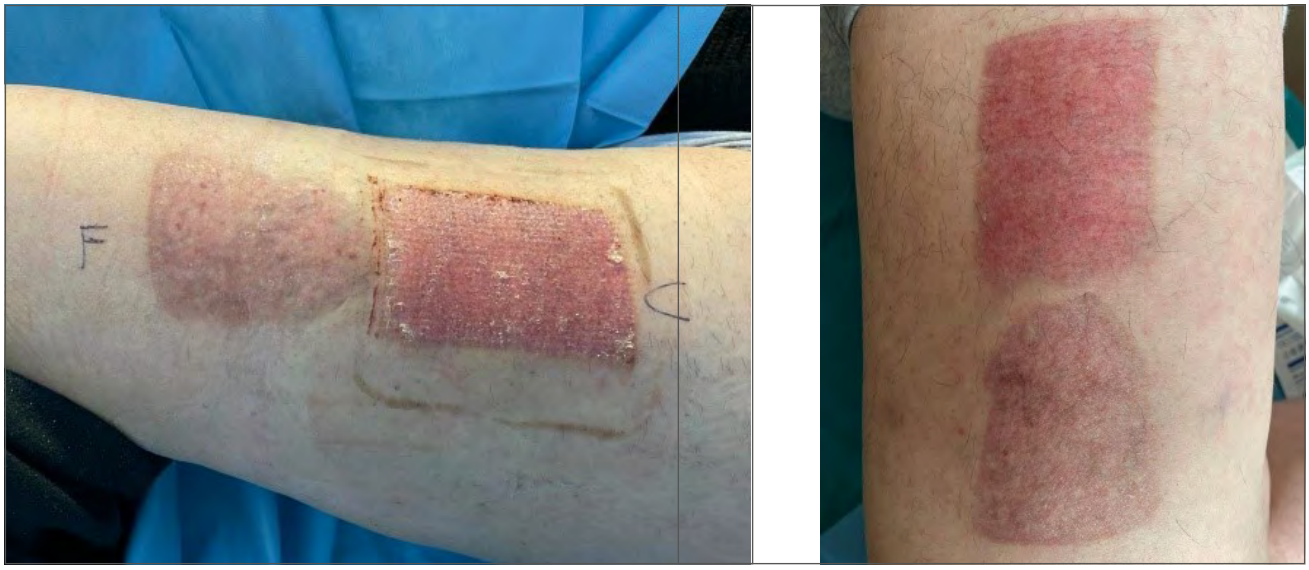
RESULTS

Patients characteristics

The study included a total of 61 adult patients aged 25 to 89 years (mean age of patients was 70.3 ± 16.5 years) all were Fitzpatrick skin type II and III. There were 36 (59%) males and 25 (41%) females. Thirty three (56%) donor sites randomly received dressing A and 28 (44%) received dressing B. The groups were homogeneous regarding their demographic characteristics. All donor sites were placed on the patients' thigh. In 5 (8%) donor sites local signs of infection occurred. Moreover, 4 patients (6%) were active smokers during the study period, 6 were ex-smokers (10%) and 51 had never smoked (84%). In the study group, there were 10 (16%) patients affected by diabetes. Split-thickness skin grafting procedures were carried out on these patients for oncologic surgery (20, 63%), traumatic injuries (8, 25%), chronic ulcers (2, 6%) and postoperative wound complications (2, 6%).
Five patients required the harvesting of two donor sites, one treated with dressing A and the other one with dressing B. In Figure 1-2 are shown the progress of the two scars in one of these patients.

Time to epithelialization

The healing time was calculated as the number of days between the surgery and the complete epithelialization of the donor site. As shown in Figure 3, the median time of healing of all patients included in the study was 22.5 days (IQR: 18.5-30.5).
Five patients, the ones whose STSG donor site got infected during the healing process, were considered outliers. Because of their abnormal healing rate, we decided to exclude their data in the time to re-epithelialization analysis. In this way we obtained a median healing time of 20 days (IQR: 16.5-25.5). The mean healing time was 22.6 ± 8.3 days.
Excluding the data of infected donor sites, the mean time to complete epithelialization for dressing A and dressing B



Figures 1-2. Skin graft harvesting in or and donor site treated with Fitostimoline® plus (F) and connettivina®bio plus (C).

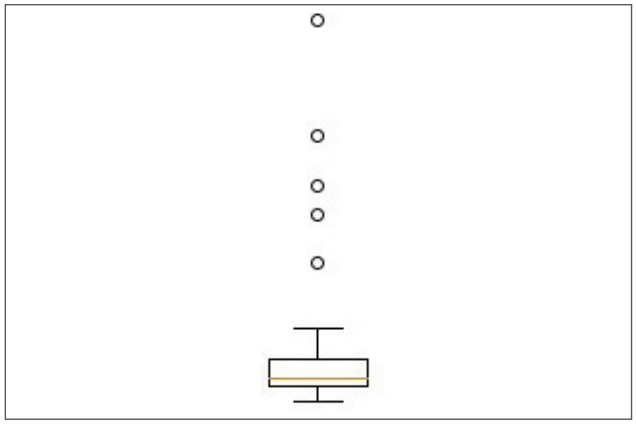


Figure 3. Box plot of median healing time of all patients measured in days.

were 23.5 ± 9.9 days and 21.9 ± 7.3 days, respectively. without any statistically significant difference between the two treatment groups (p = 0.96). Median healing time was 22 days (Q1 = 15.5 and Q3 = 26.5) for dressing A compared to 20 days (Q1 = 18.5 and Q3 = 25.3) for dressing B. The average time of re-epithelialization of the donor sites was comparable in the two treatment groups.

Scar scores

The primary endpoint of the present clinical trial was the long-term scar outcome of STSG donor sites, which was assessed 3 months after surgery. The quality of the scar was evaluated using two different scar scales: the Vancouver Scar Scale (VSS) and the Manchester Scar Scale (MSS). In both scales, a lower score means a better scar result.

Table I. Mean VSS scores by treatment group.

VSS item	Dressing A n = 33	Dressing B Plus n = 28	P value
Vascularity	1.3 ± 0.7	1.7 ± 0.9	0.21
Pigmentation	1.4 ± 0.9	1.8 ± 0.5	0.17
Pliability	0.8 ± 0.6	1.7 ± 0.8	0.001
Height	0.1 ± 0.3	0.3 ± 0.5	0.23
Total score	3.6 ± 1.9 (1-6)	5.5 ± 2 (2-9)	0.017

In Table I and in Figure 4 the VSS mean scores by treatment group are reported. The average VSS total score was 3.6 for dressing A and 5.5 for dressing B (p = 0.017). Considering now the other scar assessment scale, i.e. MSS, we found similar results. In Table II and in Figure 5, the MSS scores of dressing A and dressing B are compared, along with their statistical significance. Even

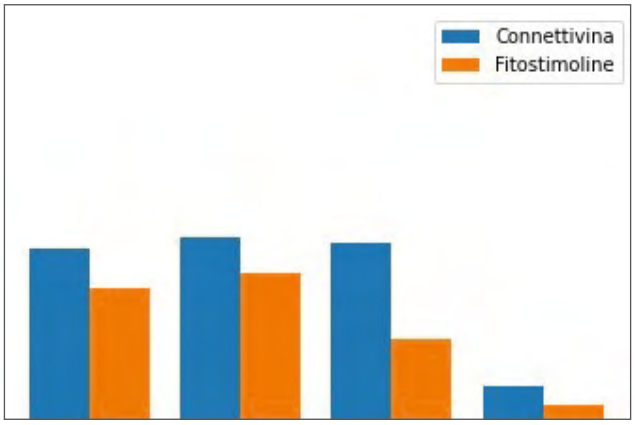


Figure 4. Bar chart showing the mean VSS scores.

Table II. Mean MSS scores by.

MSS item	Dressing A n = 33	Dressing B n = 28	P value
Colour	2.2 ± 0.9	2.9 ± 0.9	0.05
Shine	1.3 ± 0.5	1.5 ± 0.5	0.23
Contour	1.1 ± 0.4	1.6 ± 0.6	0.03
Distortion	1.3 ± 0.5	1.3 ± 0.5	0.80
Texture	1.5 ± 0.5	2.2 ± 0.7	0.006
Total score	7.4 ± 1.7 (5-10)	9.2 ± 2.5 (3-10)	0.03

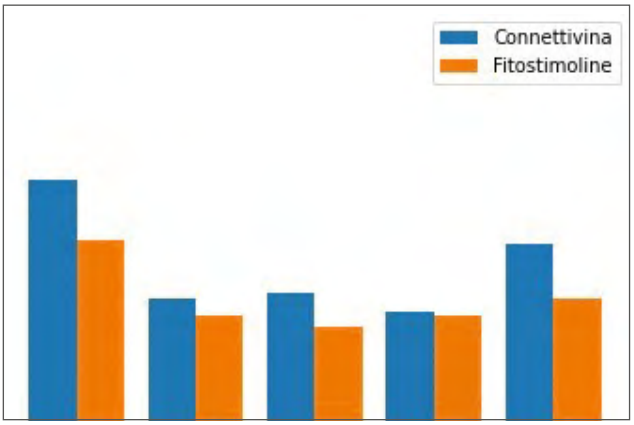


Figure 5. Bar chart showing the mean MSS score.

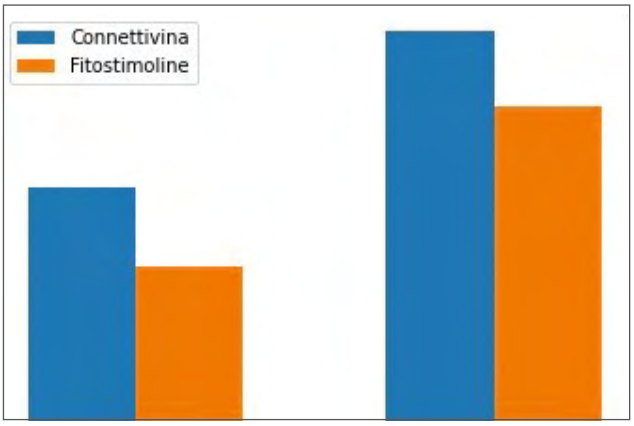


Figure 6. Comparison between VSS and MSS total scores.

in this case dressing A achieved a better long-term scarring outcome since the mean MSS total scores for dressing A were 7.4 compared to 9.2, respectively (p = 0.03).

The comparison between VSS and MSS mean total scores (Fig. 6) demonstrates that dressing A yielded better scarring results.

Figures 7-10 show some photographs that compare the scar outcome between donor sites treated with A or B dressings.

Predictors of long-term donor site scar quality

In our data analysis, we considered time to epithelialization, gender, diabetes and tobacco smoking habits to be some of the most influent factors that affect the quality of the scar.

Considering time to complete re-epithelialization, we decided to divide our group study by healing time (< 14, 14-21, > 21 days), and compared their MSS and VSS total scores (mean ± SD).

In Figure 11 and Figure 12, VSS and MSS total scores for both A and B treatment groups were shown. In Table III the total scores were compared to the healing times. For lower healing times, dressing A showed a better scar quality; instead, for donor sites that healed in more than three weeks, the scarring quality between the two medications was comparable.

Moreover, we analyzed separately the mean VSS and MSS total scores of male and female patients, to verify whether gender could be a factor that predicts long-term scar quality. Mean VSS total score for males was 4.7 ± 2.2 and for females was 4.6 ± 2.3. Moreover, mean MSS total score was 8.8 ± 2.3 and 7.8 ± 2.4 for males and females respectively. No significant differences were found in scar quality, depending on the gender of the patients, neither with VSS (p = 0.88) nor with MSS (p = 0.25).

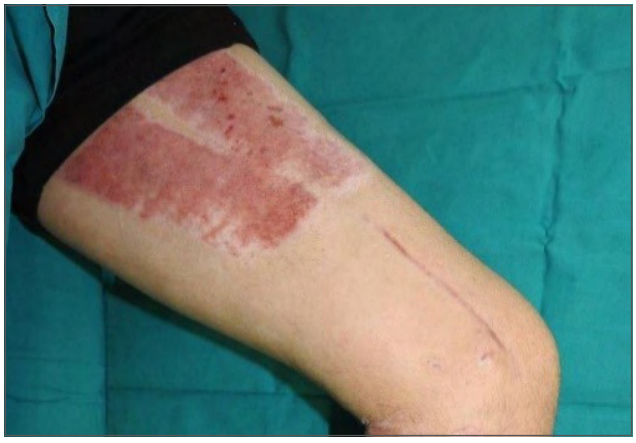
We also evaluated the comorbidities of patients as possible predicting factors, in particular diabetes and tobacco smoking habits. We considered as ex-smokers, people who quit smoking for at least 30 days. In the statistical analysis we decided to put in the same group all people who quitted smoking at least 30 days before the surgery. Mean VSS total score for smokers was 6.5 ± 3.5 while mean MSS total score was 7.5 ± 6.4. For patients who never smoked along with ex-smokers, mean VSS total score was 4.6 ± 2.1 and MSS total score was 8.5 ± 2.1 (p = 0.24 for VSS and p = 0.57 for MSS).

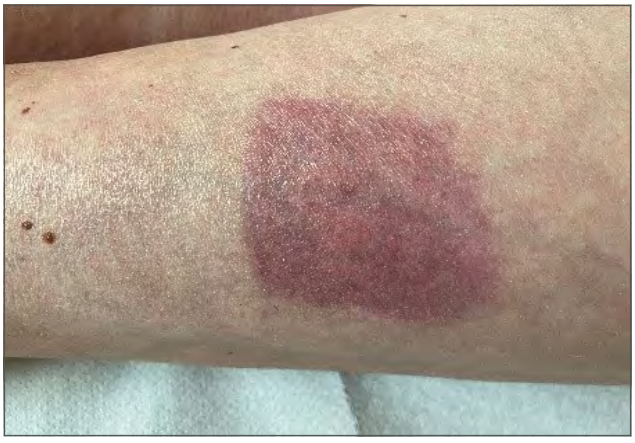
Mean VSS total score and MSS total score for donor sites of diabetic patients was 4.2 ± 3.3 and 7.6 ± 2.5, while for non-diabetic subjects was 4.8 ± 2.0 and 8.6 ± 2.4 (p = 0.60 for VSS, p = 0.40 for MSS). In our study group, patients with diabetes were 60% more likely to fully heal the donor site wound in more than 21 days (RR = 1.6).

In our study, results of pain assessment were not considered relevant and were not reported. We noticed, however, that very few of our patients complained about a significant pain at the STSG donor site. Nevertheless,

Table III. Mean VSS and MSS total scores by healing time.

Total scores	< 14 days	14-21 days	> 21 days	P
VSS	3.5 ± 3.5	4.6 ± 2.1	4.9 ± 2.3	0.60
MSS	8.0 ± 4.2	8.7 ± 2.9	8.3 ± 1.9	0.72





Figures 7-8. Donor sites treated with fitostimoline plus dressing 3 months after.

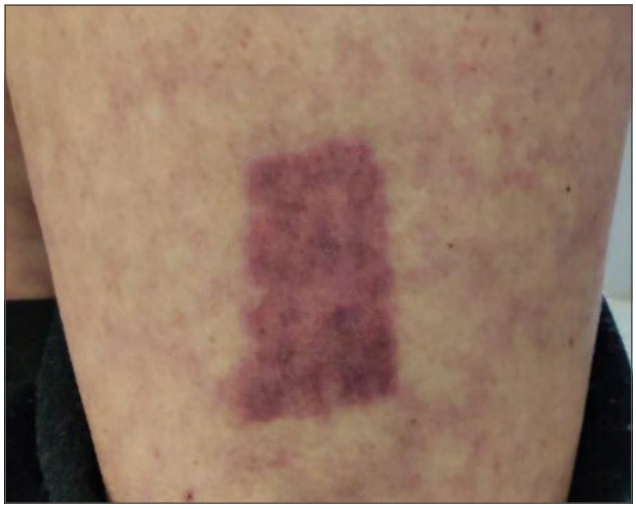


Figure 9. Donor sites treated with connettivina bio plus dressing 3 months after.

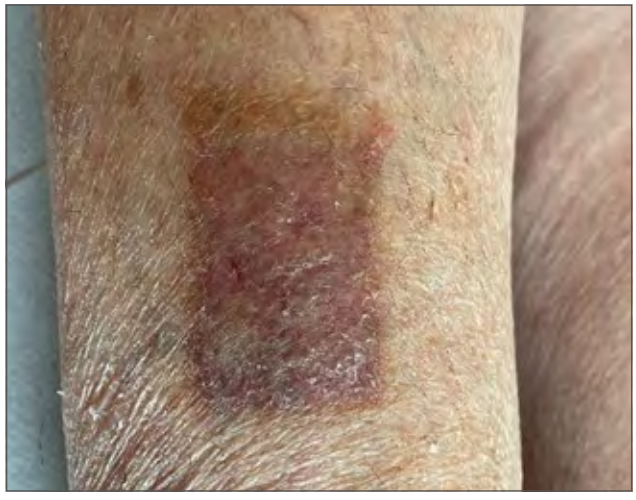


Figure 10. Donor sites treated with connettivina bio plus dressing 3 months after.

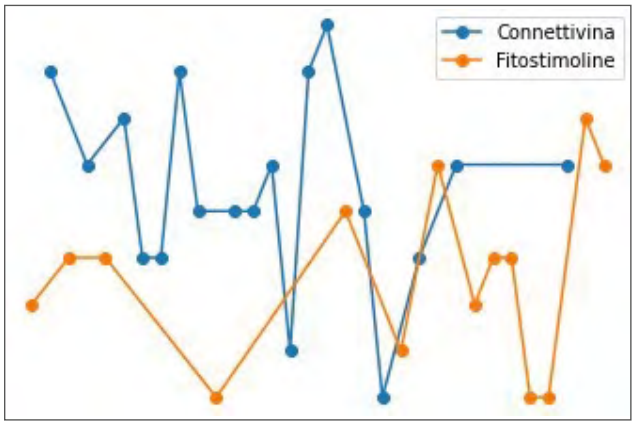


Figure 11. VSS total score.

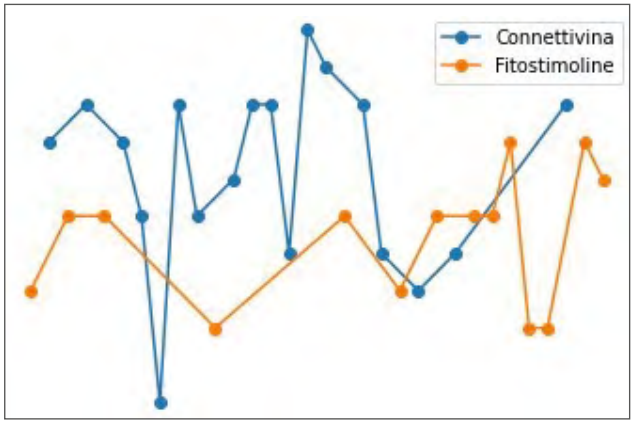


Figure 12. MSS total score.

they reported discomfort, pruritus and concerns about the aesthetic outcome. Patients who complained about high pain intensity were prevalently those whose wound got infected. Pain was scored between mild to moderate in severity. In the first days after surgery, higher pain

scores were usually recorded, even though some patients did not experience any kind of pain and most of them did not need any pain medication. In our study, only a minority of patients required rescue Paracetamol, and local pain decreased very rapidly after the first week of treatment. This trend is observed in all treatment groups in a wide range of studies. While epithelialization occurred, pruritus and discomfort at the donor site usually replaced local pain.

DISCUSSION

Split-thickness skin graft donor sites are partial-thickness wounds that require adequate care, professional management and appropriate medical products. They are another scar that needs to be accepted by the patients, despite the risk of its healing in an unsightly way. Many therapeutic approaches have been adopted, although it is not definitive which one is the best. In fact, the results of many different studies conflict and no single dressing method has been established as the most effective.

Luckies, new molecules and topical agents with exceptional properties are being continuously developed, thanks to new advanced techniques and progressive technologies. There is a substantial need for an ideal donor site wound dressing and the analyzed dressings proved themselves to be two acceptable alternatives. While there are some studies regarding the efficacy of the studied dressings, to our knowledge none of them has investigated the effect on STSG donor sites.

In our clinical trial, each patient was randomly assigned to a treatment group, either with A or with B dressings. The two groups were comparable regarding age and gender. The mean age of the whole study group was 70.3, which was quite higher than in any other similar study.

Different strategies can be used to measure healing time of donor sites. In our study, we reported the number of days between surgery and complete epithelialization of the wound. Across numerous studies, the mean time to epithelialization ranged from 5 to 35 days. In our study, mean and median time to re-epithelialization, considering all the patients enrolled, were 37.0 and 22.6 days, which were a little bit higher if compared to those in the current medical literature. However, the average age of our patients was higher than in other studies and this element could have affected our results. Moreover, some donor sites in our study group got infected after surgery, displaying redness, swelling, increasing pain and discharge from the wound. A swab culture was taken for microbiological analysis and in all cases wound cultures showed Streptococcus Aureus bacteria. The infected wound was treated first with a disinfectant solution and then an antibiotic cream such as Gentamicin was spread. A silver foam was applied as secondary dressing over the donor site wound, when low to medium exudate was present. In few cases it was also orally administered Ciprofloxacin 500 g twice a day for one week. Excluding these infected donor sites, we obtained mean and median healing time of 22.6 and 20 days respectively. Both A and B dressings provided complete healing of the wound within approximately three weeks.

The main purpose of this prospective clinical trial was to assess the ability of A and B dressings to improve scar quality in STSG donor sites. Scars of the donor sites are linearly shaped and commonly placed on the patients' thighs, arms or back.

A dressings in the form of gauzes and cream combined proved to be superior in achieving a better long-term scar result when compared with B products. In fact, Figure 11 and Figure 12 show that the scores of all the items of both scar assessment scales were lower when A dressing was applied on the donor site wound, meaning a better scar result. The characteristics that were the most different, in favor of A dressing, were pliability and texture. Not only A dressings showed better results in mean scores but also considering patients one by one.

We decided to investigate whether there was a correlation between scar quality and healing time, gender and patient's comorbidities such as diabetes and smoking habits. We discovered that patients' donor sites that took more than three weeks to heal had slightly higher (worse) both VSS and MSS scores.

On the contrary, we failed to detect any statistically significant difference between males and females quality scar.

Concerning patients with diabetes mellitus, in our study we did not find any particular difference between mean VSS and MSS total scores, but diabetic patients were 60% more likely to have a healing time longer than 21 days.

Finally, mean VSS and MSS total scores for smokers were quite similar in comparison to ex and non-smokers. For our analysis we united in the same group patients who never smoked and those who quit smoking by at least 30 days.

CONCLUSIONS

Even if STSG is a frequently performed reconstructive technique, there are very few studies that have investigated short and long-term outcomes of split-thickness skin graft donor sites. Their morbidities are often underestimated, despite donor sites being a significant cause of pain and discomfort, affecting patients' quality of life. Moreover, a consensus about the proper way of treating and dressing them has not yet been reached.

Treatment strategies vary too much and this lack of uniformity in the management of donor sites may influence negatively the clinical outcomes.
We designed this single blind randomized clinical trial to compare the final outcome of two promising innovative dressings, in order to contribute to the advancement in this research field. Both the analyzed dressings are secure and effective for this purpose, especially to effectively promote wound healing and scarring. However, the ones containing Rigenase® and polyhexanide, both as impregnated gauze and cream, demonstrated significant better scarring of the donor site. Although time to epithelialization was similar in both the treatment groups, Rigenase® and polyhexanide dressings appear to be superior than the ones based on hyaluronic acid and silver sulphadiazine in long-term scar outcome. In this trial, we have started to define a new possible guideline for the management of skin graft donor sites. More studies are necessary to further confirm our first analysis.

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Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

GP, FDA: A
FM, LS: D
GM, GBS, AZ: DT
UR, GM, MDA: S
PT, GP, VR: W

Abbreviations

A: conceived and designed the analysis
D: collected the data
DT: contributed data or analysis tool
S: performed the analysis
W: wrote the paper
O: other contribution (specify contribution in more detail)

Ethical consideration

This study was approved by the Institutional Ethics Committee of Federico II University Hospital, plastic surgery division (protocol number 00018256).

The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.
Written informed consent was obtained from each participant/patient for study participation and data publication.

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