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IDEAS AND INNOVATIONS

Preliminary results of the new lipogluing technique plus full-thickness skin graft in post traumatic lower limb reconstructive surgery

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Abstract

Soft tissue reconstruction of a complex wound in the lower leg still presents a challenge to reconstructive surgeons, especially in the foot and ankle with exposed bones. We report the preliminary results of soft tissue complex defect treatment and coverage with our new lipogluing technique plus full-thickness skin graft. From September 2015, five patients with complex soft tissue defects on the lower leg underwent the coverage procedure with our new lipogluing technique plus full-thickness skin graft. At the first surgical step after standard debridement, we fix by fibrin glue the graft of fat cells withdrawn using the standard Coleman technique. Lipoglued fat cells enhance the soft tissue cover and better supplement the final skin thickness and pliability. This allows us to achieve the ultimate goal of reconstructive procedures: the recreation of all anatomical cutaneous and subcutaneous layers. Based on this preliminary personal experience, reliable information can be given about the safety, effectiveness, and usefulness of the lipogluing technique plus skin graft. All patients were able to wear normal footwear and to return to their usual activities thanks to the good results obtained and, when necessary, to thin coverage. To date, the coverage appears durable on all patients and they do not show any secondary problems of skin ulceration or breakdown. The lipogluing technique represents an evolution of the reconstructive process that aims to augment the autologous soft tissue under the skin graft avoiding more invasive procedure, in order to obtain a skin cover that feels natural.
Level of Evidence: Level V, therapeutic study.

Keywords Lipogluing · Lipofilling · Fat grafting · Fibrin glue · Complex defect reconstruction · Artiss

Introduction

The treatment of complex soft tissue wounds in the lower leg, in particular with exposed tendinous or osseous structures, remains a challenging clinical problem in terms of functional and esthetic outcomes and one that requires the use of an advanced soft tissue management technique which should preferably be the simplest procedure that effectively solves the problem.

Lipofilling has become an excellent tool in the armamentarium of the reconstructive surgeon; it represents a technical revolution in plastic surgery and it is increasingly used worldwide because of its effectiveness in selected cases. The fat graft survival rates and the longevity of fat transplanted using Coleman's lipostructure have been demonstrated in a high number of cases with long-term follow-up [1, 2]. The autologous fat is a dynamic organ with a lot of therapeutic possibility mediated by all his different components: adipose cells, stromal vascular fraction, and stem cells. Our first idea is to achieve the ultimate goal of reconstructive procedures: the recreation of all anatomical cutaneous and subcutaneous layers. Lipoglued autologous fat (adipose cells plus fibrin glue) associated with full-thickness skin graft is our choice promising to get this kind of result.

With respect to the damage that has occurred, it is important to find a reconstructive method that takes into account not only the functional result, primary goal of reconstruction, but also the cosmetic perspective.

Flaps, although reliable, could sometimes not be available because of limited donor areas or limitations due to the local

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anatomy; also, they are sometimes not the best reconstructive choice in light of the patients' general conditions or of the desired functional and esthetics results.

The use of skin grafting alone could have very bad esthetic outcomes and on the bones, it could create problems due to poor graft take and frequent skin ulceration or breakdown in the long-term [3].

The use of tissue sealants, like fibrin glue, has increased across different surgical specialities [2, 4] because it has been shown to be a useful agent in reducing complications such as seroma, ecchymosis, skin necrosis, and wound dehiscence as it reduces post-operative wound drainage and hematoma [5, 6]. The fibrin adhesive works by achieving hemostasis on large oozing surfaces, sealing open lymphatic vessels, and adhering two raw surfaces together [7]. Fibrin sealants also serve to increase the tensile strength of tissue in comparison with natural fibrin bonds [8].

The fibrin glue (ARTISS Baxter, Deerfield, Illinois, USA) is a good adhesive capable of gluing structures together; it is used in a large number of surgical specialties and in Plastic Surgery, it is available for the placement of skin grafts and for cutaneous and subcutaneous flap attachments [9–11].

Our study explores the viability and the preliminary results of a new promising lipogluing technique to reconstruct all skin and subcutaneous tissue layers by lipoglued fat cells and skin graft, as an alternative to fasciocutaneous flaps [3].

Patients and methods

This study was conducted according to the Declaration of Helsinki developed by the World Medical Association and subsequent amendments and an informed consent was obtained in writing form each patient selected for the study.

Between September 2015 and December 2016, 4 male and 1 female patients, whose age ranged between 46 and 81 years (mean 57.6 years), were treated with the lipogluing technique plus full-thickness skin graft for soft tissue complex defects of the leg and foot. Mechanical trauma was the most common cause of the wound (4 patients), whereas one case was caused by a trauma plus thermal injury during a motorcycle accident.

Surgical technique

The reconstruction was carried out in a two-stage process. In the first stage, surgical debridement was achieved in all instances and the bony surface, when exposed, was abraded lightly to achieve, when possible, an adequate vascularized wound bed.

The wound was carefully cleansed and disinfected with a povidone-iodine solution and rinsed with physiological water, with the aim of reducing the bacterial load [12].

Fat was harvested as per the Coleman technique, under low negative pressure through manual suction with a 20-cc hand-held syringe and a blunt 3-mm cannula at the level of the abdominal region and thigh only based on patient's preferences and anatomical possibility. The fat was filtered using a metal sieve and washed with normal saline, in order to minimize the residual fluid, oil, and blood in the final material to be grafted. In order to "glue" and attach the fat tissue over the entire surface of the wound bed, we sprayed (TECHNIQUE A) the fibrin glue (ARTISS Baxter, Deerfield, Illinois, USA) according to the instructions and specifications provided by the manufacturer, so as to prepare the wound bed to receive and fix the fat grafting that was applied by a curette in a single layer of about 2 mm. Then, we sprayed the fibrin glue (ARTISS Baxter, Deerfield, Illinois, USA) over the entire surface already covered with fat cells, to stabilize the position of fat cells.

We completed the procedure by shaping, with a curette, another single, 2-mm-thick layer of fat cells, which was then covered by spraying fibrin glue (ARTISS Baxter, Deerfield, Illinois, USA) in order to fix all the fat grafting.

Alternatively (TECHNIQUE B), we prefer using a double or triple 2-mm-thick lipoglued cell layer each, set up outside (Supplemental Material Video 1: "Lipogluing Technique"), before laying it on the wound bed.

After waiting at least 5 min, we dressed the area with non-adhesive gauze.

Our adhesiveness studies between fibrin glue (ARTISS Baxter, Deerfield, Illinois, USA) and fat tissue have shown that the best fat/fibrin glue ratio is achieved by spraying at least 1 ml of fibrin glue (ARTISS Baxter, Deerfield, Illinois, USA) per 20 cc of fat grafting.

We combine the two methods to pursue the best results in covering complex defects and to achieve the best body contour possible. We dressed the lipoglued area only with non-adhesive gauze. The first dressing change was performed on day 5 or 7. Subsequent dressing changes were performed as needed.

Typically, it takes 4 to 6 weeks before the appearance of a well-vascularized tissue and before being able to cover the wound bed with a skin graft (the average waiting time was 42.5 days, ranging between 35 and 50 days); however, it may take longer in certain less-vascularized areas, with bone exposed without a periosteum or when the thickness of the lipoglued fat is more than 4 mm, (Supplemental Material Content Video 2: "Focus On: Tissue Growth in Lipogluing Technique" with all the photos that share the revascularization processes that gradually involved the lipoglued graft functioning like an autologous scaffold). At the moment of the first step of lipoglued grafting, the bacteriology was negative. Perioperative prophylactic antibiotics were prescribed in all cases according to our institutional protocol. The patients underwent weekly dressing changes until the new wound bed showed signs of a good neo-vascularization. In order to re-establish all the layers of the soft tissue defect and obtain the best functional result possible, in the second step, a full-thickness skin graft was positioned, in order to reproduce the anatomical features of a healthy skin and to maximize the overall functional and esthetic outcomes [13].

The first dressing change was performed on day 5. Subsequent dressing changes were performed as needed.

Results

All patients were followed and assessed for a complete wound healing and stability in daily life; all grafts showed satisfactory coverage without any complications such as breakdown, blister, or chronic ulcer [13] after an average post-operative follow-up of 11.5 months (range 8 to 18 months).

Complications after these procedures were minimal and related to the partial success of full-thickness skin graft; only in one case of a big thigh's area grafted (patient 4) only needed dressing until complete re-epithelization. To date, there has been no incidence of long-term skin problems.

Based on this preliminary personal experience by the author, reliable information can be given about the safety and effectiveness of the lipogluing technique plus skin graft to solve complex defects also with exposed bones.

Clinical cases

Patient 1

A 49-year-old male has had a total skin heel necrosis on his left foot when he was 19 years old, following a motorcycle accident and orthopedic treatment for femoral fracture, treated by local debridement and dressing determining a slow worsening chronic ulcer of the Achilles tendon region for the last 30 years.

After a biopsy aimed at ruling out the possibility of skin cancer, we performed radical debridement and placement of lipoglued fat grafting as described above (Supplemental Material Fig. 7).

We evidence the results of the vascularization process inside the lipoglued fat graft at 20 days and at 35 days after the first surgical procedure and the results after the placement of a full skin graft (Supplemental Material Figs. 8, 9, and 10).

Patient 2

A 46-year-old male sustained a mechanical trauma and thermal injury during a motorcycle accident which resulted in an area of necrotic skin and burned bone at the fifth metatarsus and toe of his right foot (Fig. 1). Surgical debridement was performed to remove the devitalized tissue and the bony surface exposed was abraded lightly until an adequate wound bed that, however, was not well vascularized. We have placed lipoglued fat grafting as described above (Fig. 2). We evidence the results of the vascularization process inside the lipoglued fat and the final results (Figs. 3, 4, 5, and 6).

Fig. 1 A 46-year-old male sustained a mechanical trauma and thermal injury during a motorcycle accident which resulted in an area of necrotic skin and burned bone at the fifth metatarsus and toe of his right foot (Clinical Case 2)

Patient 4

A 51-year-old female sustained a mechanical trauma and penetration injury during a Quad motorcycle accident, which resulted after primary treatment in an area of necrotic skin of her right thigh (Supplemental Material Figs. 11-12). Surgical debridement was performed to remove the devitalized tissue just to the muscles underlying and lipoglued fat grafting was placed to fill up the deep loss of subcutaneous tissue about for 14 to 20 mm of thickness (Supplemental Material Fig. 13). We evidence the results of the vascularization process inside the lipoglued fat and the results after the placement of a full skin graft (Supplemental Material Figs. 14 and 15). The appearance after 12 months showed a good contour reconstruction, with good filling of the deep subcutaneous loss of tissue and a nice cosmetic result that could be ameliorated by another session of standard lipofilling to restore completely the thigh contour. The clinical examination and the ultrasound control performed 1 year after the lipoglued graft evidence a good maintenance of thickness of subcutaneous tissue under the skin graft with an average lowering of 30% of the starting thickness of the lipoglued fat graft.

Discussion

The ideal method for the soft tissue reconstruction should offer viable tissues similar in texture and thickness to the lost ones, leaves the most inconspicuous donor site defect possible, and can be performed without compromising

Fig. 2 At the first step, surgical debridement was performed to remove the devitalized tissue and the bony surface exposed was abraded lightly until an adequate wound bed that, however, was not well vascularized and lipoglued fat was placed as described above

meaningfully other body regions if possible. The lipogluing plus skin graft technique offers all these advantages [14].

Our idea is to achieve the ultimate goal of reconstructive procedures: the recreation of all anatomical cutaneous and subcutaneous layers. Lipoglued autologous fat (adipose cells plus fibrin glue) associated with full-thickness skin graft is the first our choice promising to get this kind of result. We had in our mind the idea to better supplement the subcutaneous tissue with fat cell derived by adipose cells grafted or stem cells survived in stromal vascular tissue of lipoglued grafting. After this series of patients in our mind, we still think the lipoglued fat grafting in some way is used like an autologous scaffold and it ameliorates the microenvironment of the wound with better results than only wound dressing, vacuum-assisted system, or dermal substitute and coverage with skin graft, that in some similar cases in our experience were not able to ensure very good long-term results in those kind of problems.

We have in mind the idea in this way to re-create a subcutaneous autologous environment that could be an area of future study in order to ameliorate its features (number of fat cell derived by adipose cells grafted or stem cells survived in stromal vascular tissue of lipoglued grafting, stem cells enrichment, growth factors, etc.) and favorable to receive if it were necessary other supplement

Fig. 3 The results of the vascularization process inside the lipoglued fat graft at 15 days (left) and at 30 days (right) post first surgical procedure

Fig. 4 The results of the vascularization process inside the lipoglued fat graft at 45 days (left) and 60 days (center and right photo) post first surgical procedure, just before the second surgical step

with a session of standard lipofilling for example, to improve theoretically in an infinite way the quality of the reconstructive coverage in a challenging area, to get very good results in high demanding patients.

Fig. 5 60 days after the first step, in order to re-establish all the layers of the soft tissue defect, we placed a full-thickness skin graft taken from the inside of the thigh. Results at 15-, 30-, and 45-day post skin graft

Fig. 6 Results at 10 months after the procedure of lipogluing technique plus full-thickness skin graft in the treatment of a cutaneous, subcutaneous and osseous defect in an area of necrotic skin and burned bone at the fifth metatarsus and toe of the foot

We usually look for in the appropriate reconstructive technique with in mind the general rule that it should preferably be the simplest procedure that effectively solves the problem [12].

The reconstruction of defects in the lower leg has primarily involved the use of local or distant flaps; although these options offer adequate coverage, in many cases, the patients also experience significant donor–site morbidity and abnormality and these options often fail to provide good esthetic and functional reconstructive results.

The choice of reconstruction is influenced also by patient factors such as age, co-existing medical conditions, length of procedure, and fitness for general anesthesia. The "ideal" treatment for a particular patient should be tailored around his/her specific needs.

Leg defects can be difficult to treat and have a severe impact on patients' esthetics and functional results and quality of life. Mindful of this, we sought a new possible approach to the management of these complex defects.

The new lipogluing technique fixes the fat cell graft by the fibrin glue (ARTISS Baxter, Deerfield, Illinois, USA), a very good biological adhesive, capable of gluing structures together [15], used in a large number of surgical disciplines and in Plastic Surgery, available for the placement of skin graft and for cutaneous and subcutaneous flap attachment [16–20]. This technique allows to improve the soft tissue cover by addressing proactively subcutaneous tissue deficits and also improves skin graft long–term results.

A complete and stable coverage of the soft tissue losses was obtained in all cases and patients were able to wear their normal footwear and go back to their normal activities with an inconspicuous, neither cosmetic donor site defects. The 2-stage lipogluing technique plus full-thickness skin graft provides an alternative treatment in lower leg reconstruction, also in the case of exposed bones. The new subcutaneous autologous environment could be area of future studies in order to ameliorate its features and quality (number of fat cell derived by adipose cells grafted or stem cells survived in stromal vascular tissue of lipoglued grafting, stem cells, and growth factors enrichment etc.). It also allows to receive other supplement with a session of standard lipofilling to improve theoretically in an infinite way the quality of the reconstructive coverage in a challenging area, to get very good results in high demanding patients . It could prove very useful also in other parts of the body and it helps solve many challenging problems of reconstructive surgery [3] yielding a good functional result comparable with flap reconstruction and a better esthetic outcome.

The esthetic outcome of reconstructive surgery and minimal morbidity of the donor site have become priorities for plastic surgeons also in the reconstructive treatment of complex soft tissue defects with important functional results to be achieved.

Several publications in the plastic surgery literature underline [1, 12] the efficacy of lipofilling as a cosmetic and reconstructive procedure and propose it as a safe, neutral, biological material that is able to restore the body contour. Several studies underline the power of transferred fat to regenerate blood supply in skin disorders following radiotherapy, improving the quality of irradiated skin and in the correction of soft tissue contour deformity related to implant-based breast reconstruction [14, 20].

Autologous fat grafting has become a widespread technique for different reconstructive purposes; however, the

disadvantage is the unpredictable re-absorption rate that often necessitates repetitive procedures. The angiogenesis process is crucial for the survival of adipocytes, which are subject to apoptosis and necrosis if not supported by a network of capillary vessels by the fourth day after implantation [2]. Studies have shown that the plasmatic nutritional supply of adipocytes can only go as far as 1.5 mm into tissues and that only 40% of the fat at a distance of 1.5 mm from the boundary of the tissue block survives [2, 20]: we can assume that plasmatic nutrition and the time of revascularization play a crucial role for the survival of fat graft and determine the final clinical outcome.

The main determinant for cell survival is an appropriate, supportive microenvironment and its lack is probably the main cause of variable rate of re-absorption of lipofilling [20] and in the same way of lipogluing graft. We can use this model to evaluate the process of evolution of breast and scar's lipofilling.

The success of fat grafting depends on optimal local vascularization and the successful integration with the receiving wound bed. In patients 2 and 4, where we were be able to obtain a histological evaluation of the new wound bed during the second step just before the skin graft, we were able to better assess the concept of the adipose tissue graft re-absorption rate and to better understand what could happen in the breast reconstructive lipofilling when the microenvironment is not well vascularized and we observe a poor rate of adipose cell engraftment and a high rate of re-absorption. During the histological examination of these cases, we observed a very rare presence of adipocyte and fat cells and the new tissue reduced compared to the initial volume grafted was represented almost by extracellular matrix and granulation tissue. The results reported in the literature showed that the second fat graft performed in the same areas without any sophisticated procedures could acquire better cosmetic results and volume retention [21]. Nevertheless, we can conclude that lipogluing technique associated with full-thickness skin graft represents an attempt of the reconstructive process that aims to augment the soft tissue, in order to produce the three layers of the natural skin.

The adipose organ is a dynamic, connective tissue composed of a heterogeneous cell population and a dense microvascular system entwined within the extra cellular matrix that embeds cells in a nutritional and structural microenvironment [20]. The re-absorption phenomenon, inherent to fat cell grafting, is initially and mainly coordinated by the post-graft ischemic period, during which transplanted cells need to survive through a process of diffusion. The final outcome of fat transplantation is subsequently determined by an efficient and rapid revascularization of the graft [20].

Despite the grade of the fat cell re-absorption, the matrix of lipoglued tissue graft allows us to rebuild the subcutaneous tissue on hold of skin graft. We think the dermal layer of the full-thickness skin graft has an important role in the achievement of a stable reconstruction in a challenging area like the foot that undergoes daily stresses and pressures. All patients were able to wear normal footwear and to return to their usual activities thanks to the good results obtained that was a strong and thin coverage, when necessary. So for coverage of small to moderate size defects, we prefer use of full-thickness skin graft also if we know that we could have some problem in taking skin graft. We have had some engraftment problem only in clinical case number 4 with a full-thickness skin graft of large size (10 × 18 cm). Before surgery, we have discussed with the patient about the disadvantages of full thickness instead of split skin graft in the coverage of large defects but she has preferred to take advantage of a mini-abdominoplasty instead to have a superficial but big scar at her contralateral tight too. The conventional approach in covering a complex defect in the lower extremity especially in its distal third includes local flap and microsurgical distant transfer, but the use of these techniques could be made impossible by the large size of the defect and/or the paucity of donor site and the functional and esthetic contour's results we want to obtain because the control of flap thickness may be also challenging [13, 22, 23].

The lipogluing technique plus skin graft has proved to be effective but we have to underline that it is not without potential problems, because the biological active component of fibrin glue could give rare allergic reactions and because it is manufactured from blood plasma donations, which carries the potential risk of viral transmission. To reduce this risk, stringent controls are applied to the selection of blood donors and consecutive virus removal procedures are employed [8].

The use and the procedure of fibrin glue spraying were performed per the manufacturer's specifications and instructions. The use of fibrin sealant and these associated risks must be fully discussed with the patients before its use, as a part of informed consent [8].

Conclusions

Lipogluing technique associated with full-thickness skin graft represents an evolution of the reconstructive process that aims to augment the soft tissue, in order to produce the three layers of the natural skin. The technique is safe and is associated with minimal post-operative complications.

This technique allows a significant degree of contour restoration after tissue loss, rather than skin grafting that is inherently a two-dimensional technique and, conversely, tissue flaps often are hindered by the excessive final bulk that could alter the functionality, the wearing of shoes, and the final esthetic outcome.

Soft tissue supplementation not only improves the overall esthetic outcome but may also mitigate the risk of skin graft–related complications.

Future publications will include long-term results and, maybe, the possibility to ameliorate the results by a second new standard lipofilling in the lipoglued areas.

The lipoglued technique may offer an easy approach for managing a complex clinical problem, it does not prevent the possibility to proceed with a more complex reconstruction in

the future [22], and should be incorporated into reconstructive surgeons' armamentaria because it appears to be functionally and esthetically positive, able to cover large defects with minimal donor–site morbidity and good cosmetic results with an optimal contouring of the reconstructed area.

With the lipogluing technique plus skin graft, it is possible to achieve a thinner complete coverage of the complex defect to the foot and ankle than a fasciocutaneous or a muscle flap with a better aesthetical and functional outcome in terms of esthetic appearance and the use of normal footwear. We believe lipoglued adipose tissue graft reconstruction has the potential to play a new role beside the already established technique in the reconstructive ladder.

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Compliance with ethical standards

Conflict of interest The authors M. Verga, M. Carminati, O. Jaber, and E. Robotti declare that they have no conflict of interest.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration developed by the World Medical Association and subsequent amendments or comparable ethical standards and an informed consent for the surgical procedure and for the use of fibrin glue and lipofilling technique was obtained in writing form from each patient selected for the study.

Informed consent statement The authors M. Verga, M. Carminati, O. Jaber, and E. Robotti declare that an informed consent for the surgical procedure and for the use of fibrin glue and lipofilling technique was obtained in writing form from each patient selected for the study.

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