Original Article

Pilot Study of Additive Effect of "Offloading Ilizarov Frame" To Reduce "Reverse Sural Flap" Surgery Complications: A Clinical Trial

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ABSTRACT

Background: A reverse sural flap is an available surgical technique because it provides robust axial blood circulation to flaps with a substantially larger surface area. We aimed to assess Ilizarov frames outcome after reverse sural flaps among patients with traumatic injuries to the distal portion of the leg.

Methods: Patients with traumatic distal injury of leg in Shoha-e Tajrish Hospital in 2022-2021 were recruited and treated with reverse sural flaps. Interventional group was followed by Ilizarov frames application (group A). For the second group, just conventional dressings and proper positioning were done after surgery (group B). Between the two groups, the duration of surgery, the degree of flap swelling, the time from surgery to discharge and flap failure, surgical site infection, deep vein thrombosis (DVT), and other complications were compared using SPSS 25 software.

Results: Of 26 recruited patients, twenty consented to participate in this study. The average time from initial injury to reconstruction surgery, the mean duration of surgery, the mean time from surgery to discharge and the degree of swelling of the flap was compared between these two groups. The results showed better outcome in Ilizarov group, but the flap swelling grade was the only statistically significant factor between groups (*P* value= 0.03).

Conclusions: The use of "offloading Ilizarov frames" to protect reverse sural flaps resulted in a considerable reduction in the flap swelling. It is a safe, quick, easy, and effective technique.

Keywords: Ilizarov technique; Surgical flaps; Free Tissue Flaps; Lower Extremity

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INTRODUCTION

Traumatic injuries to the distal portion of the leg carry a significant risk of soft-tissue complications, often resulting in exposure to the bone, joint, tendon, neurovascular anatomy, and osteosynthesis material [1-4]. There are several solutions such as salvage procedures utilizing either a pedicle flap or a microvascular free flap, depending on the patient's age, the location and size of the defect, as well as the patient's condition, and

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the surgeon's experience. Amputation is a possibility if the wound is not treated appropriately[5,6]. The main advantages of local fasciocutaneous flaps include simplicity, availability, and versatility. A reverse sural flap is an available option because it provides robust axial blood circulation to flaps with a substantially larger surface area. Additionally, it is easily transposable and does not require microsurgery[1-3] .

Venous congestion is one of the most common complications after all types of flap surgery and is difficult to manage. This condition is characterized by a purplish hue, a decreased refill time, dark blood at pinprick, venous bleeding at flap borders, and increased swelling[4,5]. It can develop spontaneously or as a result of a preceding event classified as primary or delayed. Large veins are involved in primary congestion, whereas small veins are frequently involved in delayed congestion. In both conditions, it is critical to evaluate the effects of pressure on the flap's pedicle. This could be due to hematoma pressure, vein kinking, excessive tension by wound closure, or pressure from the patient's position [6,7].

In this study, Ilizarov frames were primarily used to offload and protect the reverse sural flaps. We hypothesized that Ilizarov frames would result in fewer complications and flap failures.

MATERIAL AND METHODS

A clinical trial pilot study (Registration: IRCT20211201053235N3) was conducted at a tertiary referral trauma center between June 2020 and April 2021 with approval from the facility Ethics Committee. Written informed consent was obtained, and twenty patients were enrolled in the study.

Patients who presented or were referred to Shohada-e Tajrish Hospital, Tehran, Iran with soft tissue defects in the lower leg, heel, and foot requiring soft tissue reconstruction were enrolled. Soft tissue defects resulted either from direct or crushing soft tissue injury, spoke injuries of the heel, and wound complications after previous open reduction and plate osteosynthesis for distal tibial fractures (Figure 1), calcaneal fracture, ankle fracture-dislocations, pilon fractures, Achilles

Figure 1: Wound complications after previous open reduction and plate osteosynthesis of distal tibial fracture.

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tendon repair, or reconstruction. Patients with acute fractures requiring surgical stabilization were not included.

We also excluded patients with peripheral vascular disease, chronic osteomyelitis, heavy smokers, and patients with uncontrolled serious comorbidities. All patients were initially debrided, antibiotics were prescribed based on an infection consult, and in case of suspected infection, the wound was wrapped in Vacuum-Assisted Closure until clinical and biochemical evidence indicated that the wound was healing. Before surgery, all patients received CT angiography to examine the flap artery's base. Computer-assisted randomization was used to separate patients into two groups. Ten patients had reversed sural flaps followed by Ilizarov frames application (group A). For the second group, just conventional dressings and proper positioning were chosen (group B) (Figure 2). In group A, simple two-ring frames with two pins per ring were used to elevate the lower limb (Figure 3). To guarantee proper elevation, large-diameter rings (220 mm)

Figure 2: Conventional dressings with proper positioning.

Figure 3: Simple two-ring frames with two pins per ring were used to elevate the lower limb.

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were chosen and the injured limb was eccentrically positioned in the Ilizarov rings, well above the ground.

All flaps were performed in the prone position under spinal aesthetic by a single senior orthopedic surgeon. The flaps axis was identified in both groups between the gastrocnemius muscle heads and posterior to the fibula tip. A flap was marked according to the defect dimension, plus an additional 1 cm for flap contraction and a more tension-free inset (Figure 4). The dissection began at the proximal border of the skin paddle and continued distally, including the fascia. While the distal portion of the pedicle was chosen to match the requirements for distal coverage, it was limited to 5-7 cm from the tip of the lateral malleolus. The gap between the pivot points and the defects was opened to facilitate the passage of the flap pedicle. To cover the donor sites and the space between the pivot points and the recipient area, skin grafts from the ipsilateral thighs were employed. Vaseline gauze was applied to the wounds, followed by a simple dressing and a wool dressing, with the flap's center-left open for routine checks. In none of the cases, compression bandages were used. Patients in group A were postoperatively maintained in the supine position. In contrast, group B was cared for 7-10 days in the lateral or prone position in bed, depending on the position of the flap, to avoid putting pressure on the flap's pedicle and recipient areas. For the first 24 hours, flaps were checked every two hours; for the second 24 hours, flaps were checked every four hours. Apart from that, both groups received identical postoperative care, with adequate hydration and analgesia always provided. In none of the cases was Thromboprophylaxis administered. Weight-bearing was initiated with restriction one day after surgery. Between postoperative days 3 and 5, dressings were removed. Following hospital discharge, all patients were followed weekly for the first three weeks, twice weekly for the next six weeks, and then monthly for up to six months. in group A Two weeks after surgery, the frames were removed.

Between the two groups, the duration of surgery, the degree of flap swelling, the time from surgery to discharge and flap failure, surgical site infection, deep vein thrombosis (DVT), and other complications were compared and contrasted. Results were analyzed using the *t*-test in SPSS software version 25 (IBM Corp., Armonk, NY, USA).

RESULTS

Altogether, 20 patients were enrolled. After randomization, 10 patients were in group A and 10 patients were in group B. Table 1 shows the demographics of the patients. All patients were male and had a mean age of 30.61 years (range: 14-68 yr). The mean age of patients in group A was 26.11 years (range: 14-58) and in group B was 35.11 years (range:16-68). The mean age difference between the two groups was not statistically significant (*P* value: 0.057). The difference between the mean BMI in the two groups (21.75 vs 26.12) was also not statistically

Figure 4: Longitudinal vascular axis of the flap was performed by drawing a straight line that joined the mid-popliteal point to another point midway between the lateral malleolus and lateral side of the Achilles tendon.

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Table 1: Demographic and hospitalization information of patients in the two groups

Variable	Group A n=10	Group B n=10	*P*-value*
Mean Age (Min-Max) years	26.11 (14-58)	35.11 (16-68)	0.057
BMI (Mean± SD) kg/m^2	21.75±14.05	26.12±13.00	0.090
Education level			
Non-academic(percent)	9 (90.00%)	10 (100.00%)	0.184
Academic (percent)	1 (10.00%)	0 (0.00%)	0.073
Cigarette smoking (percent)	1 (10.00%)	0 (0.00%)	0.073
Alcohol use (percent)	0 (0.00%)	0 (0.00%)	-
Drug addiction (percent)	1 (10.00%)	0 (0.00%)	0.073
Diabetic patients (percent)	1 (10.00%)	1 (10.00%)	0.186
Hypothyroid patients (percent)	1 (10.00%)	0 (0.00%)	0.073

Table 2: Comparing surgical outcome variables between the two groups

Variable		Group A	Group B	*P*-value
Duration of surgery (Mean± SD) minutes		150.00±23.71	144.00±26.03	0.091
Time from injury to surgery (Mean± SD) days		29.30±8.26	27.00±9.085	0.127
Time to discharge (Mean± SD) days		6.62±3.26	8.77±3.78	0.057
Flap Swelling Grade number (percent)	Grade 0	7 (70%)	5 (50%)	0.036
	Grade 1	3 (30%)	1 (10%)	
	Grade 2	0	0	
	Grade 3	0	3(30%)	
	Grade 4	0	1 (10%)	
Blood transfusion Number (%)		1 (10.00%)	0 (0.00%)	0.073
ICU admission after surgery number (%)		0 (0.00%)	1 (10.00%)	0.073
DVT number (%)		0 (0.00%)	0 (0.00%)	-
Flap failure number (%)		0 (0.00%)	1(10.0%)	0.073

significant (*P* value: 0.090). The distribution of original injuries or surgeries that caused the soft tissue defects was similar in both groups. In each group, there were 5 cases of fractures (distal tibia, bi-malleolar, or pilon fractures) that had undergone open reduction and internal fixation. These patients developed a skin defect with exposed metal fragments in the early postoperative period that required soft tissue reconstruction. Other causes included skin defects after Achilles tendon repair/reconstruction, and spoke injuries of the heel. These patients were also evenly distributed between the two groups. Number of patients with comorbidities such as diabetes and thyroid disorders was not significantly different between the two studied groups.

In Table 2, surgical factors and postoperative complications are compared between the two groups. The average time from initial injury to reconstruction surgery was 29.30 days (SD 8.26 days) in group A and 27.00 days (SD 9.085 days) in group B, respectively. This difference in time was not significant (P value: 0.127). The average duration of surgery was 150 minutes (SD: 23.71 minutes) in the

Figure 5: Congestion and partial necrosis of the flap in non-Ilizarov group.

group A and 144 minutes (SD: 26.03) in the group B. Although this time difference is not significant (*P* value: 0.091), it shows that the use of the Ilizarov frame did not significantly increase our operation time. The mean time from surgery to discharge was 6.62 days (Range: 3-29) in group A compared with 8.77 days (Range:5-29) in group A. This difference was not statistically significant (*P* value: 0.057), but it did exhibit a trend indicating that using Ilizarov frame could lead to a faster and safer discharge. Regarding social situations, none of the patients reported drinking alcohol. One patient had a history of smoking but stopped after admission to the hospital, and one patient had a history of substance abuse. Although the above two patients were randomized to group A, they had a good clinical outcome with their flap surgery without complications. Regarding the educational level of the patients, only one patient had a university education and was randomized to group A.

The degree of swelling of the flap averaged 0.7 in group A and 3.1 in group B. As shown in Table 2, this was the only outcome measure that showed a significant statistical difference between the two groups (*P* value=0.036). Although the differences between the groups in variables related to operative time and postoperative complications were in favour of group A, these differences were not statistically significant. In one case, the flap failed due to severe flap congestion and complete necrosis. Three cases had partial necrosis, which was treated with debridement and skin graft (Figure 5). Three distinct patients were treated for blisters in the flap using daily dressings and a variety of delayed closure techniques. These patients were a member of group B.

One patient in group A required a postoperative blood transfusion, and one patient in group B had to be admitted to the intensive care unit for close postoperative monitoring on the advice of the anaesthesia team. There were not any other complications seen such as post-operative infection, pin tract infection among studied patients and both groups did not experience late postoperative complications such as DVT, deep infection, or septic arthritis.

DISCUSSION

Fasciocutaneous flaps are popular because of their simplicity, availability, and versatility, without sacrificing muscle function, and have been used successfully in large clinical series[3,4,8,9.] The reverse sural flap is a reliable flap that can be used to reconstruct moderate to large-sized wounds in the lower leg, ankle, and heel regions [1,2,10,11]. Because this flap does not need the sacrifice of any of the distal extremity's major arteries, it is an ideal alternative for covering severe soft tissue defects in patients with vascular problems [10,12]. A systematic review of the reverse sural flap [13], showed an overall flap survival rate of 95% with a major complication rate of 14% requiring further treatment or revision surgery. The most common complication in this review was venous congestion (75.3%) followed by epidermal losses (63%) and tip necrosis (55.9%). venous congestion should be fully evaluated after surgery because it becomes irreversible after 6 to 8 hours due to severe microvascular lesions [6]. Several postoperative measures have been described to alleviate pressure on the pedicle flaps and recipient sites, including the use of pillows, modified posterior splints and modified casts [14-16]. The "flap swelling scale" can be used to determine the degree of flap swelling as a reliable predictor of flap necrosis. This scale considers factors such as congestion, skin condition, blistering, and ultimately skin necrosis [4,5] .These measures may result in longer hospital stays, additional costs, obstruct the view of the pedicle flap, donor and recipient sites, can be inconvenient, and rely on patient compliance. Additionally, none of these procedures completely relieves pressure and elevates the limb. External fixators were forced by Nappi and Drabyn in 1893 to immobilize the limb and protect the pedicle flaps[17]. This technique distributes the weight over the entire injured lower extremity, protecting it from strong shear forces while keeping the foot and leg in the correct position to avoid snapping the pedicle [12-14]. In addition, the use of external fixators allows routine examination of the condition of the flap. Ilizarov frames have been used successfully in conjunction with soft tissue flaps to treat difficult open fractures of the distal tibia [18-21] and tibial osteomyelitis [22] and to protect the flap during lower limb elevation [23]

The currently available English literature on the use of Ilizarov frames following lower leg, ankle, and heel flaps for elevation and protection of the flap is heterogeneous retrospective and limited to case series [23,24]. One retrospective study compared the outcome of heel flaps in 21 patients with Ilizarov elevation frames and 10 patients with plaster of Paris protective boots [23]. The authors found Ilizarov fixators particularly useful in patients with obesity, non-compliant patients, and patients with complex wounds requiring simultaneous sural and saphenous flaps.

We have presented a pilot Randomised Control Study on 20 patients with skin defects in the lower leg, heel, or ankle requiring soft tissue reconstructions. Reversed sural flaps were fashioned by a single senior orthopedic surgeon. These patients were randomly assigned to one of two equal and homogeneous groups based on their use of protective Ilizarov frames. In the group for whom offloading Ilizarov frames were employed, there were no flap failures. Whereas one patient in the control group underwent revision surgery due to flap failure, three patients experienced epidermal loss or blistering. Although this difference was not statistically significant (*P-value* = 0.060), this is most likely due to the small sample size in our pilot study. Flap Swelling Grade was significantly reduced when he employed the Ilizarov frame due to the raised heel from the floor. (*P-value* = 0.036). Additionally, the Ilizarov frame addresses this issue if the patient

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falls asleep and possibly loses control of his or her position.
The other inherent benefit of using frames in the setting of the lower leg, ankle, and heel flap reconstruction is that it enables patients to rest and sleep in the supine position following surgery, avoiding awkward positions in the bed that are more comfortable and physiological for the patients. Patients can sleep easily and confidently in any position that is deemed appropriate for them, as well as breath deeply and comfortably. As this study suggests, the application of a simple two rings, two pins, offloading the Ilizarov frame, does not add to the surgical time significantly. The Ilizarov frame is more well-tolerated than other methods of elevating the injured limb. The applied frames are only required for the first two weeks following surgery. Infection at the pin site was not observed in any of the cases.
This study had some limitations. Being a pilot trial, the sample size in this study was small. Although there were only 10 patients in each group, it is the only available RCT in the current literature. The previously available studies on the use of offloading and protective frames are retrospective, heterogeneous, and low-numbered. Moreover, we did not use Ilizarov frames primarily as means of fracture stabilization in this trial. The cases of open fractures, which were included in this trial, were recent fractures that were treated with plate osteosynthesis and were complicated by wound dehiscence with skin defects. The initial metalwork used for fracture fixation in these cases could be retained and the frames were purely used as means of protection, offloading the flap while allowing elevation of the limb. These patients were distributed equally between the two groups. This strategy was adopted to ensure that all patients could be treated with similar frame configurations using two large rings and only two pins for each ring. We however acknowledge that the use of Ilizarov frames can be expanded to cases with acute open lower tibia and ankle fractures requiring a simultaneous flap reconstruction for soft tissue coverage. The above limitations could be reduced by conducting a larger RCT which would not only provide more powerful evidence but would also allow the use of more rigid frames in cases of acute fractures while minimizing the effect of heterogeneity between the groups.

CONCLUSION

Utilizing "offloading Ilizarov frames" to protect reverse sural flaps led to a significant decrease in flap congestion and swelling. It is a procedure considered safe, quick, simple, and successful. Using this kind of Ilizarov frame allows patients to be supine on the bed following surgery, which enhances their comfort and ability to breathe and sleep better. The frames are removed usually in an outpatient facility.

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CONFLICT OF INTERESTS

All above authors mention that there is no conflict of interest in this study, and no benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.

REFERENCES

1. Donski PK, Fogdestam I. Distally based fasciocutaneous flap from the sural region. *Scand J Plast Reconstr Surg* 1983;**17**(3):191–6. doi.org/10.1097/00006534-198505000-00100.
2. Costa-Ferreira A, Reis J, Pinho C, Martins A, Amarante J. The distally based island superficial sural artery flap: clinical experience with 36 flaps. *Ann Plast Surg* 2001;**46**(3):308–13. doi.org/10.1097/00000637-200103000-00018
3. Ponten B. The fasciocutaneous flap: its use in soft tissue defects of the lower leg. *Br J Plast Surg* 1981;**34**(2):215–20. doi.org/10.1016/s0007-1226(81)80097-5
4. Chang SM, Wang X, Huang YG, Zhu XZ, Tao YL, Zhang YQ. Distally based perforator propeller sural flap for foot and ankle reconstruction: A modified flap dissection technique. *Ann Plast Surg* 2014;**72**(3):340–5. doi.org/10.1097/sap.0b013e31826108f1
5. Chan JKK, Harry L, Williams G, Nanchahal J. Soft tissue reconstruction of open fractures of the lower limb: muscle versus fasciocutaneous flaps. *Plast Reconstr Surg* 2012;**130**(2):284e. doi.org/10.1097/prs.0b013e31827c723b
6. Boissiere F, Gandolfi S, Riot S, Kerfant N, Jenzeri A, Hendriks S, et al. Flap Venous Congestion and Salvage

Techniques: A Systematic Literature Review. *Plast Reconstr Surg Glob Open* 2021;**9**(1). doi.org/10.1097/gox.0000000000003327
7. Malviya V, Golandaj VK, Saini A, Dadsena NK. Evaluation of Leech Therapy in Salvage of Congested Flaps: a Series of Nine Cases. Indian J Surg. 2021;1–6.
8. Saaiq M, Zimri FUK. Reverse Flow Superficial Sural Artery Fasciocutaneous Flap: A Comparison of Outcome between Interpolated Flap Design versus Islanded Flap Design. *World J Plast Surg* 2019;**8**(3):316–23. doi.org/10.53902/sojor.2021.01.000502
9. Pontell ME, Saad N, Winters BS, Daniel JN, Saad A. Reverse sural adipofascial flaps with acellular dermal matrix and negative-pressure wound therapy. *Adv Skin Wound Care* 2018;**31**(1):612–7. doi.org/10.1097/01.asw.0000527290.81581.af
10. Ciofu RN, Zamfirescu DG, Popescu SA, Lascar I. Reverse sural flap for ankle and heel soft tissues reconstruction. *J Med Life* 2017;**10**(1):94. doi.org/10.1007/s00068-015-0569-x
11. Follmar KE, Baccarani A, Baumeister SP, Levin LS, Erdmann D. The distally based sural flap. *Plast Reconstr Surg* 2007;**119**(6):138e-148e. doi.org/10.1097/01.prs.0000259203.79909.7e
12. Follmar, K.E. and Erdmann, D., 2013. Reversed sural artery flap. Pu LLQ, Levine JP, Wei FC. Reconstructive surgery of the lower extremity. Quality Medical Publishing, p.665.
13. Schmidt K, Jakubietz M, Meffert R, Gilbert F, Jordan M, Jakubietz R. The reverse sural artery flap–How do modifications boost its reliability? A systematic analysis of the literature. *JPRAS open* 2020;**26**:1–7. doi.org/10.1016/j.jpra.2020.07.004
14. Price MF, Capizzi PJ, Watterson PA, Lettieri S. Reverse sural artery flap: caveats for success. *Ann Plast Surg* 2002;**48**(5):496–504. doi.org/10.1097/00000637-200205000-00008
15. Yilmaz M, Karatas O, Barutcu A. The distally based superficial sural artery island flap: clinical experiences and modifications. *Plast Reconstr Surg* 1998;**102**(7):2358–67. doi.org/10.1097/00006534-199812000-00013
16. Zgonis T, Stapleton JJ. Innovative techniques in preventing and salvaging neurovascular pedicle flaps in reconstructive foot and ankle surgery. *Foot Ankle Spec* 2008;**1**(2):97–104. doi.org/10.1177/1938640008315379
17. Nappi JF, Drabyn GA. External fixation for pedicle-flap immobilization: a new method providing limited motion. *Plast Reconstr Surg* 1983;**72**(2):243–5. doi.org/10.1097/00006534-198308000-00027
18. Clemens MW, Parikh P, Hall MM, Attinger CE. External Fixators as an Adjunct to Wound Healing. *Foot Ankle Clin* 2008;**13**(1):145–56. doi.org/10.1016/j.fcl.2007.12.001
19. Hollenbeck ST, Woo S, Ong S, Fitch RD, Erdmann D, Levin LS. The combined use of the Ilizarov method and microsurgical techniques for limb salvage. *Ann Plast Surg* 2009;**62**(5):486–91. doi.org/10.1097/sap.0b013e318189a9e5
20. Appel III JZ, Wendel JJ, Zellner EG, Hagan KF, Shack RB, Corlew DS. Association between preoperative measurements and resection weight in patients undergoing reduction mammaplasty. *Ann Plast Surg* 2010;**64**(5):512–5. doi.org/10.1097/sap.0b013e3181cf9f7d
21. Xu J, Zhong W-R, Cheng L, Wang C-Y, Wen G, Han P, et al. The combined use of a neurocutaneous flap and the ilizarov technique for reconstruction of large soft tissue defects and bone loss in the tibia. *Ann Plast Surg* 2017;**78**(5):543–8. doi.org/10.1097/sap.0000000000000921
22. Bibbo C. Reverse sural flap with bifocal Ilizarov technique for tibial osteomyelitis with bone and soft tissue defects. *J Foot Ankle Surg* 2014;**53**(3):344–9. doi.org/10.1053/j.jfas.2013.12.008
23. Saeed S, Ahmed SK, Chinoy MA, Khan MA. Protection of heel flaps with Ilizarov fixator as an elevation frame: A case series and review of literature. *J Pak Med Assoc* 2015;**65**(11 Suppl 3):S40-4.
24. Noack N, Hartmann B, Küntscher M V. Measures to prevent complications of distally based neurovascular sural flaps. *Ann Plast Surg* 2006;**57**(1):37–40. doi.org/10.1097/01.sap.0000208946.40714.07

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