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Remission Strategies with Fat Grafting to Prevent Recurrence of Pedal Ulcerations and Pain: A Case Series

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Background: Foot deformities and gait abnormalities can result in locally elevated peak pedal pressures or atypical pedal biomechanics. Combined with underlying comorbidities such as neuropathy, stroke, atrophic fat padding and history of ulcerations, this can lead to recurrent ulcerations and pain. Pedal fat grafting (PFG) is a treatment modality that has been shown to reduce peak pressures and accelerate wound healing. This study aimed to investigate the utility of PFG to treat and prevent ulcerations.

Methods: We retrospectively analyzed medical history, demographics, wound volume at time of procedure, volume of fat injected, surgical outcomes, and presence of new wounds in 15 patients who underwent PFG at Keck Hospital between 2018 and 2023.

Results: Seventeen feet from 15 patients (63 ± 12 years old, body mass index 30.9 ± 3.1) received PFG with an average volume of fat injected of 10.7 mL and procedure time of 84.6 minutes. At the time of PFG, nine wounds were present on nine feet with an average wound volume of 1.6 ± 2.7 cm^3. Average follow-up was 6.9 months (range 1–36 months), with no complications or recurrent ulcerations since the procedure.

Conclusions: PFG is a promising treatment option for reducing peak pedal pressure and preventing ulcer recurrence in patients with various conditions. Further study is warranted for long-term follow-up. *(Plast Reconstr Surg Glob Open 2023; 11:e5232; doi: 10.1097/GOX.0000000000005232; Published online 1 September 2023.)*

INTRODUCTION

Fat grafting has been widely used to correct a variety of deformities due to the abundance of adipose tissue and ease of procurement. Autologous fat is transferable to many areas of the body without significant donor site morbidity.[1] Modern autologous pedal fat grafting (PFG) implements Coleman technique of lipoaspiration under low pressure for lipotransfer to the deformity.[2,3] Grafted adipose tissue reduces stress on tissues by absorbing impact, which protects the local anatomical structures. Moreover, it is a concentrated source of growth factors and cytokines that aid in granulation tissue formation, reduce scar tissue, upregulate angiogenesis, and mitigate inflammation.[4–6] Adipose tissue is rich in adipose-derived stem cells, which differentiate to support ectodermal and mesodermal structures. These aspects of adipose tissue allow it to potentially reverse the effects of neuropathy and peripheral artery disease.[7,8]

There are several chronic conditions that frequently result in pedal complications, which can produce elevated peak pedal pressures or atypical pedal biomechanics. Most commonly, diabetes mellitus (DM) and neuropathy result in foot wounds due to repetitive stress on the foot. Atypical biomechanics in neuropathic or neuroischemic feet lead to tissue loss and prolonged wound healing.[9] Charcot neuroarthropathy (CN) is another disorder that affects up to 35% of individuals with peripheral neuropathy and is characterized by the osteolytic destruction of pedal bones and joints, which is the predominant cause of a "rocker-bottom foot." The pathophysiology of CN

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is not fully understood but is believed to be caused by a combination of repetitive macro and microtrauma combined with a heightened pro-inflammatory response.[10] The rocker-bottom foot is a convex foot type due to midfoot collapse that many patients develop and results in a highly elevated midfoot peak pressure that causes recurrent or persistent ulcerations.[11] Other neurological conditions such as spina bifida can result in neuropathic sequalae such as foot deformities that can produce altered biomecheanics.[12]

The 5-year mortality rate for patients with diabetes with pedal ulcerations is 2.5 times higher than those without a foot ulcer. Greater than 50% of diabetic foot ulcers become infected,[13] and approximately 20% of moderate to severe foot infections result in amputation, after which mortality increases from 42% to 70% at 5 years.[14]

PFG has been successfully implemented as treatment for a number of pedal conditions such as diabetic foot ulcers, pedal fat pad atrophy, thromboangiitis obliterans, plantar fibromatosis, and plantar osteochondromas.[4,15–32] Although it has be shown that grafted lipoaspirate redistributes over time in the plantar foot surface, it retains its supportive and analgesic function.[22] Considering this, the investigators expected that PFG holds potential therapeutic benefit to treat conditions, which results in elevated localized pedal pressure by providing a mechanism to dissipate said elevated pressure. Therefore, in this case series, we present a series of patients who were treated with PFG to prevent recurrent midfoot ulcerations, lesions, and pain.

METHODS

A retrospective chart review was conducted on all patients who underwent PFG for elevated pedal pressures at Keck Hospital of USC between September 18, 2018, and January 7, 2023, by the senior author (L.S.). Data on patient demographics, anthropometrics, social habits, primary complaint for which PFG was indicated, current would characteristics, adipose tissue source procedure duration, outcome, complications, and reulcerations as of latest follow-up were collected and analyzed. Data collection and analysis were performed independently by the first three authors to ensure lack of bias and to control quality. The applicable statistical tests were performed to assess differences in procedure time, ulceration healing time, and presence of complications between body mass index (BMI), adipose sources, smoking status, and presence of comorbidities for the overall cohort and each diagnostic category.

RESULTS

We report 15 cases in which 17 feet were fat grafted primarily due to recurrent ulcerations secondary to neuropathic and/or ischemic conditions or developed atrophic fat padding and increased peak pressures that were at high risk for reulceration.

Seventeen feet (eight right) were fat grafted in 15 patients, eight with CN, 10 with DM, and two with spina bifida (five women) with an average age of 63 ± 10 years, average BMI of 30.9 ± 3.9. Nine patients had current ulcerations or similar lesions at the time of operation with

Takeaways

Question: Can fat grafting be utilized to prevent recurrence of pedal ulcerations and pain that result from atypical gait biomechanics?

Findings: Conditions that present with gait abnormalities and related atypical biomechanics which frequently result in severe pedal pain and recurrent ulcerations can be effectively treated using modern fat grafting techniques.

Meaning: Fat grafting is an effective treatment to prevent recurrent pedal ulcerations and pain.

average dimensions of 1.09 ± 0.61 × 1.05 ± 0.79 × 0.38 ± 0.26 cm and volume of 1.6 ± 2.7 cm^3. The average volume of fat injected was 10.7 ± 8.6 mL. Eleven patients received autologous fat (nine from the lower abdomen, one from the thigh flank region, and one from a subtalar joint lipoma) and four received Leneva allograft adipose matrix, with the procedures taking an average of 74.6 ± 26.6 minutes. Fat grafting donor sites were selected based on the ease and safety of access as well as relative abundance of adipose tissue. Further details regarding the technique of autologous fat grafting are outlined in Simonacci et al.[33] Autologous fat grafting took an average of 81.1 ± 23.8 minutes, with the Leneva allograft adipose matrix procedures taking only 56.8 ± 28.7 minutes ($P = 0.06$). Nine of the fat grafts were performed concurrently with an exostectomy of a bony prominence contributing to the pedal complication. Latest postoperative follow-up appointments ranged from 1 to 36 months with an average of 6.9 ± 8.8 months postoperative, with no complications and no reulceration or related pedal lesions since the procedure in any patient. Because there were no postoperative complications or reulcerations, it was not possible to determine if there is a relationship between this and the independent variables outlined. Moreover, no significant relationship existed between procedure time or healing time and any of the independent variables outlined. A summary of the characteristics of the fat grafting procedures and patients can be found in Table 1.

Charcot Neuroarthropathy

Nine feet (five right) were fat grafted in eight patients with CN with an average age of 65.5 ± 7.0 years, average BMI of 31.8 ± 2.7, and mean time since diagnosis of 3 ± 1 years. All patients had experienced chronic or recurrent midfoot or forefoot ulcerations, five of whom had current ulceration at the time of operation with average dimensions of 0.74 ± 0.38 × 0.78 ± 0.33 × 0.3 ± 0.13 cm and volume of 1.45 ± 3 cm^3. The average volume of fat injected was 15.6 ± 9.5 mL; all patients received autologous fat (seven from the lower abdomen, one from the thigh flank region), with the procedures taking an average of 78.1 ± 25.7 minutes. Five of the nine autologous fat grafts were performed concurrently with an exostectomy of a bony prominence contributing to the recurrent ulcerations. Latest postoperative follow-up appointments range from 4 to 36 months with an average of 11.2 ± 10.4 months postoperative and average healing time of 33 ± 36 days, with no complications and no reulceration since the procedure.

Table 1. Summary of the Characteristics of the Fat Grafting Procedures and Patients Who Received Fat Grafting

		Full	CN	Spina Bifida	DM
Gender	Masculine	10	5	0	8
	Feminine	5	3	2	2
Feet	Right	8	5	1	6
	Left	9	4	2	5
Ethnicity	White	6	4	1	5
	Hispanic	3	3	0	3
	Other	3	0	0	0
	Asian	2	1	1	1
	Asian Hispanic	1	0	0	1
Age	Mean	63	65.5	50.5	66
	STD	12	7	24.7	7.6
BMI	Mean	30.9	31.8	24.9	31.7
	STD	3.9	2.7	6	2.6
Surgery duration (min)	Mean	74.6	78.1	91.5	76.7
	STD	26.6	25.7	2.1	28.3
Total fat injected (mL)	Mean	10.7	15.6	3	13.9
	STD	8.6	9.5	0	8.7
Ulcer dimensions (cm)	Mean	1.09×1.05×0.38	0.74×0.78×0.30	1.00×0.50×0.30	1.10×1.13×0.39
	STD	0.61×0.79×0.26	0.38×0.33×0.13	0.00×0.00×0.00	0.65×0.82×0.27
Ulcer volume (cm^3)	Mean	1.6	1.4	0.2	1.9
	STD	2.7	3	0	3.1
Longest postoperative follow-up (mo)	Mean	6.9	11.2	3	9.3
	STD	8.8	10.4	2.8	10
Fat donor site	Lower abdomen	9	7	1	8
	Leneva adipose matrix	4	0	1	1
	Thigh flank	1	1	0	1
	Subtalar joint lipoma	1	0	0	0

Seven patients had DM, six had chronic hypertension and hyperlipidemia, two had chronic kidney disease, two had coronary artery disease, two were immunocompromised, and one had spina bifida. Three patients were current smokers with an average of 20 ± 12 pack-years. None of the comorbidities or social habits had a significant relationship with outcome or healing time.

Diabetes Mellitus

Eleven feet (six right) were fat grafted in 10 patients with DM with an average age of 66 ± 7.6 years and average BMI of 31.7 ± 2.6. All patients experienced chronic or recurrent midfoot or forefoot ulcerations, seven of whom had current ulcerations at the time of operation with average dimensions of 1.10 ± 0.65×1.13 ± 0.82×0.39 ± 0.27 cm and volume of 1.9 ± 3.1 cm^3. The average fat volume injected was 13.9 ± 8.7 mL, eight patients received autologous fat (seven from lower abdomen, one from thigh flank region), and two patients received bioengineered fat grafts (Leneva allograft adipose matrix), with procedures taking an average of 76.7 ± 28.3 minutes. Latest postoperative follow-up appointments range from 3 to 36 months with an average of 9.3 ± 10.0 months postoperative and an average healing time of 33 ± 36 days, with no complications and no recurrence of ulceration since the procedure.

Seven patients had CN, six had chronic hypertension and hyperlipidemia, two had chronic kidney disease, two had coronary artery disease, one was immunocompromised, and one had Agent Orange exposure. Two patients were current smokers with an average of 20 ± 12 pack-years, and two were former smokers. None of the comorbidities or social habits had a significant relationship with outcome or healing time.

Spina Bifida

Three feet (one right) were fat grafted in two patients with spina bifida, with an average age of 50.5 ± 24.7 years and average BMI of 24.9 ± 6. One patient was immunocompromised with CN, chronic hypertension, and hyperlipidemia. Both patients experienced chronic or recurrent midfoot or forefoot ulcerations, and one had a current ulceration at the time of operation with dimensions of 1×0.5×0.3 cm. Both patients received 3 mL of the Leneva allograft adipose matrix, with procedures taking an average of 91.5 ± 2.2 minutes. Both grafts were performed concurrently with an exostectomy of a bony prominence contributing to the recurrent ulcerations. The latest postoperative follow-up appointments for these patients were at 1 and 5 months with no complications and no recurrence of the ulceration since the procedure.

Other

Three other patients received fat grafting for pedal complications secondary to conditions other than CN, DM, or spina bifida, which serve to provide insight into the range of patients appropriate for autologous and allogenic fat grafting.

A 66-year-old man with Parkinson disease and BMI of 28.5 presented with a 1.8×0.6×0.3 cm verrucous lesion on

the left foot. Excision of the lesion and ostectomy of the fifth metatarsal base was performed in combination with 3 mL of Leneva allograft adipose matrix grafting to accelerate healing, improve comfort, and prevent lesions as a result of the biomechanical manifestations of the excision and ostectomy. The patient had no complications and the surgical wound fully healed by 14 days with no notable lesion development as of 1 month postoperative.

A 44-year-old man with a BMI of 36.09 presented with chronic sesamoiditis secondary to pedal fat pad atrophy and arthritis. Three milliliters of Leneva allograft adipose matrix were grafted below the sesamoid and surrounding area to relieve pressure and reduce inflammation. The patient had no complications and no notable sesamoid discomfort as of 1 month postoperatively.

A 74-year-old woman with bilateral coxarthrosis and BMI of 32.3 presented with a subtalar joint lipoma causing significant pain and pedal inflammation. Three milliliters of Leneva allograft adipose matrix along with 7 mL of autologous fat from the resected lipoma were grafted over first through fourth metatarsal heads as well as portions of the forefoot to reduce inflammation, accelerate healing, and reduce risk of complications as a result of the biomechanical manifestations of the procedure. This operation was performed concurrently with percutaneous Achilles tendon lengthening and a second digit hammertoe repair. The patient had no complications, lasting pain, or notable lesions as of the 2-month postoperative follow-up appointment, and all surgical wounds were healed.

DISCUSSION

Conventional treatment protocols of pedal ulcerations include surgical debridement, off-loading, infection monitoring, and vascular reconstruction. However, after ulcerations heal, recurrence occurs at a rate of 40%–55%.[11,34] Typical wound healing takes 117 days (95% confidence interval, 93–40) and recurrence occurs after an average of 67 days (95% confidence interval 47–87).[34] Biomechanical dysfunction is generally not resolved after the ulceration is healed. Neuropathy or loss of protective sensation continues to contribute to inflammation and reulceration. Newly epithelialized skin and scarring are prone to reulceration. These factors increase the risk of ulcer recurrence, even with appropriate therapy for the original ulceration.

In the series presented here, all 17 pedal locations that were treated with PFG achieved full clinical recovery with no reulceration. Visual and palpable inspection of the grafted area reveals increased fullness and turgor. This may reduce the impact shear and normal stress on the peak pedal pressure areas, which is likely the primary driver of the analgesic effect observed in patients experiencing painful sensation. This also likely contributes to the lack of recurrence, prevention of new pedal lesions, and discomfort in all 15 patients. The reported mitigation of pain along with the relatively quick recovery may support the proposed regenerative effects of ADSCs and other therapeutic factors abundant in adipose tissue on peripheral arteries and nerves as well as the surrounding tissue.[4–8]

Additionally, the anti-inflammatory factors present in adipose tissue likely serve to combat the pro-inflammatory response observed in CN and DM, thereby inhibiting the upregulation of the osteolytic activity.[10] This may not only prevent further exacerbation of biomechanical deformities but also partially reverse it in some cases as a result of the pro-osteoblastic shift; however, further investigation is needed to confirm this.

The relatively heterogenous and limited sample size of this series limits the robustness of conclusions drawn. Moreover, the limited number of objective outcome measures introduces potential for qualitative bias. Although the sample, which is heterogenous in regard to demographics, comorbidities, and social history, improves the generalizability of the study, it introduces confounders, which make it difficult to make strong predictions. A follow-up study with a relatively larger and homogenous sample size with objective assessments regarding gait assessment, pain scores, or even radiological evaluation would provide more robust insight into the benefits of this treatment.

CONCLUSIONS

The cases outlined in this series support the therapeutic utility of PFG to regions of elevated peak pressure secondary to a range of conditions to treat and prevent recurrent or persistent ulcerations. Moreover, the observations provide insight into the potential mechanisms of action of this approach. Although a larger scale study with long-term follow-up data is needed to provide enough support for the use of PFG as a standard of care and to confirm all therapeutic mechanisms, the data presented here provide considerable support for such an investigation.

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DISCLOSURES

The authors have no financial interest to declare in relation to the content of this article.

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