Volumetric Analysis in Autologous Fat Grafting to the Foot

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Hot Topic Video

Background: Pedal fat grafting is a safe, minimally invasive approach to treat pedal fat pad atrophy. Prior randomized controlled trials demonstrate that the fat as measured directly under the metatarsal heads disappears between 2 and 6 months after fat grafting, despite patients having relief for 2 years. The authors aim to use magnetic resonance imaging to further assess three-dimensional volume of fat in the foot after autologous fat grafting to help explain the mechanism for improved pain.

Methods: A prospective study was performed using magnetic resonance imaging before and at 6 months after pedal fat grafting to assess changes in the three-dimensional morphology of the fat.

Results: Seventeen patients (six men and 11 women) underwent injections with a mean volume of 5.8 cc per foot. At 6 months, patients demonstrated increased tissue thickness ($p = 0.008$) and volume ($p = 0.04$). Improvements were seen in pain ($p < 0.05$) and activity ($p < 0.05$). Foot pressures and forces were significantly decreased and positively correlated with increased fat pad volume ($p < 0.05$).

Conclusions: Pedal fat grafting significantly increases metatarsal fat pad volume. The distribution of the fat may contribute to lasting clinical relief in these patients. (*Plast. Reconstr. Surg.* 144: 463e, 2019.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

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THERAPEUTIC

Fat pad atrophy of the forefoot is common, affecting approximately 30 percent of patients older than 60 years.[1] Although often age-related, it may be caused by abnormal foot mechanics, obesity, steroid use, or collagen vascular disease.[2–4] Displacement or atrophy of the fat pad can lead to osseous prominences in the foot that may be seen with painful skin lesions. Fat pad atrophy may result in significant pain or compensatory gait, leading to callus formation or ulceration. In sensate patients, the pain can lead to emotional and physical pain, leading to productivity and financial losses.[5–9]

Various procedures have been described to augment atrophied fat pads; however, many of these techniques have failed to demonstrate sustained tissue thickness over time.[10–12] Our group previously published our results from the first clinical trial to apply standardized fat grafting techniques for pedal fat pad atrophy.[13,14] This study served as a proof-of-concept and highlighted the effectiveness of fat grafting in significantly improving pain and disability and also decreasing foot pressures and forces at 2 years.

Our prior randomized, crossover clinical trial demonstrated that patients treated with standard-of-care padding got worse, with decreased tissue thickness over time. In our fat grafting group, the tissue thickness under the metatarsal heads was measured by ultrasound and discovered to return to baseline

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thickness between 2 and 6 months, despite long-lasting pain relief out to the 2-year study endpoint. We hypothesize that, despite our previous finding of decreasing tissue thickness over time, the volume of fat that is injected into the foot is retained at 6 months and likely redistributes around the metatarsal heads to support them long term. We used magnetic resonance imaging to validate this hypothesis of volume retention, in comparison to our standard ultrasound measurements, to further understand changes that are occurring in the foot when autologous fat is used to treat plantar fat pad atrophy.

PATIENTS AND METHODS

Trial Design

Seventeen adults who experienced pain from fat pad atrophy were recruited into an institutional review board–approved, prospective, case series. The overall purpose of this study was to use magnetic resonance imaging to determine the three-dimensional volumetric changes in the soft tissue of the foot after fat grafting. Inclusion criteria consisted of foot pain under the head of the metatarsals, a diagnosis of fat pad atrophy by a foot and ankle specialist, and an interval of 6 months after any surgical intervention or steroid injection to the foot. Exclusion criteria included uncontrolled diabetes mellitus (hemoglobin A1c level > 7.0 percent), open ulcerations, infection (including osteomyelitis), systemic disease that would render the fat harvest and injection procedure unsafe to the patient, pregnancy, known coagulopathy, and tobacco use within the previous 12 months.

Medical, surgical, social, and activity histories were obtained. Vital signs including temperature, blood pressure, height, weight, and body mass index were obtained. Any prior foot injury, surgery, or previous foot ulcerations were noted. A physical examination and complete foot examination were documented, including vascular, neurologic, dermatologic, and gait evaluations.

On completion of the screening visit, phlebotomy was performed to assess serum complete blood count with differential, comprehensive chemistry panel, coagulation studies, erythrocyte sedimentation rate, albumin, and hemoglobin A1c. Standardized two-dimensional photographs of the foot, including any lesion pattern, were captured.

Intervention

Surgical consent was provided, and surgical procedures were performed at the University of Pittsburgh Medical Center Aesthetic Plastic Surgery Center. Subjects received local anesthesia (lidocaine 1% with epinephrine 1:100,000) at the site of aspiration of the fat grafts (i.e., abdomen, thighs, or flanks), and a tumescent solution (500 ml of normal saline, 10 ml of 2% lidocaine, and 1 ml of 1:1000 epinephrine) was injected into the harvest site. A tibial nerve block and a forefoot Mayo block were performed with a 50:50 mixture of 2% lidocaine 0.5% bupivacaine without epinephrine. A blunt-tip multihole hollow cannula was used to aspirate approximately 50 to 100 ml of fat tissue through a stab incision made with a no. 11 blade. Liposuction was performed under a low, consistent negative pressure using 10-ml syringes to limit trauma to the adipocytes. Incisions for donor sites were closed with benzoin and Steri-Strips (3M, St. Paul, Minn.).

A standard Coleman technique was used to process the fat, where the harvested fat graft was placed in centrifugation at 3000 rpm for 3 minutes.[15] The resultant fat was decanted, oil was wicked using absorbent gauze, and the high-density fraction (bottommost 1 ml of each 10-ml syringe) was transferred to a 1-ml syringe for injection into the foot. An 18-gauge needle was used to make an entry site between the first and second toes and the fourth and fifth toes on the plantar aspect of the foot, allowing for a cross-hatch injection pattern. Occasionally, injections were performed from the dorsal aspect. A 0.9-mm blunt cannula was used to inject the 1-ml syringes of fat into the foot.

Postoperatively, subjects walked out of the clinic in comfortable sneakers with padded insoles, allowing for offloading of the fat-grafted region. Subjects were instructed to limit strenuous activity for 4 to 6 weeks, including barefoot walking. All procedures were performed by the same surgeon (J.A.G.). No subjects received additional treatment of fat grafting or underwent any other surgical intervention to the foot during the clinical trial.

Measurement of Tissue Thickness

Ultrasound (Terason Ultrasound Imaging System, Version 4.7.6; Terason, Burlington, Mass.) was used to measure plantar tissue thickness under each metatarsal head. Ultrasound was performed by the same clinician at every visit, excluding the 2-week postoperative visit.

Magnetic Resonance Imaging Analysis

Initial preoperative magnetic resonance imaging was performed at 1.5 T using T1-weighted spin echo, T2-weighted fast spin echo with or without fat suppression and short-TI inversion recovery sequences in sagittal, coronal, and axial planes. Three-dimensional volumetric reformatted imaging was performed using Vitrea (Vital Images, Minnetonka, Minn.) with surface rendering, and emphasis on the underlying forefoot fat pads. Postoperative imaging was performed at an approximately 6-month interval with similar imaging parameters.

Preoperative and postoperative imaging included characterization of the location and appearance of the adipose tissue in the plantar forefoot surrounding the second through fourth metatarsal heads. Overall percentage change in fat pad volume was measured.

In addition, attention was paid to the presence of subchondral bone marrow edema both preoperatively and postoperatively. Metatarsophalangeal joint angles were also measured and compared. All preoperative and postoperative imaging was reviewed by a musculoskeletal-trained radiologist with 7 years of experience.

Measurement of Pain and Disability

Foot pain and subject disability were measured by the Manchester Foot and Disability Index, a validated assessment of the foot that includes components of pain, function, appearance, and work/leisure activities.[16] In addition, ability to perform activities of daily living and sports-related activities was assessed by the Foot and Ankle Ability Measure.[17] The questionnaires were administered at every visit, excluding the operative visit and 2-week postoperative visit.

Measurement of Stance and Gait Force and Pressure

The Tekscan HR Mat pressure measurement system and Research Foot Module (Tekscan, Inc., South Boston, Mass.) were used to obtain pedobarographic data to assess baseline plantar foot forces and pressures. Subjects were weight-calibrated to measure forces and pressures applied while standing, then recalibrated for walking. Standing measurements were captured from an average of 150 seconds. Walking measurements were captured from an average of a minimum of three passes for each foot at a self-selected speed. The pedobarograph was performed at every visit, excluding the operative visit and 2-week postoperative visit.

Statistical Analyses

Statistical analyses were performed with IBM SPSS Windows Version 24.0 (IBM Corp., Armonk, N.Y.). The Kolmogorov-Smirnov and Shapiro-Wilk normality tests were conducted. Paired t tests were run to determine difference in means between parametric data and Wilcoxon rank sum tests were used to evaluate differences in medians for nonparametric data. Tests were two-sided and significance was set to the level of $p < 0.05$, $p < 0.01$, or $p < 0.001$, as indicated. All outlier data (2σ) were removed before analyses. Data for injected feet only were evaluated, to avoid diluting the results with unaffected foot measurements. Correlations were determined by the Pearson coefficient at a confidence level of $p < 0.05$. All data are presented as mean ± SEM.

RESULTS

Participant Characteristics

Seventeen fat pad atrophy patients (11 women and six men) were enrolled into the study and retained throughout the 6 months to study completion. Average age at screening was 57.5 ± 2.8 years, and average body mass index was 26.0 ± 1.5 kg/m^2. Neither age nor sex was found to have any correlation to any outcome. Body mass index was negatively correlated to volume increase ($p = 0.043$, $r = -0.52$) (i.e., with higher body mass indexes, a lower increase in volume was measured) and reported pain outcomes ($p = 0.033$, $r = -0.394$) (i.e., with higher body mass indexes, a lower improvement in pain was reported).

Causes for fat pad atrophy include failed neuroma surgery, prior foot surgery, steroid injections, and overuse. Fat pad atrophy was diagnosed in 31 feet where 15 subjects underwent bilateral fat grafting injections and two subjects underwent fat grafting in only the one injured foot. An average of 5.8 ± 0.4 cc of fat was injected into the left foot, and an average of 5.8 ± 0.4 cc of fat was injected into the right foot.

Subjects experienced postoperative bruising of the donor site and feet, soreness, and pain. No patients experienced infection, hematoma, seroma, or oil cysts. No perioperative antibiotics or narcotics were used. No serious adverse events or unanticipated events occurred.

Tissue Thickness Outcomes

Figure 1 displays fat pad thickness measured over time. Fat pad thickness is lowest at baseline ($p < 0.0001$) and highest immediately postoperatively ($p < 0.0001$). Then, at 2 months postoperatively, fat pad thickness decreases and settles to the same thickness measured at 6 months postoperatively ($p = 0.144$), remaining thicker than at baseline ($p = 0.008$).

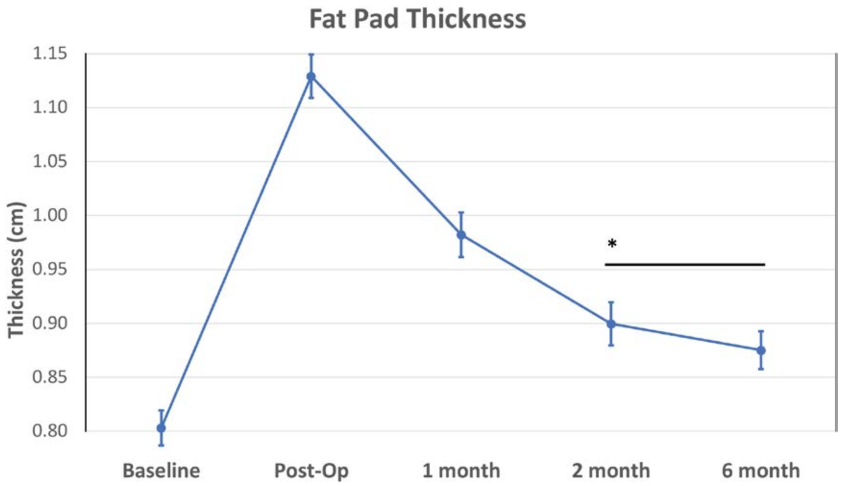

Fig. 1. Fat pad thickness measured over time by ultrasound.

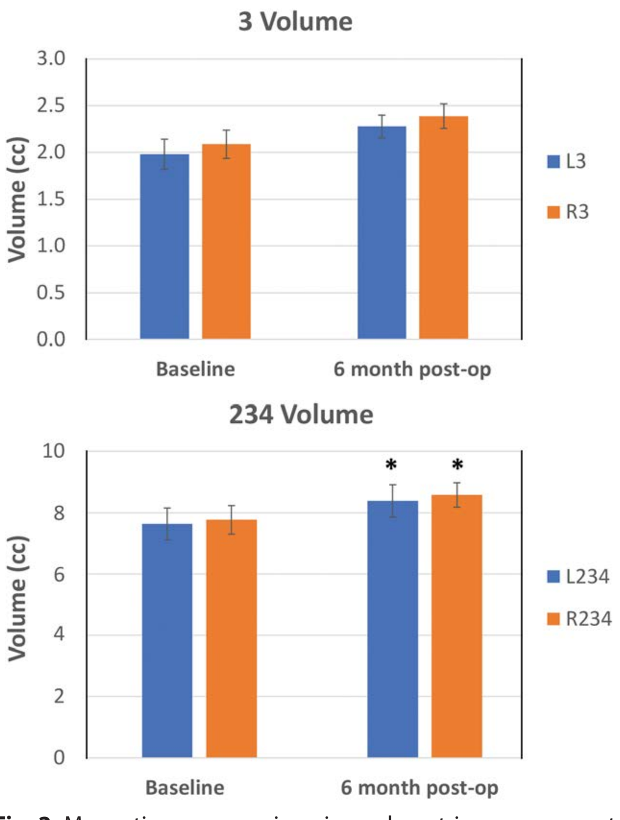

Fig. 2. Magnetic resonance imaging volumetric measurements obtained at baseline and 6 months postoperatively.

Magnetic Resonance Imaging Analysis

Figure 2 highlights volumetric measurements obtained at baseline and 6 months postoperatively. There was no difference in means between L3 or R3 fat pad cross-sectional area at baseline and 6 months postoperative ($p > 0.05$). L234 volume and R234 volume were both significantly higher at 6 months postoperatively than at baseline ($p = 0.04$). Fat volume measured under 3 and 234 were found to be positively correlated ($p = 0.001$, $r = 0.567$). Figure 3 demonstrates the fat pad as seen on magnetic resonance imaging.

Only four of our 17 patients (23.5 percent) showed any signs of marrow edema on either their preoperative or their postoperative magnetic resonance imaging scan. In one patient, the edema improved postoperatively; in another, it was unchanged; and in the final two, it was actually a new finding postoperatively. Metatarsophalangeal joint angles on magnetic resonance imaging at baseline averaged 154.0 ± 1.7 degrees and, at 6 months postoperatively, 155.0 ± 1.6 degrees, with no significant difference in means between the time points ($p = 0.819$) (Fig. 4).

Pain and Disability Outcomes

Manchester Foot and Disability Index scores were surveyed at each time point, where a lower score indicated improved functionality, pain, appearance, and work/leisure activities; in addition to Foot and Ankle Ability Measure scores, where a higher score indicated improved ability to perform activities of daily living and sports. Function scores were lowest (most improved) at 6 months postoperatively ($p < 0.05$) (Fig. 5), and pain scores were lowest (most improved) at 2 and 6 months postoperatively ($p < 0.05$). No changes in appearance were revealed throughout the study ($p > 0.05$). Work/leisure scores were lowest (most improved) at 6 months postoperatively ($p < 0.05$). Both activity of daily living and sports scores were highest (most improved) at 6 months postoperatively ($p < 0.05$).

Pearson correlations indicated that improved functionality according to the Manchester Foot

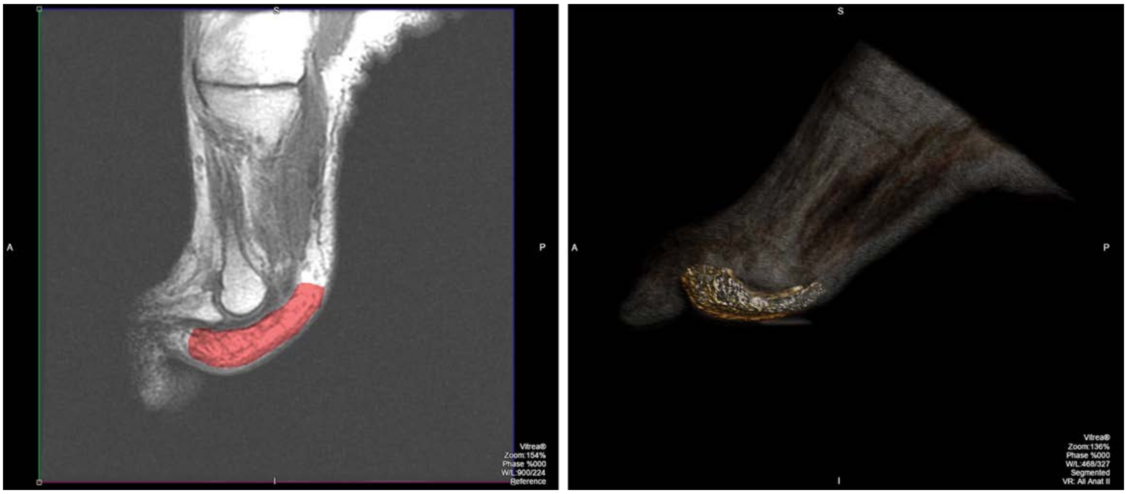

Fig. 3. (*Left*) Selection of the fat pad volume on the sagittal T1 sequence for measurement. (*Right*) Three-dimensional model showing the actual volume of postprocedural fat on the background of the patient's soft tissues.

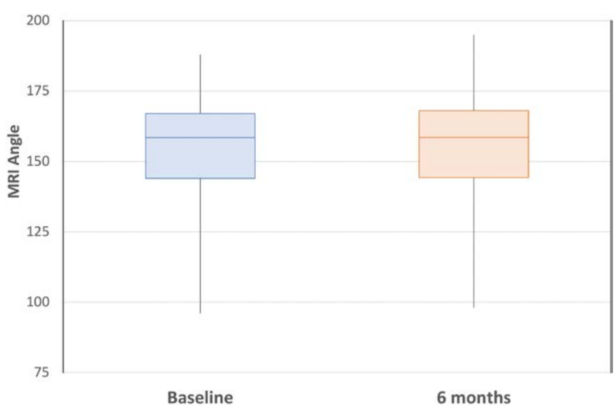

Fig. 4. Magnetic resonance imaging (*MRI*) angle measurements obtained at baseline and 6 months postoperatively. *Boxes* represent medians; *lines* represent ranges.

and Disability Index was directly correlated to improved pain, appearance, work/leisure, activities of daily living, and sports ($p < 0.05$), and improved pain scores were directly correlated with improved functionality, appearance, work/leisure, and activities of daily living ($p < 0.01$). Increase in pain scores directly correlated to worsened reported work/leisure and function outcomes in both groups ($p < 0.05$).

Stance and Gait Force and Pressure Outcomes

Standing force was lowest at 6 months postoperatively ($p < 0.05$) (Fig. 6) and standing pressure was lowest at 2 and 6 months postoperatively ($p < 0.05$). Walking forces and pressures were both highest at baseline ($p < 0.01$), then decreased throughout the study.

Decreases in walking forces and pressures were found to be positively correlated with increases in fat pad volume ($p = 0.013$, $r = 0.441$; and $p = 0.032$, $r = 0.382$, respectively). Improvements in reported work/leisure and activities of daily living scores were found to be positively correlated with decreases in standing forces ($p = 0.024$, $r = -0.431$; and $p = 0.043$, $r = 0.362$, respectively) and pressures ($p = 0.003$, $r = -0.562$; and $p = 0.009$, $r = 0.465$, respectively).

DISCUSSION

Although our group's prior work has already demonstrated the effectiveness of fat grafting in significantly improving foot-related pain and disability, this study is the first to show a significant increase in retained volume over time. This confirms our hypothesis that, whereas plantar tissue thickness as directly measured under the metatarsal head may decrease over time, injected fat is retained and remains supportive while redistributing around the metatarsal heads. Three-dimensional imaging is better than ultrasound at assessing volume retention in the ball of the foot.

An interesting finding in our study is that higher body mass index correlated to less improvement in fat pad volume and pain reduction. Despite padding patients' insoles and instructing them to avoid strenuous activity postoperatively, it is challenging to totally offload the grafted region in these subjects. Thus, the greater a patient's weight, the more pressure that will be applied to the grafted fat, and this may lead to a less-favorable outcome. An alternative hypothesis is that the quality of fat in patients with a high body mass may not be as favorable. Although this should not necessarily exclude patients with a higher body mass from undergoing

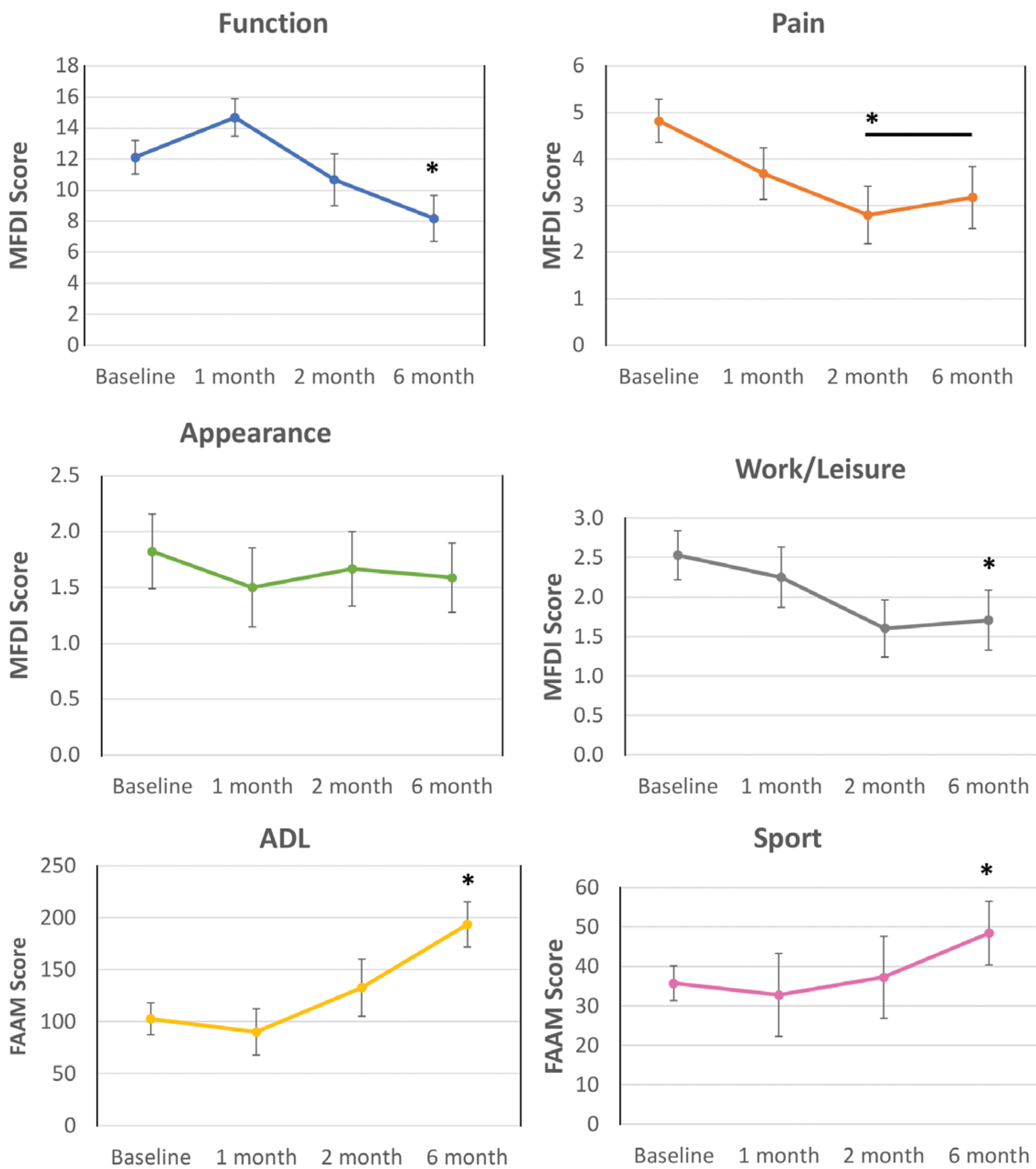

Fig. 5. Pain and disability outcome scores. *MDFI*, Manchester Foot and Disability Index; *ADL*, activities of daily living; *FAAM*, Foot and Ankle Ability Measure.

pedal fat grafting, this is something on which they should be counseled preoperatively. It is also worth noting that all patients in our study were either uncontrolled or well-controlled diabetics without sequelae such as peripheral neuropathy. The application of pedal fat grafting to diabetics with peripheral neuropathy remains unstudied, but we hypothesize that this would lead to greater difficulty with offloading the grafts and less-favorable outcomes.

Although several patients in our study with hammertoes appeared to have less toe deformity following pedal fat grafting, analysis of the metatarsophalangeal angle failed to reveal any significant change in toe position postoperatively. Hammertoes cause a retrograde force, leading to greater plantar flexion and prominence of the metatarsal heads at the ball of the foot, with fat pad displacement just behind the toes. Therefore, it may be ideal for addressing osseous deformities (e.g., bunions, hammertoes) in conjunction with fat grafting for these patients.

A limitation of this study is the 6-month follow-up, which was attributable primarily to funding of the study. Although our study shows a significant increase in volume at 6 months, we also observed

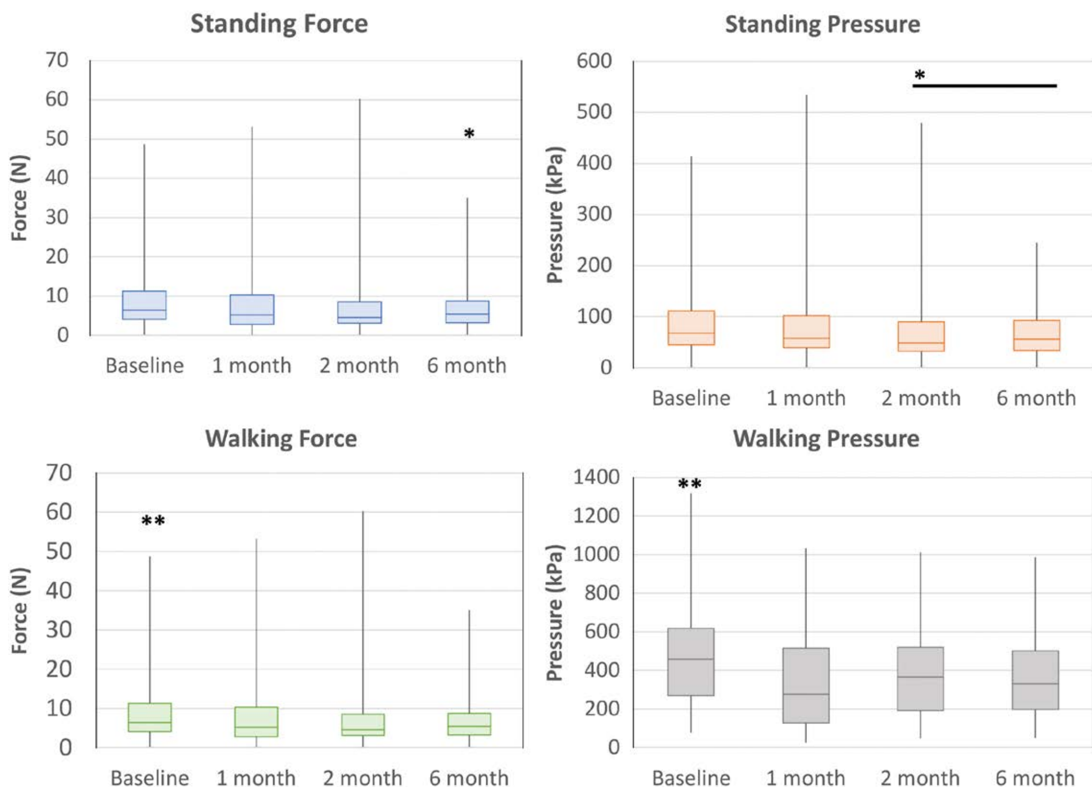

Fig. 6. Stance and gait force and pressure outcomes represented in box-and-whisker plots.

increased tissue thickness at this time point, and it remains to be seen how volume might change over a longer period. Further magnetic resonance imaging at 1 or even 2 years will help answer the question of whether volume is retained and correlated with improved pain. Another limitation is the small sample size of our cohort. A larger sample may reveal more significant information regarding bone marrow edema, metatarsal angle, and volume over time. Forefoot fat pad atrophy is often bilateral. We decided to offer the procedure for both feet if patients had pain in both feet, to avoid the need for a secondary operation. Our outcomes might have been different if we had operated on just one foot at a time, allowing for better pressure relief of the operated foot and potentially better recovery and fat take.

Another possible explanation for the long-term improvement in patient outcomes following pedal fat grafting relates to the quality, rather than the quantity, of fat in the metatarsal fat pads. Studies have shown that the biomechanical properties of plantar soft tissues change with advancing age, with increasing fat pad stiffness and reduced compliance likely contributing to the development of foot-related problems.[18–20] Thus, perhaps a qualitative biomechanical change in the metatarsal fat pad following pedal fat grafting could account for long-term symptomatic improvement. We are currently investigating the stem cell characteristics of the fat used in our foot fat grafting cases and aim to correlate it to clinical findings in the near future.

CONCLUSIONS

Pedal fat grafting leads to a significantly increased volume in the metatarsal fat pads seen at 6 months, which correlates with improved function and pain, along with decreased foot forces and pressures. Further studies will show whether this increased volume is maintained longer, or whether the qualitative rather than quantitative changes in the fat pads are contributory as well.

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