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ORIGINAL ARTICLE

The plantar fat pad and the diabetic foot – a review

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Abstract

There has been much debate concerning the pathologic consequences of diabetes on the plantar fat pad and its subsequent association with the development of a foot ulcer. This review article documents two theories regarding pathophysiology in diabetic foot ulcer formation as they are related to the plantar fat pad and discusses current treatment options for this pathophysiological phenomenon. Traditionally, fat pad atrophy in diabetic patients was thought to result as an irregular arrangement of collagen fibrils within the septal walls as a result of glycation as well as diminishing adipocyte size due to thickened septal walls. Contrary to this traditional theory, a model depicting distal fat pad migration from under the metatarsal heads has been described in the diabetic patient. Such pad migration renders the metatarsal heads vulnerable to increased pressure, which, in turn, predisposes to foot ulceration. This migratory fat pad theory plays a significant role in approaches to the prevention of diabetic foot ulceration and subsequent amputation. Various methods of fat pad supplementation and claw toe management are impacted by the pathophysiological changes described and new avenues of therapy may be based on these changes.

Introduction

The rise of the fast food industry and the impact of an increasingly sedentary life have progressively resulted in diabetes becoming one of the most common chronic diseases with a global burden that will have a great impact on modern society. Hyperglycaemia and glycation end products (AGE) are associated with multiple pathologic consequences including heart disease, renal disease and cataracts. In addition, neuropathic foot ulceration is of particular concern as it can lead to amputation.

Hyperglycaemia leaves many tissues susceptible to injury; in particular, excess glycation of the arteries that supply the nerves of the lower extremities can cause nerve damage, resulting in diabetic neuropathy (1). This neuropathy not only impairs the individual's ability to detect various stimuli, but can also cause a conformational change in the shape of the foot and/or toes, both predisposing the patient to foot ulceration. As diabetes progresses, deep bacterial penetration of the ulcer and poor circulation allow infections to take hold and spread throughout the lower limb (2), often precipitating amputation.

Given that the morbidity associated with amputation includes the risk of another amputation, it is essential to elucidate the pathogenesis of ulcer formation in the diabetic foot. For quite some time, the traditional theory of ulcer formation in the diabetic foot revolved around an atrophy of the plantar fat pad that acts to relieve pressure applied during gait. Allied to this thinning of the plantar fat pad, the triad of ischaemia, neuropathy and increased susceptibility to infection, sets the stage for diabetic foot ulceration (DFU). Recently a newer theory has been proposed, which describes a migration, rather than atrophy, of such adipocytes as the cause in ulcer formation. This model has relevance to ongoing interventions aimed at the prevention of DFU – supplementation of the fat pad, prevention of migration, or both, are relevant strategies that may be adopted depending on the background pathophysiology.

Key Messages

- fat pad migration in the claw foot deformity causes thinning of the plantar fat pad
- newer methods for fat pad supplementation include lipotransfer/stem cell injections

The plantar fat pad

In order to fully understand the pathological process in which diabetes can lead to ulcer formation, it is necessary to review the anatomy of the plantar fat pad itself as well as its comparison with other fat pads throughout the body. Simply put, a fat pad is essentially a collection of adipocytes surrounded by a regular arrangement of fibrous tissue septa, which acts primarily as a shock absorber besides providing insulation and protection.

The plantar fat pad, in particular, has unique characteristics that enable its performance as a prototypical shock absorber. Specifically, interactions among nerves, blood vessels and adipocytes allow the pads of the heel and the metatarsals to assume the weight-bearing role that is an essential quality of the human foot. The plantar fat pad consists of globules of fat surrounded by fibrous tissue septa; these septa, in turn, anchor the adipocytes in a firm position via attachments to the skin and the bones of the foot (3). The septal walls consist of a parallel arrangement of collagen fibrils (4).

The normal heel (calcaneal) fat pad consists of a thick epidermis, a collagen-rich dermis, an elastin-rich reticular dermis and a superficial subcutaneous layer, which is separated from the deeper subcutaneous layer by horizontal septa. The deeper subcutaneous layer, in turn, has a greater elastin content than does the superficial subcutaneous layer. Finally, the deep subcutaneous layer is connected to the collagen-laden plantar aponeurosis, which is superficial to the calcaneus (5).

Sensory branches of the plantar nerves innervate the fat pad in the metatarsal region. Interestingly, the density of nerve branches at the metatarsal heads is about twice as great as that in the more proximal regions of the metatarsals (3). The common plantar nerve also sends two branches to the heel fat pad, with the distal branch supplying the lateral aspect of the pad and the proximal branch coursing through the medial aspect. The nerves in the fat pad were also seen to penetrate the septal wall to eventually terminate within the dermis. A special mechanical baroreceptor, the Vater Pacini corpuscle is also found in the fat pads but not in the dermis.

The posterior calcaneal branches of the posterior popliteal artery supply the heel fat pad. The plantar arteries and arterial twigs of the posterior calcaneal artery supply the medial fat pad. As seen with the nerves, the vasculature runs through the septal wall, eventually arriving in the dermis (3).

When analysing the anatomy of the plantar fat pad, it is important to compare it with other fat stores and fat pads in the body. Adipose tissue that is responsible for mechanical strength and support, as that found in the plantar fat pad, boasts firm fibrous tissue septa rich in elastin. On the other hand, fatty tissue that serves the function of energy storage has relatively loose fibrous tissue thereby making it incapable of supporting much weight (6).

Plantar fat pad and the diabetic foot

As noted earlier, traditional thinking revolved around the notion that plantar fat pad atrophy contributed to foot ulceration in diabetic patients. Many believed, and still do, that the fat pad cells begin to decrease in size owing to low perfusion to the fat pad as a result of microangiopathy associated with the increased glycation products that are characteristic of diabetes (7). This process would thereby thin out the fat pad itself, causing increased plantar pressure and subsequent ulcer formation.

Buschmann *et al.* compared atrophic diabetic heel fat pads to normal, healthy pads. Histomorphological analysis was undertaken after excision of a weight-bearing portion of the heel from four atrophic feet, obtained after amputation, and four normal cadaveric feet. Analysis revealed a mean 30% smaller surface area and 16% smaller diameter of adipocytes in the atrophic pad when compared with the normal heel pad. Moreover, the overall decrease in volume observed in the atrophied fat pads resulted in a thinner superficial layer that was less capable of absorbing pressure during gait. The septa that surround the fat globules were 10–25% thicker than normal and contained a greater percentage of elastic tissue that led to the appearance of fragmentation in certain cases (5). Finally, perineural fibrosis and hypertrophy of Schwann cells was observed in atrophic fat pads; this was not the case in normal pads.

Hsu *et al.* later highlighted a change in the collagen fibrils that are found in the septal walls of the plantar fat pad (4). Specifically, they remarked that unlike the characteristic seen in non-diabetic patients in which collagen fibrils were found in a regular, parallel orientation to one another, those found in diabetic feet were described to have lost this regular arrangement and were instead distorted and fragmented. It was surmised that these changes in collagen fibres were due to glycation products that caused abnormal cross-linking among adjacent collagen molecules predisposing these patients to DFU (4).

Although there was a lack of overwhelming evidence supporting fat pad atrophy in the diabetic foot ulcer, this theory remained the predominant perspective until 2009 when Waldecker *et al.* documented the role of the metatarsal fat pad in the progression of ulceration. Plantar metatarsal fat pads of patients with diabetes and peripheral neuropathy were compared with those of healthy individuals using histological and computer planimetry. The results of the study indicated that there was no statistically significant difference in mean cross-sectional area of adipocytes between diabetic, neuropathic patients and healthy individuals (7). These findings are a direct contradiction to those observed in Buschmann's trial, in which the calcaneal fat pads in diabetic patients exhibited a relative decrease in size in comparison to those in healthy subjects (5). Other publications also showed a variation in results; for example, Gooding *et al.* demonstrated the significance of calcaneal and metatarsal fat pad atrophy in the development of foot ulceration (8), whereas Robertson *et al.* found no such association (9). Clearly, there must be an underlying cause for a reduction in the size of the metatarsal head fat pad other than atrophy of the fat pad.

It is well known that diabetes is associated with excess blood glucose; noteworthy is the concept that excess glycation of arteries supplying nerves of the lower extremities can lead to nerve damage, or diabetic neuropathy (1). This neuropathy,

which eliminates sensation in the foot, impairs the ability of the feet to detect various stimuli such as pain. As such, patients may distribute excess body weight on inflamed areas and develop calluses. A subsequent break in the skin at these wounded areas may ultimately cause ulcers to develop (2). Neuropathy may also cause changes in the shape of the toes or the entire foot. In particular, the toe deformity, also called hammer/claw toe, was the independent variable isolated and analysed for its association in the development of DFU by Bus *et al.* in 2004.

In this study, the thicknesses of the sub-metatarsal head (sub-MTH) fat pads, among other dependent variables, was compared among three groups: a diabetic experimental group with peripheral neuropathy and toe deformity; a diabetic control group with neuropathy but without toe deformity; and a healthy control group. Interestingly, it was found that dependent variables such as sub-MTH and sub-phalangeal fat pad thicknesses and thickness ratios were comparable in the two control groups without toe deformity. It was only the experimental group with toe deformity and neuropathy that differed from the two control groups when it came to these three variables. Thus, the mean sub-MTH and sub-phalangeal fat pad thicknesses were 2·5 mm and 9·1 mm, respectively in the experimental group; 6·0 mm and 7·6 mm, respectively in the neuropathic control group; and 6·0 mm and 7·7 mm, respectively in the healthy control group (10). These findings demonstrated that the peripheral neuropathy did not, in itself, cause the fat pads to thin out; a much more plausible explanation involved a variation in toe angle, which defines the degree of deformity. This was the only difference between diabetic control and experimental groups. Thus the first identifiable association of thinning of the sub-MTH fat pad was the toe angle – the greater the angle, the thinner the pad.

In some severe cases, an absence of sub-MTH fat pads was seen altogether.

This concept was further developed by Bosjen-Moller (11) who speculated that as the sub-MTH fat pads are connected to the proximal phalanx, hyperextension of the toes, as seen in claw/hammertoe, will result in a distal displacement of the fat pads. Specifically, a patient with hammertoe will exhibit a metatarsophalangeal (MTP) joint that protrudes upwards, while the proximal interphalangeal (PIP) joint bends downward. In the case of claw toes, the MTP joint projects upward and both the PIP and distal interphalangeal (DIP) joints project downward (12). These abnormal joint configurations subsequently result in plantar fat pad displacement (Figures 1 and 2).

This migration phenomenon not only explains the dependence of the sub-MTH fat pad thickness on the toe angle, but also supports the notion that the sub-phalangeal fat pad becomes thicker as the sub-MTH fat pad migrates toward it. Furthermore, a more drastic migration that is seen in extreme toe deformities in some patients may result in a break between the distal and proximal halves of the sub-MTH fat pads owing to the absence of support in this area altogether.

Figure 1 depicts the relationship of joint configuration on the plantar fat pad (yellow) in a healthy individual. Figure 2 portrays the concept of fat pad migration to such a degree that

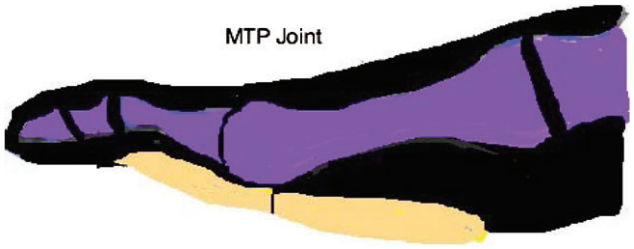

Figure 1 Schematic – healthy individual, normal fat pad.

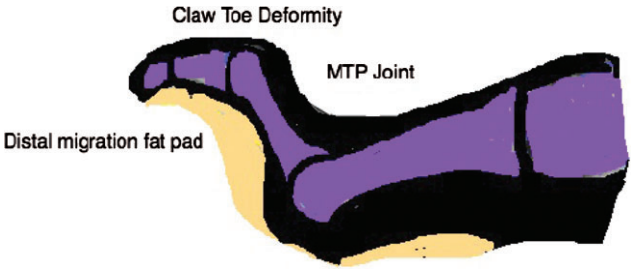

Figure 2 Migration of fat pad with claw toe deformity.

the proximal and distal halves of the pad become completely separated from one another. Furthermore, the MTP joint in the patient with claw toe deformity protrudes upward and the interphalangeal joint in the same patient projects downward. These observations are essentially absent in the healthy individual.

As the sub-MTH fat pad is a major shock absorber of the foot, the distal migration of the fat pad in patients with toe deformity leaves the foot susceptible to ulceration as plantar pressure is greatly increased. The bulk of the increased pressure appears to impact the second and third metatarsal heads (13) setting the stage for ulceration. The sequence of fat pad thinning together with the triad of vascular, nerve and immune system abnormalities in the diabetic patient sets the stage for DFU and potential amputation.

Although claw/hammer toe deformity is a common finding among patients with diabetes, it is important to emphasise that the prevalence of such deformities is not unique to diabetes. According to Farndon *et al.* (14), there was no statistically significant difference in diabetic versus non-diabetic patients concerning the incidence of toe deformity; claw/hammer toes were almost equally found in both groups. Furthermore, it was also noted that the prevalence of sensory neuropathy was significantly greater in the diabetic population, suggesting that although neuropathy can play a role in the development of foot deformity, it cannot be the sole cause as an equal proportion of non-diabetic patients are also afflicted by such deformities. As such, more research is required in order to fully elucidate the relationship between peripheral neuropathy, among other factors, and incidence of toe deformities.

Current treatment and future considerations

One of the major causes of claw/hammertoe deformity is diabetic neuropathy; delay or prevention of nerve damage

is vital in hindering the progress of foot ulcer formation or avoiding it altogether. As such, glucose monitoring and stringent food care are essential.

In the instance in which diabetic neuropathy has developed, patients with claw/hammertoes may experience pain that impairs mobility as well as renders them susceptible to foot ulcer development. Pain associated with claw and hammertoe deformities is related to increased friction between the toes and the shoes. Thus wider, more comfortable shoes should be worn, utilising soft gel pads if necessary.

In some cases, changing shoes may be sufficient to correct the deformity and relieve pressure and pain in the foot. However, in more severe cases, surgical intervention may be necessary. In such cases, earlier intervention is generally associated with a less complicated procedure as well as greater patient satisfaction (15). In short, a surgical procedure on the foot will entail a restoration of the toe joint so that function can be reassumed. This process may involve either directly straightening the toes subsequent to releasing the adjoining tendons or straightening the knuckle to its normal position if the toes are too rigid to manipulate. Furthermore, it is not uncommon for a pin to be placed in the toe joint to ensure proper healing; a major advantage of its use is that the pin rarely needs to be removed after surgery as it causes no further discomfort or harm (15). Postoperatively, the patient is advised to wear a special shoe for at least the first week, after which time athletic shoes may be permitted. Although exercise is not allowed for 6–8 weeks, it is important to gradually resume activities under the supervision of a podiatrist.

Tarsal decompression is an additional surgical technique that has been tried in an effort to improve the peripheral neuropathic effects, the intent being to reduce pressure on the tibial nerve to improve sensation. Aszmann *et al.* demonstrated that upon performing decompression of the posterior tibial nerve at the ankle in diabetic patients, a mean 69% of these nerves displayed improvement in sensibility after almost 2 years. Furthermore, a significant percent of non-decompressed nerves exhibited worsening of neuropathy (16). In a similar study, decompression of the posterior tibial nerve resulted in significant pain relief, and to a lesser extent, increased nerve sensation. Of particular importance in this study, however, was the observation that no new ulcers developed subsequent to nerve decompression (17).

In addition to the treatment options listed above, silicone injections have been used to reduce plantar pressures, and consequently, the incidence of foot ulceration in diabetic patients. Two separate articles (18,19) have promoted silicone use as a safe shock absorber citing the material's inertness, capability to be sterilised, absence of carcinogenic properties, and non-inflammatory characteristics. Van Schie *et al.* (20) demonstrated increased plantar tissue thicknesses and decreased peak plantar pressures over their matched controlled subjects at 24 months after the first injection (20). However, there are potential problems with free silicone injections and the advent of newer autograft options (below) provides safer alternatives.

Finally, the use of soft tissue implantation (autografts and allografts) to alleviate the consequences of plantar fat pad pathology has recently gained momentum. In the case of allograft use, Rocchio *et al.* (21) implanted acellular human dermal matrix into plantar tissue to increase thickness in patients with thinned out fat pads; 25 patients were followed up at 1, 3, 6 and 12 months intervals postoperatively, and thicknesses, detected by ultrasound, increased from 5·01 mm, preoperatively, to 7·52 mm after 1 month, 7·18 mm after 3 months, 7·16 mm after 6 months, and 7·03 mm after 1 year (21). Thus 90% of the mean thickness of the plantar tissue measured 1 month postoperatively was retained at 1 year.

Mulder (22) reported the successful use of an allograft in a patient who exhibited significant loss of the plantar fat pad after a motor vehicle accident. At the 6-week postoperative visit, the heel pad allograft was still present and the patient was satisfied with both the cosmetic and pain-reducing results of the procedure. This procedure was also conducted successfully in two other cases. Thus allograft pad implantation appears to be an alternative for supplementing the plantar fat pad but long-term results in larger numbers are still needed to assess efficacy of this technique.

As far as autograft is concerned, our laboratory is interested in fat lipotransfer autografting, using the patient's own fat harvested via liposuction. Not only does lipotransfer/grafting serve as a potential for fat generation but transfer of stem cells found within the mix is thought to be advantageous in combatting the diabetic diseases process, especially with respect to the angiogenic potential of these cells. Unique lipotransfer techniques are being utilised to facilitate stromal vascular fraction and adipocyte implantation. Results will be published in forthcoming articles.

Another worrisome complication of diabetes is the Charcot deformity that can occur in diabetic patients who also have a peripheral neuropathy. As is typical in diabetic peripheral neuropathy, nerve damage prevents the patient from feeling pain; as such, any small trauma may be sufficient to result in development of Charcot deformity because the patient will continue to put weight on the injured foot. The Charcot foot, which is characterised as being red, swollen and deformed, carries a prevalence of 0·15–2·5% in the diabetic population (23). Furthermore, Alamo Family Foot and Ankle Care reports a recurrence risk of less than 5% (23). Just as is the case with foot ulceration seen in diabetic patients, there is an increased risk of mobility issues and possible amputation associated with the Charcot foot; thus, rapid detection and treatment are keys to full recovery.

Conclusion

The once popular theory of diabetes resulting in atrophy of the various anatomical components of the fat pad has been challenged by the notion that a migration in the support tissue of the foot, rather than a morphological evolution of its cells, results in the apparent thinning of the fat pad, which then causes increased plantar pressures with predisposition to subsequent ulceration. Given that diabetes has become a major health concern throughout the world, its consequences are grave, and that multiple theories defining the development of ulceration exist, it is imperative to continue research on the matter so that efficient treatment and prevention techniques can be realised. Treatment options such as the use of protective orthotics, surgical interventions, silicone injections,

tarsal decompression and soft tissue augmentation have all been studied. Of particular interest is the application of autografting as the combination of fat generation and stem cell implantation may offer a promising alternative for plantar fat pad regeneration in the diabetic foot. Regardless of the avenue of treatment decided upon, quick detection and action are critical in alleviation of morbidity associated with the DFU.

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