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Invited Review

The role of rehabilitation in the management of diabetic foot wounds

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ABSTRACT

Diabetes is one of the most common health problems worldwide. Diabetic foot wounds (DFWs) are hazardous complications of the disease. Patients are often referred to rehabilitation facilities at later stages of the diabetic complications, particularly after amputation surgery. There are potential benefits of rehabilitation practices in preventing and managing DFWs. Therefore, rehabilitation needs to be more involved in the management of DFWs and should be in all stages of diabetic care. In this review, we discuss literature data to bring rehabilitation perspective to the multidisciplinary management of DFWs.

Keywords: Diabetic foot, exercise, foot ulceration, plantar pressure, rehabilitation.

Diabetes mellitus (DM) is one of the leading causes of morbidity and mortality worldwide. Its prevalence is 16.5% in Turkey, and this number has been increasing constantly.[1] Diabetic foot wounds (DFWs) develop in 12 to 25% of all DM patients. Foot wounds are a serious health problem that negatively affects the quality of life and may result in major amputations. In addition to the difficulties experienced by the patient, the estimated financial burden of DFWs on our country is also quite high. According to a study conducted in tertiary healthcare institutions, the economic cost of a patient with DFWs is US$ 976 per person, while of a diabetic patient without a wound is only half of that in our country.[2] Meanwhile, several studies have shown that the probability of recurrence is 70% within five years. Considering both the morbidity and the financial impact, prevention of the development of DFWs becomes the most important goal of the healthcare providers to diabetic patients.

Peripheral neuropathy and vasculopathy are the main causes of DFWs. When sensory loss is severe, the protective senses of the plantar surface diminish, and feet become vulnerable to trauma and minor injuries. Vasculopathy, as another contributing factor causes tissue ischemia and prepares the area for wounds. However, in recent years, factors other than neuropathy and vasculopathy are thought to contribute to wound development, such as gait abnormalities, balance disorders, muscle dysfunction, and joint restrictions. These factors, per se or combined, lead to abnormal plantar pressure distribution pattern and put the foot under risk of ulceration.[3] Data from several studies have suggested that rehabilitation can prevent or treat DFWs by modifying these etiological factors.

Management of DFWs is a multidisciplinary teamwork, and infectious diseases specialists, endocrinologists, plastic and reconstructive surgeons, orthopedic surgeons, physical medicine and rehabilitation specialists, cardiovascular surgeons,

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diabetes nurses, diabetic wound care nurses, physiotherapists, podologists, dieticians, and social workers are the members of this team. In this review, we discuss the contribution of rehabilitation to the prevention and management of DFWs.

The role of rehabilitation in the management of DFWs can be evaluated in two periods: pre-wound and post-wound rehabilitation.

Prevention of diabetic foot wounds within the context of rehabilitation

Neuropathy & Vasculopathy

Currently, exercise is recommended for all diabetic patients owing to its positive effects on blood glucose regulation. On the other hand, the benefits of exercise in controlling peripheral neuropathy and vasculopathy require more attention.

Although there are multiple forms of diabetic neuropathy, the most common form is distal symmetrical sensorimotor polyneuropathy with an insidious onset.[4] Due to impaired tactile sensation, individuals with advanced polyneuropathy cannot detect trauma to their foot. In addition, balance and motor control would be affected by the loss of proprioceptive sensation. When motor neurons are also recruited, the loss of muscle strength would also be detected. These impairments altogether change the normal mechanical loading on the foot and lead to increased ulceration risk. Since this involvement mostly starts from distal and, then, progresses to proximal, the foot is the first body part to be exposed to the risk of injury with a minor trauma.[5,6]

The preventive effects of exercise on the development of polyneuropathy are primarily thanks to the control of blood glucose level and insulin resistance. Exercise also supports microvascular function and fat oxidation, reduces oxidative stress, and increases neurotrophic factors (Table 1).[7] Studies have shown that aerobic and resistive exercises reduce the risk of neuropathy development in diabetic patients.[8-10] A study which examined nerve fiber density with skin biopsies demonstrated that diet and exercise for one-year significantly increased the nerve fiber density.[11] In a systematic review including 418 patients, physical activity and exercise increased the nerve conduction velocities and peripheral sensory function.[12] A recent systematic review showed that aerobic exercises might positively affect nerve function in patients with diabetes, but optimal dosage still remains unclear.[13]

TABLE 1
Effects of exercise preventing the development of diabetic neuropathy

Controls body weight
Controls blood glucose level
Increases insulin sensitivity
Improves microvascular function
Increases fat oxidation
Increases neurotrophic factors

In addition, previous studies have demonstrated the positive effects of exercise on ongoing polyneuropathy. Both aerobic and aerobic plus resistive training have shown to improve nerve conduction velocities and neuropathic symptoms.[7,14,15] A recent randomized-controlled trial (RCT) investigated the effects of sensorial and gait training on proprioception, nerve function, and muscular activation in patients with diabetic peripheral neuropathy (DPN).[16] In this study, a rehabilitation program including wall slides, bridging exercises, prone plank, sit to stand, wobble board exercises, one leg stance, heel and toe raise, tandem stance gradually progressed to different grades using unstable surface and gait training with different patterns of walking were conducted thrice a week for a total of 24 sessions. The results of this study demonstrated a significant improvement in proprioception and nerve function.

A much-debated question is whether exercise is safe for individuals who already have neuropathy. There is a common concern regarding exercise-induced foot wounds in patients with DPN due to the impaired protective sensation. For many years, diabetic patients who had neuropathy were advised to avoid weight-bearing exercises. In contrast, recent researches have demonstrated that physical activity reduces risk for skin breakdown.[17-20] Also, aerobic exercises have shown to improve neuropathic symptoms and stimulate repair and branching of cutaneous sensory fibers.[7,21] However, weight-bearing exercises should not be prescribed to patients who have advanced foot deformity or open foot wounds. Also, patients with absent protective sensation must avoid repetitive weight-bearing activities, such as treadmill walking.[7]

Vasculopathy is one of the most important complications of diabetes. As well as neuropathy, endothelial dysfunction and inflammation are also associated with DFWs, leading to ischemia in the tissue. Another contribution of vasculopathy for the development of DFWs is that diabetic patients with

peripheral vascular disease have claudication and, therefore, their walking speed declines. Due to the reduced walking speed, the time spent in the stance phase of the foot is prolonged. Thus, the plantar surface is exposed to pressure for a longer time period, leading to an increased risk of DFWs. Using the most appropriate exercise programs, claudication and fatigue of these individuals can be reduced and their functional capacity can be increased. It is also known that exercise has positive effects on endothelial function, oxidative stress, and the formation of inflammatory responses.[22,23] Moreover, physical activity can reduce the risk of DFWs by increasing tissue perfusion. A study showed that an intermittent walking program (more than 30 min, thrice a week) significantly improved the walking speed and distance in patients with claudication.[24] Other studies revealed that walking for 1 h, four times a week as a home-based exercise program led to an increase in the walking speed and quality of life in diabetic patients with vasculopathy.[25,26] Taken together, these studies indicate that walking and intermittent walking improve the walking speed and, thus, reduce the risk of vasculopathy-related DFWs.

To prevent complications of diabetic neuropathy and vasculopathy, walking and supervised exercise should be an integral part of the rehabilitation of diabetic patients. The recommendation of the American Diabetes Association (ADA) for type 2 DM patients is to perform at least 150 min of moderate-intensity aerobic exercise and/or 90 min of vigorous aerobic exercise per week.[27] According to the 2019 update of the Clinical Practice Guideline for Diagnosis, Treatment, and Follow-up of. Diabetes Mellitus and Its Complications issued by the Diabetes Working Group of the Turkish Endocrinology and Metabolism Association, diabetic patients are advised to perform aerobic exercises (e.g., walking, running, swimming) and exercises to increase muscle strength two to three times a week.[28] In addition, it is emphasized that flexibility and balance exercises are helpful to increase mobility, particularly in elderly patients. This guide also provides a detailed information on blood glucose control for diabetic patients who desire to exercise, and diabetes complications that may be associated with exercise. Contraindications to exercise in patients with diabetes are also described (Table 2).

Joint stiffness

Diabetic patients have an increased connective tissue thickening and stiffness in all of their main tendons and ligaments. This is clinically relevant, particularly in the foot-ankle complex, as it leads to abnormalities in plantar pressure distribution.[29-31] There are a number of reasons for tissue stiffness such as glycosylation of collagen of the Achilles tendon and plantar fascia, ongoing inflammation, microvascular damage, and trauma.[32,33]

The stiffness of Achilles tendon and plantar fascia reduces the mobility of the foot and ankle, affecting all the rockers of the foot during walking, and decreases the shock absorption of the foot during the stance phase of the gait. Furthermore, the stiff Achilles tendon leads to an increase in the tensile force it exerts on the calcaneus. Foot dorsiflexion is restricted and plantar fascia becomes more tense, causing a cavus-type plantar loading, resulting in an increased load on the metatarsal heads.[34-36] Together with the impaired plantar sensation, foot wounds become inevitable under these overloaded areas.

Recent studies have shown that Achilles tendon lengthening surgery reduces peak plantar pressures and accelerates healing of the wounds in the treatment of chronic diabetic foot ulcers.[37,38] Based on these data, we can assume that the easiest way to treat foot and ankle joint limitation is not to allow its development. It has been observed that stretching exercises applied to the ankle and plantar fascia reduce plantar fascia tension and arch deformation.[39] Also, ranges of motion exercises appear to significantly reduce the peak plantar pressures.[40,41] However, the effectiveness of stretching exercises in preventing wound formation is still unclear in the long-term. Therefore, diabetic patients should be instructed to perform stretching and range of motion exercises for Achilles tendon, plantar fascia, triceps sura, and hamstring muscles (Figures 1 and 2).

TABLE 2
Contraindications of exercise in diabetic patients[22]

Unstable plasma glucose levels
Uncontrolled hypertension
Severe neuropathy leading to sensory loss
Active cardiovascular disease
Proliferative retinopathy (intensive exercises are contraindicated)
Vitreous bleeding
Severe hypoglycemia within the last 24 h
Hypoglycemia unawareness
Blood glucose level >250 mg/dL and ketone (+)

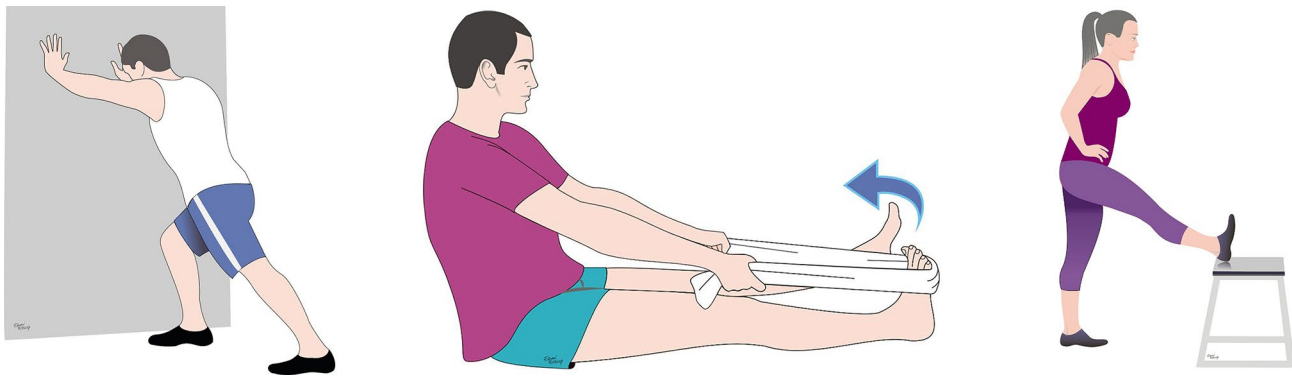

Figure 1. Lower extremity stretching exercises that can be advised to diabetic patients *(with the permisson of Erman Ertung).*

Balance

Balance requires visual, somatosensorial, and vestibular systems to work together. Although all these afferent and efferent systems may be affected to some extent in diabetic patients, the main problem in patients with polyneuropathy arises when the somatosensorial system is involved. Individuals with diabetes have a higher postural sway, regardless of age.[42,43] A study have revealed a positive correlation between the hind foot peak plantar pressure and body oscillations.[44] Impaired postural control along with the muscle weakness, joint limitations and foot deformities may lead to changes of plantar pressure distribution which may contribute to the increased risk for plantar wounds.[45]

Several studies have suggested that exercise programs for diabetic patients can improve balance and reduce risk of falls within 6 to 12 weeks.[46,47] Balance exercises can positively affect the plantar pressure distribution and may reduce the risk of wound development. To date, however, there has been no research in the literature examining the direct association between balance training and DFWs.

Gait disturbances

Gait abnormalities are observed in diabetic patients as a result of neuropathy, joint limitations, muscle dysfunction, and foot deformities. Due to DPN, patients cannot receive tactile information from the ground and, also, there is a lack of

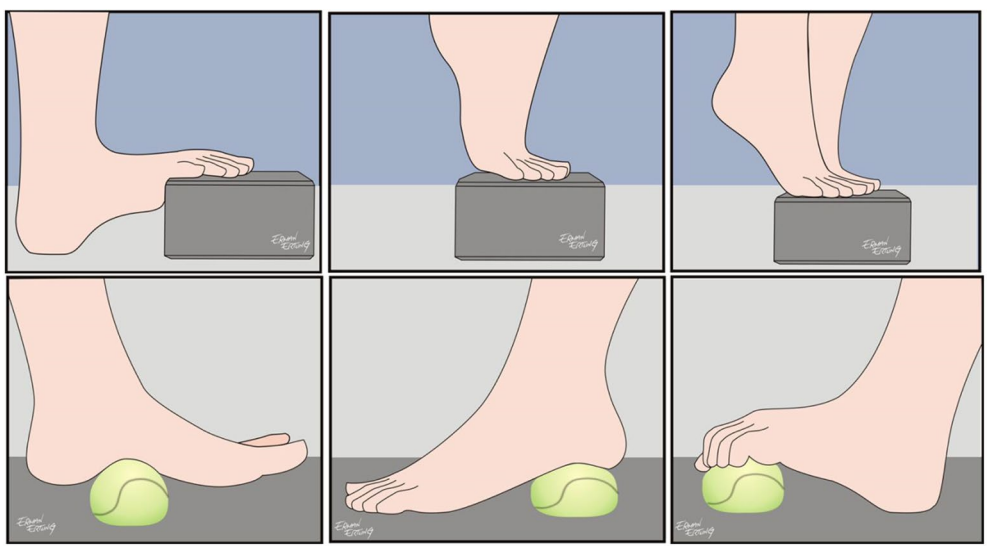

Figure 2. Plantar fascia stretching and myofascial release techniques *(with the permission of Erman Ertung).*

proprioceptive inputs from foot and ankle joints. As a result, individuals develop a more cautious and slow walking pattern against falling.[45,48] In addition, a different activity pattern of the muscles has been observed during walking in individuals with diabetes, independent of polyneuropathy.[49] A co-contraction observed in the agonist and antagonist muscles of the ankle and knee. As a consequence, the walking speed decreases and the stance phase of the gait is prolonged,[48-50] which may increase the risk of plantar wound development by prolonging the exposure time to pressure.

During gait, load transfer patterns under the foot also differ in patients with diabetic neuropathy. Due to the rigidity of the joints, mild pronation of the foot during normal gait does not occur, and the helical movement in the stance phase cannot be observed.[34,36,48] Therefore, the pressure center shifts much more medial than the physiological transition point, causing abnormal loadings on the sole of the foot which may increase risk for DFWs.[51]

To adjust gait abnormalities, muscle atrophy and joint mobility should be restored with exercises that include range of motion, balance, aerobic and resistive training. Increased postural stability and muscle quality would positively affect walking performance, thereby, reducing the risk of wound development by preventing incorrect loading on the plantar surface.

To date, several studies have focused on different gait modifications to reduce forefoot plantar pressure in diabetic patients with neuropathy. Two different studies demonstrated mild reduction in forefoot peak plantar pressures, when participants with neuropathy were instructed to pull their leg forward from the hip to initiate the swing phase of the gait rather than push off. However, the authors suggested that the patients were unable to use this pattern long term.[52,53] Brown et al.[43] reported a reduction in peak plantar pressures under forefoot with using the "step to" gait in patients with DPN. Studies evaluating the impact of biofeedback-based walking strategy in patients with DPN have shown that the insoles with biofeedback provide safe and balanced plantar pressure distribution, if there is no foot deformity.[54,55] In recent years, retro walking has been a popular treatment in rehabilitation. The walking cycle, which we start with heel strike in our normal gait, starts with finger contact when we walk back and forth, and this affects the entire plantar pressure distribution. In a study, a decline in forefoot plantar pressure was observed after a total of 12 weeks of back-walking exercise.[56] Taken together, these studies suggest that gait modifications may be able to balance plantar pressures in patients with diabetes. On the other hand, the method chosen should be sustainable and should not disrupt the patient's natural posture and create additional harmful biomechanical loads.

Management of DFWs within the context of rehabilitation

Although our main goal is to prevent DFW formation, they inevitably occur in 12 to 25% of diabetic patients. A positive contribution can be made to wound healing with rehabilitation practices.

The impact of exercise in diabetic wound healing

The main goals of exercise prescription in patients with DFWs are to prevent new wounds on the contralateral side, to help glycemic control, to prevent the side effects of immobility, and to accelerate the healing of the wound.

Individuals with foot wounds often become bedridden or a wheelchair user, until the wound heals. Immediate mobilization of these patients is necessary to avoid complications of immobilization, particularly loss of muscle strength and pressure sores. As well as providing glycemic control, exercise would also have positive effects on diabetic wound healing by increasing vascularization around the adjacent area. Providing better blood circulation of the wound bed facilitates the formation of new granulation tissue and increases nutrition and oxygenation.

In case of a present wound, loading on the affected extremity can be harmful due to its negative effect on wound healing and presence of wound dressing materials, negative pressure devices or tissue flaps on the affected area. Therefore, exercises must be either partial weight bearing or non-weight bearing. Depending on the condition of the wound, non-weight bearing or partial weight bearing aerobic exercises such as swimming, static cycling should be prescribed as a part of the treatment plan.[57] While prescribing exercise programs to individuals with unilateral wounds, care should be taken not to overload the healthy side to prevent new wounds. In future practice, it seems possible to use treadmills with lift assistance to provide motion without harmless loads on wounded feet. In a study conducted in our country, there was a significant decrease in wound sizes of patients who were instructed to do ankle-foot range of motion exercises for 12 weeks.[58] In the light of these data, we suggest that ankle and foot range of motion exercises should be recommended for all individuals with DFWs

(Figure 3). In addition, aerobic exercises should be added to the treatment plan for patients without contraindications.

Offloading braces are frequently used in individuals with DFWs, and there are concerns that they can be injurious by causing excessive loads on the healthy side. In addition, offloading braces can impair balance and, when the decreased sensorineural impulse and muscle dysfunctions of these patients are taken into account, the risk of falling increases inevitably.[59] It is also the responsibility of our branch to select the correct assistive walking device suitable for the patients' age and physical performance and to teach how to use them. Also, balance exercises should be given to these patient groups. Additionally, correction of the leg length discrepancies with a shoe lift to the healthy side is important in providing body balance and preventing back pain. These types of shoe lifts can be provided as custom made or over the counter products (Figure 4).

The role of physical therapy modalities in wound healing

Physical therapy modalities have been used in wound healing for many years. The most commonly used modalities are electrical stimulation (ES), ultrasound (US), and phototherapy. There are many reviews in the literature comparing these methods with each other and/or with placebo. Physical modalities are shown to have a positive impact on wound healing.[60-62] However, there is no definite consensus regarding their superiority to each other. Although we have briefly summarized the use of physical therapy modalities for wound healing in terms of subject integrity, this issue should be discussed with a detailed review, which is out of the scope of this article.

Electrical stimulation

Electrical stimulation helps us to direct the desired cells in the tissues to the target area with the help of its polarity. With ES, macrophages, epidermal cells, and inactive neutrophils are migrated to the cathode, while neutrophils, fibroblasts, mast cells, platelets, lymphocytes and keratinocytes are located at the anode. In the inflammation phase of the wound healing (within the first 20 days), the negative pole is recommended to be placed close to the wound. Therefore, cells against inflammation can be attracted near to the wound site. Close placement of the positive pole to the wound site is preferred, if necrosis is dominant and there is no inflammation at the

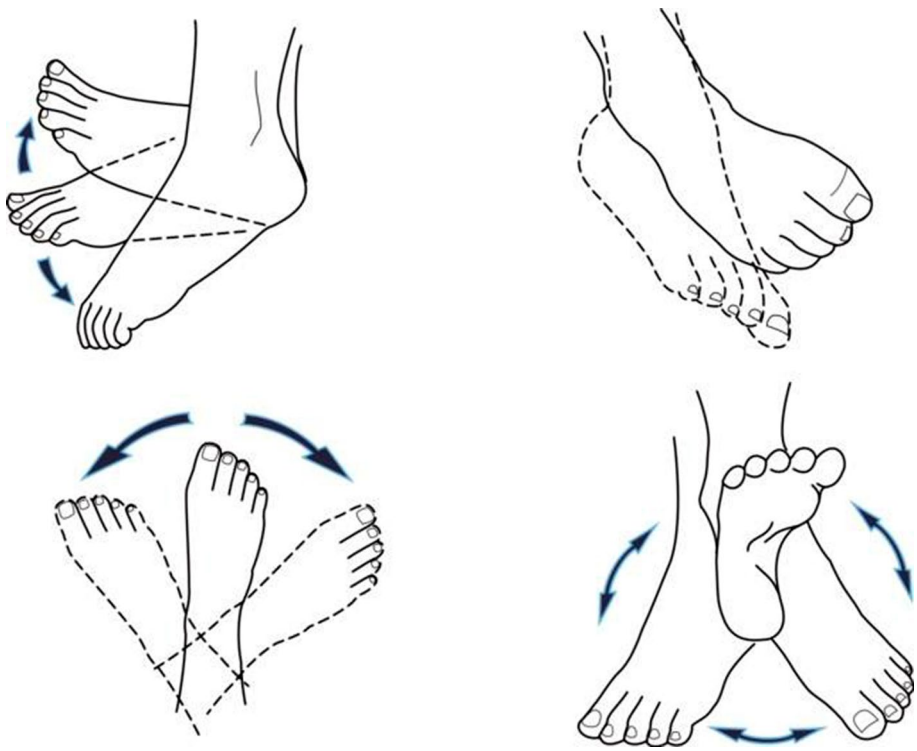

Figure 3. Foot and ankle range of motion exercises should be given even the patient had a wound or not *(with the permission of Erman Ertung).*

Figure 4. Correction of the leg length discrepancy with a shoe lift to the healthy side in a patient using off-loading brace *(with the permission of Ottobock®).*

wound or if the wound healing is in the proliferative phase.[63] The mechanism of electrical currents on wound healing is summarized in Table 3. There is still uncertainty regarding clinical impact of ES on wound healing.[64-66] Also, appropriate current types and dosages still remain unclear. A meta-analysis revealed the use of symmetrical biphasic, monophasic or square-wave pulse waveforms in high-quality RCTs and found all of them to be effective regarding wound healing rates.[67] In our clinic, we prefer using high-voltage pulsed currents with current parameters of 60 to 120 pps frequency, 40 to 100 µsec pulse width, and 45 to 60-min treatment duration.

Ultrasound

Non-thermal effects of US are predominantly responsible from tissue healing. The increasing rate of protein production by fibroblasts, vasodilatation, promotion of macrophage responsiveness are the main mechanisms of tissue repair obtained from US. There are a number of qualified studies showing that US accelerates the healing in diabetic wounds. A qualified RCT revealed that US, applied on DFWs at a frequency of 40 kHz, provided a faster healing.[68] An *in vivo* study indicated that non-contact, low-frequency US therapy thrice a week exhibited a better neovascularization and wound closure in a humanized excisional wound model.[69] A controlled study found that US delivered through a mist of saline to the wounds accelerated the repair process in diabetic mice.[70] A recent study also revealed a significantly faster reduction in the wound size with a low-frequency (20 kHz) and low-intensity US.[71] Although there is still uncertainty regarding effectiveness and dosage, low-intensity and low-frequency US therapy seems to be effective on wound healing.

Phototherapy

Phototherapy is another treatment modality which has a stimulating effect on cells and accelerates wound healing (Table 4). Low-level laser therapy (LLLT) is known to increase collagen production, vasodilatation and nerve conduction velocity, and reduce bacterial growth, as well.[63,72,73] Animal studies have demonstrated potential beneficial effects of LLLT on wound healing.[72-74] A meta-analysis of seven RCTs including 194 patients reported that

TABLE 3
Effects of electrical stimulation on tissue healing

Attracting cells to the wound area
Release of cell contents to the environment by disrupting cell membrane functions
Reducing edema
Antimicrobial activity
Increasing protein synthesis
Increasing circulation and tissue oxygenation

TABLE 4
Effects of phototherapy on tissue healing

Increasing ATP production
Increasing collagen production
Controlling inflammation
Reducing bacterial growth
Increasing vasodilation
Increasing nerve conduction velocity and regeneration

ATP: Adenosine triphosphate.

LLLT promoted a faster granulation formation with shorter wound closure time and alleviation of foot ulcer pain.[75] Although the ideal LLLT parameters for wound healing have not been established yet, an energy density between 5 and 24 J/cm^2 is considered to be the most effective range.[76,77] In the literature, it is suggested that energy under this intensity would not be sufficient for healing, whereas higher doses can inhibit healing.[77-79]

In conclusion, with appropriate aerobic, strengthening, balance and flexibility exercises, the risk of diabetic wound development can be reduced. Wound healing also benefits from exercise and physical therapy modalities. Additionally, it is important to mobilize patients who have DFWs to minimize complications of prolonged immobilization. In the light of the literature review, rehabilitation is safe and effective in preventing and managing DFWs.

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