

Advances in Basic and Clinical Research on Diabetic Foot Ulcers

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Abstract: *Diabetic foot ulcer (DFU) is one of the most severe complications of diabetes, involving complex pathological mechanisms such as neuropathy, vascular abnormalities, and infections. In recent years, with advances in treatment technologies and the promotion of multidisciplinary team (MDT) care, DFU diagnosis and treatment have improved significantly. Traditional therapies, including dressings, debridement, and negative pressure wound therapy (NPWT), remain critical in basic treatment. Meanwhile, emerging therapies such as stem cell therapy, growth factor therapy, continuous oxygen diffusion therapy (CODT), and antimicrobial materials offer new hope for treating refractory ulcers. However, DFU's high recurrence rate and poor long-term prognosis remain major challenges, closely associated with blood glucose fluctuations, infections, and psychosocial factors. MDT approaches have significantly improved cure rates and quality of life but face limitations in implementation at primary healthcare levels. Future research should focus on large-scale, multicenter studies with long-term follow-up while strengthening psychological support and personalized management. This would promote comprehensive advancements in DFU diagnostic and therapeutic strategies, ultimately improving patient outcomes and quality of life.*

Keywords: Diabetic foot ulcer, Multidisciplinary Team Care, Emerging Therapies.

1. Introduction

Diabetic foot ulcer (DFU) is among the most common and severe complications of diabetes. It significantly reduces patients' quality of life and increases healthcare costs and mortality risks. DFU development involves multiple pathological mechanisms, including neuropathy, vascular abnormalities, and infections. Recent advancements in treatment technologies and MDT care have improved DFU diagnosis and treatment. However, the high incidence, recurrence, and mortality rates of DFU remain clinical challenges. This article reviews recent progress in understanding DFU pathogenesis, treatment approaches, and recurrence prevention strategies.

2. Pathogenesis of Diabetic Foot Ulcers

The development of DFU is complex, resulting from interactions between neuropathy, vascular disease, and infection. Peripheral neuropathy caused by hyperglycemia is a major pathological basis for DFU. It impairs sensory, motor, and autonomic nerve functions, leading to sensory loss, muscle atrophy, and skin trophic changes, creating conditions for wound formation [1]. Moreover, diabetes-induced microcirculatory dysfunction and macrovascular disease exacerbate ischemia and hypoxia in foot tissues, further hindering wound healing [2]. Chronic low-grade inflammation is another critical mechanism. Overproduction of pro-inflammatory factors such as IL-1 and TNF- α , combined with reduced anti-inflammatory factors, inhibits wound healing, while abnormalities in macrophage and neutrophil function increase infection risk [3]. In addition, shear forces and pressure concentration play key roles in DFU formation, particularly in the arch and heel, where sustained mechanical stress causes micro-damage to the skin and deep tissues [4]. In summary, DFU is the result of multifactorial interactions. Future research should explore these interrelationships to develop precise therapeutic

interventions.

3. Treatment Approaches for Diabetic Foot Ulcers

3.1 Traditional Therapies

3.1.1 Traditional Dressing Therapy

Traditional dressing therapy is a foundational approach widely used in clinical practice. It provides a protective and healing environment for wounds, promoting ulcer recovery. Common dressings include gauze, breathable dressings, and hydrocolloid dressings, which effectively protect wounds, prevent external contamination, and alleviate pain [5]. However, treatment outcomes are influenced by ulcer size, depth, and patients' glycemic control. Traditional dressings alone may not achieve optimal results for deep or severely infected ulcers [6]. Thus, combining traditional dressings with other methods, such as debridement and antibiotic therapy, is essential for comprehensive treatment [7].

3.1.2 Debridement

Debridement is a crucial component of DFU treatment. It removes necrotic tissue, pus, and infection sources, improving the wound healing environment. Studies have shown that debridement significantly accelerates wound healing and enhances cure rates for severe ulcers [6]. However, debridement may cause pain, bleeding, and secondary infections, requiring professional guidance [8]. Despite potential side effects, debridement remains indispensable, particularly for extensive or complex ulcers.

3.1.3 Negative Pressure Wound Therapy

Negative pressure wound therapy (NPWT) has become a core technology in DFU treatment. By promoting local blood flow,

reducing exudate, and improving the wound environment, NPWT demonstrates significant efficacy. It shortens healing time, particularly for chronic and refractory ulcers [9]. However, high costs and equipment complexity limit its use in primary care settings. Developing portable and low-cost NPWT devices is a priority for future advancements.

3.2 Emerging Therapies

3.2.1 Continuous Oxygen Diffusion Therapy

Continuous oxygen diffusion therapy (CODT) is gaining attention for DFU treatment. It provides continuous oxygen supply, improving tissue oxygenation and promoting wound healing. Studies have shown that oxygen diffusion enhances microcirculation, accelerates wound repair, and reduces hypoxia-induced inflammation [10]. However, individual variability in efficacy and high costs hinder widespread adoption. Further research is needed to optimize its application conditions [11].

3.2.2 Growth Factor Therapy

Growth factors such as epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and fibroblast growth factor (FGF) regulate cell proliferation, migration, angiogenesis, and tissue repair at the molecular level, accelerating DFU healing [12]. While growth factor therapy improves healing rates and reduces recurrence, challenges such as degradation and stability need to be addressed. Future research on slow-release systems and delivery methods could enhance its clinical utility.

3.2.3 Stem Cell Therapy

Stem cell therapy is a promising frontier in DFU treatment. Mesenchymal stem cells (MSCs) are particularly effective due to their immunomodulatory and anti-inflammatory properties. Studies have demonstrated that MSCs accelerate healing by secreting growth factors and cytokines and promoting angiogenesis [13]. However, long-term safety and efficacy require further validation.

3.2.4 Antimicrobial Materials

Antimicrobial materials play a critical role in preventing DFU infections. Common materials include silver dressings, honey, antibiotic-coated materials, and natural antimicrobials. These materials effectively inhibit microbial growth, reduce infections, and promote healing [14]. Advances in nanotechnology have enhanced the antibacterial efficacy of silver and copper-based materials.

4. Recurrence and Risk Factors

4.1 High Recurrence Rates

Diabetic foot ulcer (DFU) has alarmingly high recurrence rates, with 40%-60% of patients experiencing recurrence within one year and over 70% within five years [15]. This trend not only exacerbates patient suffering but also imposes substantial burdens on healthcare systems, including increased hospital admissions and prolonged treatment

durations. Moreover, recurrent ulcers often lead to higher risks of infection, amputations, and poor overall quality of life. Addressing these high recurrence rates necessitates robust prevention strategies, including patient education, adherence to footwear recommendations, and consistent glucose management.

4.2 Risk Factors

Key risk factors for recurrence include blood glucose fluctuations, infections, and lipid metabolism disorders [16]. In particular, hyperglycemia contributes to impaired wound healing and recurrent tissue damage. Chronic neuropathy and advanced age further compound these risks, as they contribute to diminished sensory feedback and increased vulnerability to injuries. Studies have also identified vascular complications, such as peripheral arterial disease, as significant predictors of ulcer recurrence [17]. Comprehensive risk assessments, including glycemic control, vascular evaluation, and infection surveillance, are critical in developing personalized treatment plans to mitigate recurrence risks effectively.

5. Long-term Prognosis and MDT Care

5.1 Long-term Prognosis

The long-term prognosis for DFU patients remains grim, with studies reporting a five-year mortality rate of up to 50% following ulcer healing [18]. These outcomes are often attributed to underlying comorbidities, such as cardiovascular disease, renal impairment, and persistent hyperglycemia, which contribute to systemic complications. Early identification of high-risk patients through biomarkers and imaging techniques may improve survival rates. Preventive measures, including regular foot screening, optimal pressure redistribution through customized footwear, and early treatment of minor injuries, are essential in reducing ulcer recurrence and improving long-term outcomes [19].

5.2 MDT Care

Multidisciplinary team (MDT) care has emerged as a cornerstone in managing DFU, integrating expertise from endocrinology, cardiovascular medicine, infectious diseases, surgery, and physical rehabilitation. Studies show that MDT approaches significantly enhance healing rates, reduce recurrence, and improve patients' quality of life [20]. For instance, MDT interventions can facilitate early detection and management of complications, including infections and ischemia, through coordinated diagnostic and therapeutic strategies. Incorporating patient education, dietary counseling, and psychological support further bolsters adherence to treatment regimens and promotes overall well-being [21]. Implementing MDT care in both inpatient and outpatient settings is pivotal for addressing the multifaceted challenges of DFU management. By expanding early preventive measures, leveraging technological advancements, and fostering MDT collaborations, healthcare systems can reduce the long-term burden of DFU and improve patient outcomes.

5.3 Psychosocial Factors in the Intervention of Diabetic Foot Ulcers

Traditional diabetes management has primarily focused on physiological indicators, often neglecting the psychological health of patients. Psychosocial factors play a crucial role in the treatment outcomes of diabetic foot ulcer (DFU) patients. Studies have shown that depression, anxiety, and low levels of social support are major contributors to poor treatment adherence among these patients [22]. Poor adherence directly affects ulcer healing rates and increases the risk of recurrence. To address this issue, the integration of psychological interventions and social support mechanisms into DFU management is essential. These interventions may include counseling, stress management programs, and support groups tailored to the needs of DFU patients. Additionally, providing adequate patient education on disease management and fostering a supportive care environment can empower patients to take an active role in their treatment. Future DFU management should emphasize a comprehensive approach that integrates psychological support, patient education, and personalized care strategies. This holistic model can enhance treatment adherence, improve healing outcomes, and ultimately elevate the quality of life for DFU patients. Furthermore, longitudinal studies and large-scale trials are needed to evaluate the long-term benefits of such integrated care models in diverse patient populations.

6. Research Deficiencies and Future Directions

Despite significant progress in the diagnosis and treatment of diabetic foot ulcers (DFUs) in recent years, the following issues remain:

- (1) **Insufficient Multi-Center, Large-Scale Studies:** Most current studies involve small sample sizes and are predominantly single-center studies, which lack representativeness.
- (2) **Lack of Long-Term Follow-Up Data:** Many studies fail to systematically evaluate the long-term prognosis of patients after healing.
- (3) **Inadequate Psychological Support:** The psychological state and lifestyle habits of patients significantly affect treatment adherence and recurrence risk, but these factors have not received sufficient attention.
- (4) **Limited Multidisciplinary Collaboration:** Current research primarily focuses on single treatment methods, lacking integrated, cross-disciplinary studies.

In summary, research on DFUs still faces numerous challenges. To address these issues, future studies should integrate multi-center data, conduct large-scale prospective research, emphasize long-term follow-up, focus on patients' psychological health and personalized management, and promote multidisciplinary collaborative treatment models.

7. Conclusion

The treatment and management of diabetic foot ulcers is a complex and multi-faceted process. In recent years, advancements in both traditional and emerging therapies have significantly improved the diagnosis and treatment of DFUs. Additionally, the promotion of multidisciplinary collaborative

treatment models has provided new directions for clinical practice. However, the high recurrence rate and poor prognosis remain clinical challenges. Future efforts should focus on multi-center clinical research integration, long-term follow-up, and psychological support for patients to further improve treatment outcomes and enhance their quality of life.

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