Diabetic foot ulcers, a comprehensive approach – Review

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ANDREEA GROSU-BULARDA
RĂZVAN NICOLAE TEODOREANU
CARMEN MIHAI
FLAVIA FRANCESCA LIȚĂ
FLORIN-VLAD HODEA
IOAN LASCĂR
ALEXANDRU CHIOTOROIU

ABSTRACT – REZUMAT

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Diabetic foot ulcer represents a very severe complication of diabetes mellitus, often requiring foot amputation, leading to morbidity and higher mortality rates. Around one in six diabetic patients develops foot ulcers over their lifetime. Promoting a series of preventive measures including systemic control of diabetes and other comorbidities along with local foot care proved to be a valuable strategy. In addition to rigorous, active prevention, multidisciplinary therapeutic management of diabetic ulcers includes offloading techniques, ulcer debridement, advanced dressings and diabetic foot surgical treatment. In this article, we analyze each component of this sequential treatment plan, with emphasis on current indications and resources, having as main goals decreasing complication rate and morbidity, improving the quality of life and life expectancy of diabetic patients.

Keywords: *diabetic foot ulcers, treatment, dressings, surgery, prevention*

Ulcerul piciorului diabetic, o abordare exhaustivă – Sinteza literaturii

Ulcerele piciorului diabetic reprezintă o complicație foarte severă a diabetului zaharat, adeseori necesitând amputația segmentului afectat, determinând morbiditate severă și creșterea ratei mortalității în această populație. Aproximativ unul din șase pacienți diabetici dezvoltă ulcere la nivelul piciorului pe parcursul vieții. Promovarea unor serii de măsuri preventive, cum ar fi controlul sistemic strict al diabetului și al altor comorbidități, împreună cu îngrijirea locală a piciorului sunt strategii eficiente în reducerea morbidității. Prevenția activă și riguroasă și abordarea multidisciplinară terapeutică a ulcerelor diabetice include tehnici de descărcare a presiunii de pe membrul afectat, debridarea ulcerelor, pansamente moderne și tratamentul chirurgical al piciorului. În acest articol, analizăm fiecare componentă a planului terapeutic secvențial, cu accent pe indicații curente, având drept obiectiv principal reducerea ratei complicațiilor și morbidității, cu creșterea calității vieții și speranței de viață a pacienților cu diabet zaharat.

Cuvinte-cheie: *ulcerul piciorului diabetic, tratament, pansamente, chirurgie, prevenție*

INTRODUCTION

The foot is highly susceptible to mechanical trauma, due to its weight load absorbing properties during locomotion. Involving the most distal part of the neurovascular network, chronic wounds may result in patients with conditions such as peripheral vascular disease, biomechanical deformities, but most importantly in those with diabetes mellitus. Non-healing chronic wounds can potentially determine loss of the limb. In addition, these types of wounds were proven to increase mortality risk independent of other factors [1].

Diabetes mellitus represents a severe chronic condition leading to significant systemic complications and quality of life impairment, being the seventh cause of death in the United States population [2, 3]. According to the International Working Group on the Diabetic Foot a diabetic foot amputation occurs every 20 seconds and affects over 1 million individuals each year. There were 425 million people with diabetes worldwide in 2017, a number anticipated to rise to 629 million by 2045 [4]. Around 15% of diabetic patients develop foot ulcers over their lifetime [5]. Arteritis and small vessel thrombosis, neuropathy (potentially ischemic in origin) and big vessel atherosclerosis are the three basic components of diabetic vascular disease. When combined, these are almost certain to produce impairment in weight-bearing regions [6, 7]. Diabetic foot ulcers are generally deeper and more commonly infected than other leg ulcers, reflecting the diabetic's usual experience with severe end vascular ischemia and opportunistic infection [8]. The duration of the condition will raise the disease's incidence and mortality risk due to uncontrolled infection [8, 9]. It is known that associated infection is the most common cause of diabetes-related admission to the hospital and remains one of the major pathways to lower-limb amputation [4]. Non-healing diabetes ulcers associating soft tissue infection may complicate with severe bone infection-osteomyelitis, requiring aggressive surgical treatment and associating a higher risk of major lower limb amputation necessity [10].

THERAPEUTIC STRATEGY

Treatment of diabetic foot ulcers involves a multidisciplinary team consisting of general practitioner, diabetologist, podiatrist, orthotic devices specialist, infectious disease doctor and surgical specialists-vascular surgeon, general surgeon, plastic surgeon and orthopedic surgeon [7]. Preventive measures are mandatory, an essential strategy being patient education on adequate systemic treatment of diabetes and self-care of affected foot [7, 11]. Controlling diabetes, smoking and obesity, as well as frequent foot inspections, callosity removal (in neuropathic foot), daily moisturizing, regular toenail trimming, and well-fitting footwear, are all important measures in preventing diabetic foot complications [12, 13]. In diabetic patients, glucose level should be strictly monitored (including glycosylated hemoglobin HbA1c), as it was observed that inadequate glycemic control represents a primary determinant for the occurrence of diabetic ulcers [7, 14].

In addition to continuous, active prevention, the following represent the main components of the therapeutic management of diabetic ulcers: offloading techniques, ulcer debridement, advanced dressings and diabetic foot surgery.

Offloading

Many foot ulcers have a biomechanical component as part of the etiology. Increased plantar pressure has been linked to a variety of structural abnormalities in the foot. Claw toe deformity, hammer foot, hallux valgus or Charcot's neuro-arthropathy are the most common anomalies in patients with diabetes and they can cause severe disruption to the foot's architecture, as well as a higher occurrence in local foot pressures [7, 15–17]. Repetitive damage to the foot must be prevented by lowering pressure and shear forces on the sole of the foot, allowing existing wounds to heal and high-risk regions to be protected against recurrent ulcers. The importance of ulcer off-loading is growing, since it has been noted that if the foot is not appropriately offloaded (in high-pressure areas), even after the ulcer has healed, therefore increasing the risk of recurrence [18, 19]. Furthermore, even in a well-perfused limb, poor off-loading of the ulcer has been shown to be a key cause of ulcer healing delay [20, 21].

The International Working Group on the Diabetic Foot (IWGDF) recommends a non-removable knee-high offloading device as a first choice offloading treatment for healing a neuropathic plantar forefoot or midfoot ulcer in a diabetic patient. Second and third choices, in case of contraindications and patient non-compliance, removable knee-high and detachable ankle-high offloading could be used. The fourth choice of offloading therapy implies appropriately fitting footwear paired with felted foam [22]. If non-surgical offloading fails, surgical offloading interventions (internal offloading) are recommended [19].

Debridement

Debridement of all chronic wounds is recommended to remove surface debris and necrotic tissues. It promotes granulation tissue development and can be accomplished surgically, enzymatically, biologically or through autolysis. Debridement lowers bacterial count while increasing local growth factors production. This approach also diminishes pressure, assesses the wound bed status, and promotes wound drainage [7, 20, 23].

Mechanical debridement includes abundant washing, high-pressure irrigation or pulsed lavage, used as the initial step of the surgical procedure, facilitating necrosis removal [7]. Surgical debridement performed in sterile conditions, in the operating room is the gold standard procedure; hyperkeratosis and dead tissue are quickly and effectively removed until a healthy bleeding ulcer bed is created. If significant ischemia is suspected, vigorous debridement should be delayed until vascular evaluation and, if required, a revascularization treatment should be conducted [24, 25].

Collagenase, papain, a mixture of streptokinase and streptodornase, and dextrans are agents used for enzymatic debridement. These can remove necrosis while causing minimal damage to healthy tissue. Enzymatic debridement is recommended for ischemic ulcers, despite its high cost, in case of exceeding pain sensation during surgery [26]. Compared to saline moistened gauze and selective sharp debridement, biochemical debridement using Clostridia collagenase ointment resulted in a statistically significant decrease in wound surface after 12 weeks [27].

Endogenous proteolytic enzymes disintegrate sloughy, necrotic tissue in a natural process known as autolytic debridement, a process enhanced by dressings such as hydrocolloids, hydrogels and films. The use of dressings that produce a moist wound environment allows host defence systems (neutrophils, macrophages) to remove devitalized tissue utilizing the body's enzymes, such as collagenase, elastase, myeloperoxidase, acid hydroxylase, and lysozymes [7, 28].

Dressings

Dressings have improved wound management and healing of diabetic foot ulcer. These dressings should initiate and promote the production of healthy granulation, as well as accelerate the epithelization process [7, 29]. Thus, the main properties of such dressings should be the provision of moisture, capability to enhance growth factors production, antiseptic capacity, oxygen permeability, the ability to stimulate autolytic debridement, long and efficient time of action with sustained drug release [7, 30]. Since ulcer differ in location, depth, scarring, contraction, infection, pain, as well as the patient's biological status, multiple types of dressings may be employed, either passive, active or interactive. Passive ones provide protection and ensure exudate absorption. Active and interactive dressings stimulate local cellular and growth factor activity. These are beneficial in chronic wounds, with high adaptability, providing a more suitable environment. Categories of diabetic foot ulcer dressings can be split into hydrogels, hydrocolloids, alginates, foams, silver-impregnated, textiles and films [7, 30, 31]. Table 1 presents current advanced dressings useful for treating diabetic foot ulcers [7, 32–35].

Table 1

SOME CHARACTERISTICS OF PROTECTIVE OVERALLS USED IN THE STUDY [10]

Dressing type	Action mechanism and advantages	Indication	Disadvantages	Examples
Alginate	Absorbs wound exudate Induces autolytic debridement Provides moisture control Conforms easily to wound bed Absorbs wound exudate	Highly exuding wounds Bleeding wound bed Cavities Can be combined with silver dressings	Should not be used on dry/necrotic wounds or friable tissues Can be adherent during removal	Sorbalgon (HARTMANN USA, Inc.) Algicell Alginate Wound Dressings (Integra LifeSciences Corp) High Gelling alginate (3M Health Care)
Film	It provides a “breathable” barrier, blocking bacteria, while allowing oxygen Wound can be properly inspected due to its transparency Can be combined with alginate or hydrogel dressings	Low exuding wounds Cavities	Removal may be difficult; therefore, one should be attentive to damaged skin around the wound Not to be used in infections Provides no absorption Exudate may accumulate underneath, prompting removal	Tegaderm Transparent Film Dressing (3M Health Care)/ Adhesive Transparent Dressings (Comfort Release) Mepore Film Dressing (Mölnlycke Health Care US, LLC)
Foams	Enhanced absorption of wound exudate Provides moisture control Provides thermic and mechanical protection Ease of use Long-lasting up to seven days Conforms easily to wound bed	Highly exuding wounds Cavities	May cause maceration May cause dermatitis induced by adhesive compounds It can be bulky	Mepilex (Mölnlycke Health Care US, LLC) ALLEVYN (Smith+Nephew, Inc. HydroCell Foam Dressing (Integra LifesSciences Corp)
Hydrocolloid	Provides moist environment Induces autolytic debridement Absorbs exudate Long lasting	Low/moderate exuding wounds	May cause maceration May cause excess granulation tissue Not to be used on dry/necrotic high exuding wounds Can cause unpleasant odor Should not be used in infections	Cardinal Health Hydrocolloids (Cardinal Health) GentellDermatell (Gentell) Hydrocolloid Dressing (Smith+Nephew, Inc.)
Hydrogel	Absorbs wound exudate Provides wound hydration Cooling subjective sensation Induces autolytic debridement Can be used with silver dressings for further antimicrobial activity	Low/moderate exuding wounds Dry wounds	May cause maceration Should not be used in infections, especially anaerobic	DermaPlex Gel (MPM Medical) Dermagran Amorphous Hydrogel Dressing (Integra LifeSciences Corp)
Silicone	Protects newly formed tissues Provides comfort Are amongst most atraumatic dressings	Low/moderate/ high exuding wounds Can dry out if left too long	May cause silicone induced sensitivity	Mepiform Soft Silicone Gel Sheeting ((Mölnlycke Health Care US, LLC) Silicone Gel Sheet (Smith+Nephew, Inc.)
Silver	Provides antiseptic effect Can be combined with other dressings Reduces odor Improves subjective pain sensation Can be used for prolonged periods	Low/moderate/ high exuding wounds Infected wounds	May cause sensitivity to dressing May cause discoloration	PolyMem Silver Non-Adhesive Dressing (Ferris Mfg. Corp) Atrauman Ag (HARTMANN USA, Inc.)
Textile dressings	Used as primary or secondary sterile dressing Protect wound from contamination Absorb exudate Allow wound specific treatments with antiseptic or antimicrobial solutions	Low/moderate/ high exuding wounds Infected wounds	Require more frequent dressing changes Pain and bleeding in case of wound adherence	Woven and non-woven fibers: cotton, polyesters Sterile gauze pads

Textile dressing

Textile dressings provide the advantage of being highly available, allowing for wound secretion inspection, being easy to use by all healthcare workers and being affordable due to the low cost. Thus, they provide a very reliable form of dressing for patients with chronic diabetic foot ulcers. Textile dressings are to date the most often used type when treating diabetic foot ulcers. In order to gain an optimal wound healing environment, efforts were made to define and establish accurate parameters for each class of textile dressings.

Functional model of hemostatic material based on conventional technology (weaving)

The calculation of the design parameters of the woven structure is achievable by considering the field of material use and the values generated by its theoretical design, respectively: degree of corrugation, structure phase, special structure phases (a and b), geometric densities of warp and weft yarns, critical geometric densities, minimum geometric density/structure phase (including special phases), simultaneous minimum geometric density, critical technological density. The input data for the calculation of the parameters listed above, as well as the values obtained, are presented in tables 2 and 3 and figure 1.

Table 2

INPUT DATA AND DESIGN PARAMETERS		
Input data	**Unit**	**Values**
Length density of warp//weft yarns	-	280 dtex × 2/54f/150Z// 300dtex × 2/54f/100Z
Diameter of warp//weft yarns	mm	0.216//0.224
Geometric density in warp//weft	mm	0.476//0.476
Critical geometric density	mm	0.440
Simultaneous minimum geometric density	mm	0.38105
Critical technological density	yarn/10 cm	227.3
Wave height for warp//weft yarn in phase "a"	-	0.06129//0.37871
Wave height for warp//weft yarn in phase "b"	-	0.37871//0.06129
Phase number "a"	-	2.3809
Phase number "b"	-	7.6191
Design parameters	**Unit**	**Values**
Density in warp//weft	yarns/10 cm	210//210
Fabric width	mm	120
Total number of warp yarns	yarns	265 yarns (252 background+ 8 edge and weaving + 5 reserve)
Pattern	-	ajour (according to the programming scheme – fig. 1) base (RB2/2; P3 3/ 3 3)
No. heald frames	-	8
Encrypted drawing	-	-(1-2-2-1-3-4-4-3-5-6-6-5-7-8-8-7)-
Encrypted card	-	-(2-3-6-7/3-4-7-8/2-3-6-7/1-4-5-8/1-2-5-6/1-4-5-8)-
Weaving machine type	-	Jakob Mueller/150mm/cams/max.12 heald frames

Table 3

MINIMUM GEOMETRIC DENSITY ON STRUCTURE PHASES				
Structure phase	h_U **(mm)**	h_B **(mm)**	l_U **(mm)**	l_B **(mm)**
I	0	0.4400	0.4400	0
II	0.0540	0.3860	0.4366	0.2111
a	0.0612	0.3780	0.4357	0.2252
III	0.0810	0.3590	0.4324	0.2543
IV	0.1620	0.2700	0.4090	0.3474
V	0.2160	0.2160	0.3833	0.3833
VI	0.2700	0.1620	0.3474	0.4090
VII	0.3590	0.0810	0.2543	0.4324
b	0.3780	0.0612	0.2252	0.4357
VIII	0.3860	0.0540	0.2111	0.4366
IX	0.4400	0	0	0.4400

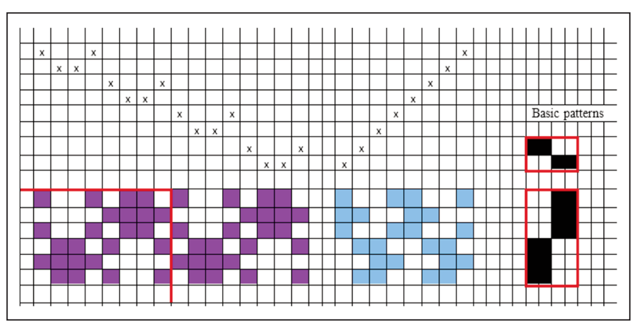

Fig. 1. Schematic diagram for combined ajour connection

Functional model of hemostatic material based on unconventional textile technology

Unconventional textile materials (non-woven fabrics) are based on textile support (consisting only of fibres) which is subjected to a consolidation process with or without consolidation materials, reinforcing bodies or sources of consolidation.

Taking into account the requirements imposed by the field of clinical use, researchers from INCDTP, Romania have designed and achieved a functional model of hemostatic material, on a technological flow that includes the following phases: mixing bed formation, detachment, mixing, carding – folding and mechanical consolidation – interweaving. It should be noted that the interweaving is performed only with the fibrous layer, so without depositing on woven textile support, because the fibres have low tensile strength and elongation at break: max. 1 cN, respectively max. 2%. The consolidation of the fibrous layer was achieved by mechanical interweaving procedure using interweaving needles, GROZ-BECKERT type, with the specification 15 x 16 x 36 x 3½ R221 G 82012.

Negative pressure wound therapy (NPWT)

Negative pressure wound therapy (NPWT) is a novel therapeutic option for diabetic foot ulcers. It uses a special pump (vacuum-assisted closure) to apply intermittent or continuous sub-atmospheric pressure to a resilient open-celled foam surface dressing, silver coated, with an adhesive drape to maintain a closed environment [36, 37]. NPWT is now approved for complicated diabetic foot wounds, although it is not recommended for patients who have an ongoing bleeding lesion. This technique results in a larger proportion of healed wounds, a shorter time for wound closure, a more rapid granulation, lowering the risk of secondary amputation [37–39]. Over the first four weeks of therapy, negative pressure wound dressings reduces wound size more efficiently than saline gauze dressings. NPWT is a cost-effective, simple-to-use, and patient-friendly approach of treating diabetic foot ulcers that aids in early wound closure, reducing complications, and therefore ensuring a better outcome [37].

Surgical treatment

The surgical approach ranges from minor interventions for foot ulcers to extensive reconstructive procedures for Charcot deformities and soft tissues related anomalies. The most important step is to diagnose and treat as soon as possible soft tissue and bone infections. Nonvascular foot surgery, vascular foot surgery, and in some cases, necessity amputation are all options for diabetic foot surgical management [7, 40].

A thorough evaluation should be performed, analysing the complexity of soft tissue defects and musculoskeletal pathological features. Vascular status of the foot is the main concern and should be always addressed prior to any reconstructive attempt. Corroborating the aforementioned findings, a comprehensive approach is presented in figure 2, integrating the surgical options for diabetic foot [41–43].

The reconstructive ladder represents the surgeon's therapeutic options ranging from the simplest procedures (primary closure and secondary intention healing), step by step to the most complex (microsurgical transfer free flaps). An alternative reconstructive paradigm is represented by the reconstructive elevator, directly selecting the most appropriate surgical procedure, taking into consideration particular patient characteristics in order to obtain optimal form and function [42, 44].

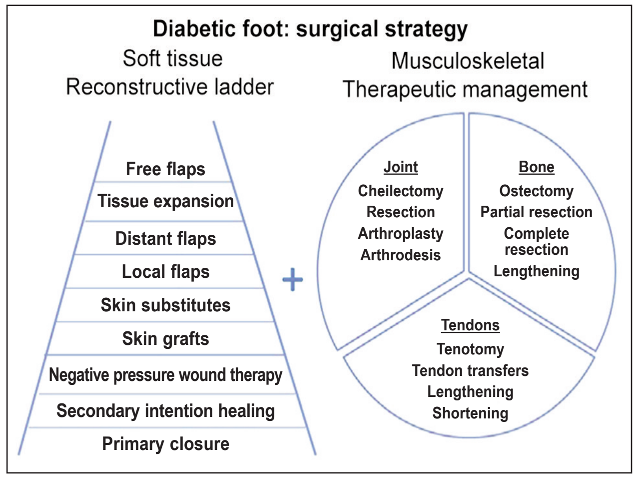

Fig. 2. Surgical strategy for diabetic foot

A sequential approach is usually employed to restore foot architecture through musculoskeletal interventions. The main therapeutic goal is to obtain the diabetic patient satisfactory ambulating status, having in mind an individualized approach for each patient. For long term immobilized patients, without gait rehabilitation potential, amputation should be considered, to avoid long hospitalization and morbidity [41, 45]. In selected active patients, adequate quality of life may be restored with a leg amputation rather than having a sequel limb. On the other hand, in patients with severe systemic status and multiple comorbidities, unable to ambulate with a prosthetic device, limb salvage is indicated, ensuring a better quality of life than amputation [45]. Amputation indication should be thoroughly assessed, given that it was observed that major amputations are associated with a higher mortality rate [45, 46].

Conceptually surgical interventions can be classified as elective, preventive, curative and emergent nonvascular foot surgery, all aiming at correcting abnormalities that may increase plantar pressure [47, 48]. Each class of foot surgery is distinguished not only by its wound status but also by its risk of subsequent amputation [48]. Elective surgery (Class I) refers to reconstructive procedures used to address deformities or excessive plantar pressures in people without neuropathy or a history of ulceration. In the absence of open wounds, prophylactic (Class II) operations are performed in neuropathic patients to limit the risk of ulcers or repeated ulceration. When open wounds are present, Curative surgery (Class III) is frequently used for regions with chronically elevated peak pressure, or as an alternative to partial foot amputation by performing joint resection, eliminating underlying bone prominences (surgical decompression), osteomyelitis and draining underlying abscesses. To limit

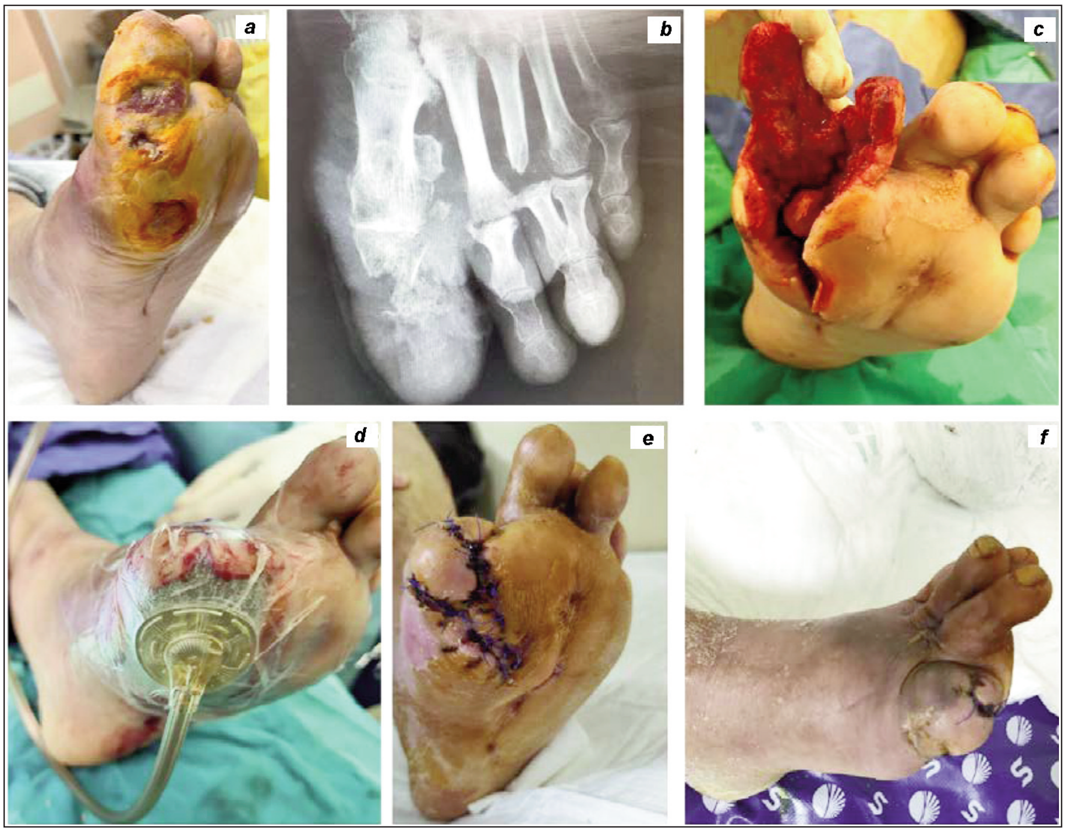

Fig. 3. Photography of: *a* – clinical aspect of extensive osteomyelitis of left hallux in a type II diabetes patient; *b* – radiologic aspect revealing bone lysis; *c* – aspect after surgical debridement imposing left halluces amputation; *d* – negative pressure wound therapy was further used; *e* and *f* – foot aspect after secondary closure when the wound was stabilized and the infectious process was eradicated

the course of infection, emergent interventions (Class IV) are done for severe or ascending infections (wet gangrene, necrotizing fasciitis, etc) [7, 47–50]. As the name implies, the latter of the aforementioned procedures are performed in an emergency setting and typically consist of open amputations at the foot level with additional fasciotomies [51]. Figure 3 presents the case of a patient needing emergency treatment, with amputation necessity for the first ray of left foot and subsequent surgical treatment.

CONCLUSIONS

Therapeutic management of diabetic foot ulcers implies a systematic, multidisciplinary approach in order to reduce severe complication, avoid lower limb amputation and decrease overall morbidity and mortality rates. The current strategy able to provide optimal results includes adequate preventive measures (patient education, strict control of blood glucose levels, self-care of the foot) and prompt initiation of specific treatment including wound correct debridement, offloading, topical use of advanced dressings, negative pressure wound therapy and surgical treatment which ranges from minor interventions for foot ulcers, to extensive reconstructive procedures for vascular restoration, bone deformities and soft tissues related anomalies.

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Authors:

ANDREEA GROSU-BULARDA[1], RĂZVAN NICOLAE TEODOREANU[1,2], CARMEN MIHAI[3],
FLAVIA FRANCESCA LIȚĂ[1], FLORIN-VLAD HODEA[1], IOAN LASCĂR[1,2], ALEXANDRU CHIOTOROIU[2,4]

[1]Clinic of Plastic Surgery, Aesthetic and Reconstructive Microsurgery,
Clinical Emergency Hospital Bucharest, Romania

[2]UMF Carol Davila Bucharest, Romania

[3]National Research Development Institute for Textiles and Leather, Bucharest, Romania

[4]General Surgery Clinic, Clinical Emergency Hospital Bucharest, Romania

Corresponding author:

RĂZVAN NICOLAE TEODOREANU, MD, PHD
e-mail: rteodoreanu@yahoo.com