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Factors involved in burn wound healing – short review

Tiberiu Paul NEAGU[1], Mirela TIGLIS[2], Ileana PERIDE[3], Ioan LASCAR[1]

[1]Department of Plastic Surgery and Reconstructive Microsurgery, "Carol Davila" University of Medicine and Pharmacy Bucharest, Romania
[2]Department of Anesthesia and Intensive Care, Emergency Clinical Hospital of Bucharest, Romania
[3]Department of Nephrology, "Carol Davila" University of Medicine and Pharmacy Bucharest, Romania

ABSTRACT

Burns represent one of the worldwide leading causes of injury. Burn wounds are associated with increased mortality and morbidity, especially the impaired quality of life due to hypertrophic scarring, scar pain and itching, paresthesia, and contractures. To properly influence the burn wound healing, it is important to establish a correct classification of the acute injury and to understand the main phase of burn wound healing process. There are various local and systemic factors that can be influenced to obtain proper healing. The most important factors include local necrosis and infection, increased local pressure and edema, anemia, hypoxia, hypotension, the presence of important chronic disease and medication, immunosuppression, nutritional status, age, and body constitution. After adequate fluid resuscitation and patient stabilization, the main step is represented by the detachment of the devitalized tissues and rapid coverage of the lesion. There are various methods to be used, like autologous or allogenic skin grafting, the use of skin substitutes, or tissue bioengineering. Knowing all these aspects, allows clinicians to properly define a therapeutic management for patients presenting severe burns.

Keywords: burn, wound healing, delayed healing, dressing, skin grafting

INTRODUCTION

Worldwide reports show that burns are one of the fourth leading types of injury, along with car accidents, falls, and physical aggression / violence [1]. A burn injury can mainly be caused by fire, heat, hot liquids, electricity, friction, or chemical solutions [2]. It is responsible for increased mortality and morbidity among hospitalized patients [3]. After the acute phase, the patient's quality of life is influenced by the scar marks, the scar pain and pruritus, the hypertrophic scarring, paresthesia symptoms, contractures development, and the need for reconstructive surgery [4,5].

Proper diagnosis of the burn lesion is the most important factor, in determining the correct treatment. Starting from this, wound classification establishes the diagnosis. Therefore, burn wounds are classified as follows [1,2]:

- first-degree burns (superficial thickness) – involvement of the epidermis;
- second-degree burns (partial or intermediate thickness) – involvement of the epidermis and dermis, associated with blister formation;
- third-degree burns (full-thickness) – may involve not only all skin layers but also the adjacent muscles and bones.

To properly understand which factors and how the burn wound healing can be influenced, in addition to the burn wound classification, it is necessary to have a global view of the phase of burn care, from the appear-

Corresponding authors:
Mirela Tiglis
E-mail: mirelatiglis@gmail.com

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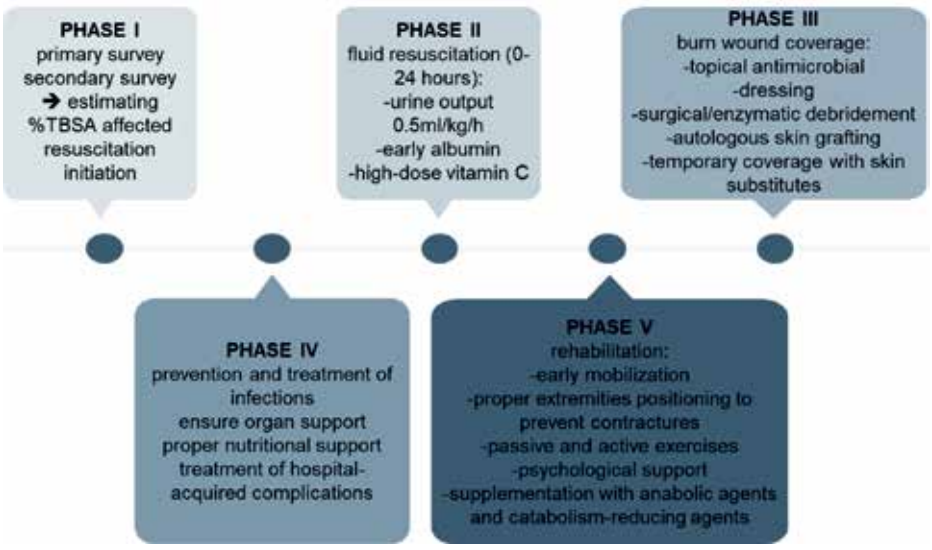

FIGURE 1. *Burn care main phases*
*TBSA = total body surface area (*adapted after Jeschke MG, van Baar ME, Choudhry MA, Chung KK, Gibran NS, Logsetty S. Burn injury. Nat Rev Dis Primers. 2020 Feb 13;6(1):11)*

ance of the acute injury to the rehabilitation stage, as shown in Figure 1 [2,6-8].

Burn wound healing involves four different stages: hemostasis (vascular constriction, clot formation with subsequent bleeding control of the injury site), inflammation (local neutrophil and lymphocyte infiltration, monocyte differentiation to macrophages, secretion of tissue growth factors), proliferation (fibroblast migration, collagen synthesis, angiogenesis, re-epithelization), and remodelling (synthesis of extracellular matrix, collagen remodelling, vascular maturation, scar tissue formation, wound contracture) [2,9,10].

FACTORS INFLUENCING BURN WOUND HEALING

The primary goal after fluid resuscitation and proper supportive care is wound coverage, to prevent burn lesion sepsis. The actual standard of care involves early surgical excision or enzymatic debridement, in the first 48-72 hours after patients' stabilization, and rapid coverage, to reduce the inflammatory mediators' release, reduce blood loss, and therefore decrease the mortality and morbidity rates [11-13]. Burns usually lead to prolonged healing time, especially second- and third-degree lesions, with a greater risk of microbial infections and increased morbidity (risk of amputation, hypertrophic scars, chronic pain, impaired quality of life) [14, 15].

The main methods of burn wound coverage are:

- various dressings: topical antibiotic ointment (bacitracin, polymyxin, mycostatin), silver sulfadiazine ointment, liquid solutions (sulfamylon, silver nitrate, acetic acid) [16-18];
- biosynthetic wound dressing: hydrocolloid dressing, polyurethane film dressing, hydrogel dressing, silicon-coated nylon dressing [18-20];
- vacuum therapy (negative pressure wound therapy and vacuum-assisted closure): stimulates the proliferation process and accelerates wound healing, increased the local blood flow, and promotes angiogenesis [21,22];

TABLE 1. *Local and systemic factors which influence burn wound healing*

necrosis	devitalized tissues delay wound healing – should be removed
desiccation	epithelization is faster if the local environment is moist and hydrated
maceration	a rapid removal of urine or fecals (proper hygiene) keep skin integrity
infection	invasion into deeper tissues, destruction of granulation tissues – proper topical and systemic antibiotic should be used
trauma/edema	the local blood supply is affected + limitation of the local nutrients exchange + obstruction of the venous and lymphatic return, and the healing cannot begin
local pressure	the blood supply (capillary) is disrupted – delayed healing
anemia	a low hemoglobin level decrease oxygen-carrying capacity
hypotension	low tissular perfusion pressure – delayed healing
ischemia	malnourishment of the adjacent tissues, cell death – impairs and delays wound healing

TABLE 2. *Patient's related factors which influence burn wound healing*

age	in older patients (compromised immune system, ineffective inflammatory response, hormonal imbalances, low cellular turnover, poor nutritional status, and hydration) the healing process is slower – prolonged hospitalization
gender	higher mortality in women (different hormonal and inflammatory responses in men and women)
body type	obese patients (poor blood supply in the adipose tissue, protein malnutrition) have a delayed wound healing
stress	reduced levels of pro-inflammatory cytokine, hormonal imbalances – delayed wound healing
nutritional status	albumin, prealbumin, transferrin, lymphocyte – markers of malnutrition – monitored regularly
chronic diseases	various chronic diseases delay the healing process: coronary artery disease, diabetes mellitus, cancer, peripheral vascular disease, chronic obstructive pulmonary disease, chronic kidney disease, cirrhosis
chronic medication	glucocorticoids and non-steroidal anti-inflammatory drugs – decrease collagen production, suppress the immune system aspirin inhibit platelet action and cell destruction
immunosuppression	due to medication or cancer – impaired wound healing
radiation therapy	through skin ulcers and hypertrophy impairs the healing
vascular insufficiency	chronic wounds and ulcers decrease the local blood supply and tissues integrity
smoking	vasoconstriction + hypoxia – delays wound healing
alcoholism	reduced resistance to infections – delayed wound healing

- autologous skin grafting: sheet split thickness / meshed split-thickness / full-thickness sheet [9,23];
- allogenic skin grafting: human cadaver and pig skin, fish skin, artificial skin grafts (tissue engineering through 3D-bioprinting and electrospinning) mycelia (the vegetative part of fungi) [24-26];
- stem cells: bone marrow-derived mesenchymal stem cells (ability to differentiate to skin fibroblasts), adipose tissue-derived mesenchymal stem cells (can differentiate to fibroblasts, favours regeneration of the damaged tissues) [27,28].

Burn wound healing is influenced by local factors, in relation to the lesions, systemic factors because of the general impact of the burn trauma, or factors related to the patient clinical status and associated comorbidities [1,9,10,22,29-32]. All these factors are presented, and their effects are explained in Table 1 and Table 2.

CONCLUSION

Burn wound management remains a complex problem, requiring periodic and judicious assessment, along with optimum intensive care measures. The key point to successfully managing the burn wound is to establish a proper diagnosis of the acute lesion. There are various local, systemic, and patient-related factors influencing the tissue healing process which must be known, to be sanctioned in time.

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