How Can Refractory Ulcers be Treated with Surgery?: The Role of Wound Surgeons in Debridement

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ABSTRACT

Foot ulcers due to diabetes or/and arteriosclerosis obliterans frequently result in an intractable condition which is refractory to treatment. In order to overcome such a condition, establishing a treatment modality based on the tissue, infection/inflammation, moisture balance, and edge of wound (TIME) concept to clinically perform wound bed preparation (WBP), as advocated by Schulz, is important. Therefore, the following steps are essential: 1) control and treat the disease-causing chronic wounds and 2) evaluate the wounds as per the TIME concept and perform local treatment at the proper timing. The core of this treatment concept is considered to be debridement. Debridement is a procedure carried out to protect the surrounding tissue by cleaning the wound of infectious and necrotic tissues, and this is crucial for chronic foot diseases. Our current strategy consists of two steps: initial medical treatment and subsequent aggressive treatment of the lesion. Our method of performing maintenance debridement, using trafermin spray and aggressive conservative therapy using NPWT, makes TIME-based wound bed preparation possible. Proper debridement at the proper time contributes to the success of this treatment. In this paper, we report the essential factors for debridement and our methods of debridement.

Key words: debridement, NPWT, TIME concept, trafermin, wound bed preparation

Introduction

Chronic wounds are wounds that do not proceed to the healing process for some reason, and foot ulcers related to diabetes and peripheral arterial disease (PAD) are known to be difficult to cure and may lead to amputation. However, from recent opinions of patients and informed consent-based treatment planning, it is obvious that patients hope to save their limbs1-4. Patients with chronic ulcers are usually in critical condition, and they possibly cannot endure limb salvage operations. Thus, the establishment of a treatment based on the tissue, infection/inflammation, moisture balance, and edge of wound (TIME) concept5 for clinical wound bed preparation (WBP)6, as advocated by Schulz, becomes essential for those patients. However, the TIME concept must always be part of a patient’s systemic evaluation7. Therefore, we have concluded that the following steps are essential: 1) controlling and treating the disease-causing chronic wounds and 2) evaluating the wounds as per the TIME concept and performing local treatment at the proper timing. The core of this treatment concept is debridement. Debridement is a procedure carried out to protect the surrounding tissue by cleaning the infectious and necrotic tissues in the wound, and it is crucial for chronic foot diseases.

TIME concept

For the purpose of transforming the chronic wounds to treatment-reactive wounds, Schultz advocated the concept of WBP. He defined WBP as the treatment for promoting the healing power of the organism itself and promoting the efficacy of other healing factors. The TIME acronym (tissue, infection/inflammation, moisture balance, and edge of wound) was developed to provide a framework for a structured approach to WBP in the clinical field8. Following these four points, observation/evaluation/treatment of chronic wounds is performed. 1) The tissue refers to inert tissue or exogenous...
material on the surface of the wound, 2) infection/inflammation refers to the cause of the wound and evaluation of the necessity of antibiotics or local sanitation for infection control, 3) moisture balance refers to the evaluation of cause and control of wound exudate, and 4) edge of wound refers to the evaluation of the condition of wound edge epithelization or the formation of dermal pockets. It has been 10 years since this TIME concept has been advocated, and the science of wound healing, especially in molecular biology, has been advancing during this time. In particular, 1) understanding of biofilms in chronic wounds, 2) negative-pressure wound therapy (NPWT), 3) advancement of local antibiotics, and 4) understanding of the role of inflammatory markers and protease in chronic wounds and molecular biology of wounds are evident. Due to this progress, the TIME concept became the guiding principle for more effective evaluation/treatment/control of chronic wounds.

**Chronic wounds and infection**

For initiating wound healing, it is important to understand the difference between acute wounds and chronic wounds. In acute wounds, unless there is surgical site infection (SSI), the wound will not be exposed to bacteria and will be healed; thus, prevention of infection becomes vital.

On the other hand, in a chronic wound, there is continuous formation of bacterial colonies on its surface, so infection control is crucial. Therefore, it is necessary to know the mechanism of infection and biofilm formation. Generally, an infection occurs when the bacterial population is $1.0 \times 10^7$ colony-forming units per gram (CFU/g), but realistically, this does not happen in the clinical situation. When there is a hematoma in the wound, necrotic tissue, or exogenous materials, even 200 CFU/g can lead to wound infection, and most infections have this pattern. Therefore, the most important step is to eliminate infective factors from the surface of the wound to prevent infection. Thus, debridement and drainage are the most vital steps in preventing wound infection. A biofilm is a complex microbial community, consisting of bacteria embedded in a protective matrix of sugars and proteins (glycocalyx). They are contributing factors for continuous chronic inflammatory changes in the wound surface, and there are biofilm bacteria in almost all chronic wounds. The problem with these biofilms is that they induce chronic inflammatory reaction, so reducing biofilm formation and preventing its restructuring are important processes. Thus, debridement is an essential treatment, and various methods of debridement have been established. It is said that biofilm bacteria recover to their original level 3 days after debridement, so repeated debridement (maintenance debridement) is necessary. We perform maintenance debridement for all chronic wound cases to eliminate biofilms, prevent recurrence, and induce acute healing of the wound.

**Debridement methods**

The following methods of debridement are popular: 1) autolytic, 2) enzymatic, 3) mechanical, 4) chemical, 5) biological (maggot therapy), and 6) sharp/surgical.

There are advantages and disadvantages for each method, and it is important to properly combine or separately use them for each situation. Recently, it has been found that NPWT can soften the necrotic tissues to enable sharp debridement. When NPWT and other methods of debridement are combined, the elimination of infected materials and exudates can be expedited, leading to granulation and epithelization. This combination supports the TIME concept. We often perform sharp/surgical debridement, and one of the methods we pay attention to is maggot therapy. Maggot debridement therapy (MDT) is performed to treat intractable wounds by using the larvae of certain flies to selectively intake necrotic tissues. There have been records of doctors using larvae to treat wounds thousands of years ago in Aborigine and Myanmar, and maggot therapy has been around for ages. Moreover, through experiences during the war, it was found that wounds treated with maggots tended to heal fast. In 1928, John Hopkins University proved this therapy to be effective using clinical evidence. Specifically, maggots selectively dissolve and intake necrotic tissues and do not damage the surrounding normal tissues, so the vascularity of the surrounding area is unharmed. Normally, revascularization is said to be necessary before debridement if the ulcer is under SPP 35 mmHg because debridement may cause ischemia of the surrounding tissues by destroying the balance. However, maggot therapy can be applied to ischemic cases. This concept applies to surgical debridement as well, and proper debridement that does not affect the vascularity of the tissues is necessary.

The debridement methods we usually perform are as follows:

1) Frequent debridement by the bed side (maintenance debridement)
2) No over-debridement during treatment
3) No debridement of the normal tissues
4) Prevent damage to vascularity by debridement
5) Keep the debridement to a low bleeding level (no hemorrhage)
6) Proceed under periosteum when resection of necrotic bones is necessary
7) Observe the wound every day and create a wound environment in which proper procedures can be performed for each wound condition
8) Preserve as much skin tissues as possible
Strategies used at our institution

In our strategies, after performing diabetic control, vasodilation/PTA, LDL apheresis, and bone marrow or peripheral blood mononuclear cell transplantation, we proceed to local active treatment of the wound. To shorten the healing time, we actively perform surgical debridement instead of chemical debridement using ointments and begin treatment based on cleansing. Surgical debridement is frequently performed at the bedside (maintenance debridement). Lastly, we eliminate biofilms and necrotic tissues completely, but we try to avoid over-debridement during each procedure. When necrotic tissues diminish and granulation appears, trafermin (bFGF) spray (Fiblast®, Kaken, Japan) is used. The surface of the ulcer covered by necrotic tissues is like the area damaged from radiation, and when granulation becomes visible on the surface, this indicates the wound is ready to react to the treatment. We call this wound condition mixed with whitish necrotic tissues and granulation “Strawberry milk sign” (Fig. 1), and it is an important timing in our treatment. Trafermin is a pharmaceutical product containing a genetic recombinant factor that induces benign granulation by angiogenesis and fibroblast growth, and it is best used in this “Strawberry milk sign” stage. After the disappearance of necrotic tissues, NPWT is carried out. We call this condition with almost no necrotic tissues and good granulation “Strawberry sherbet sign” (Fig. 2). NPWT was established as a treatment for intractable ulcer with exposure of bones due to trauma or infectious pressure ulcer. NPWT removes excessive edema fluid with increase in afterload on capillary vessels and veins, which promotes wound healing. It also allows movement and growth of tissue surrounding the wound in response to the mechanical force of suction pressure. These mechanisms of NPWT make it an ideal treatment for ischemia-based ulcers such as diabetic/PA-D foot ulcers. By the time NPWT is used, the wound can be said to heal within approximately 1 month. As mentioned before, preservation of as much skin as possible plays an important role at this time in the treatment process.

Our method of performing maintenance debridement, using trafermin spray, aggressive conservative therapy, and NPWT makes TIME-based WBP possible. Proper debridement at the proper timing contributes to the success of this treatment. Therefore, it is important to observe the wound carefully by developing the ability to judge the conditions of the wound and by attaining proper debridement skills.

Case report (Fig. 3)

Patient: 51-year-old male.

The patient underwent peripheral blood mononuclear cell transplantation twice at our institution a few years ago due to Buerger disease on his right leg. He visited us for an ulcer on his left first and fifth toes with progressive ischemia this time. Our institution was not able to perform peripheral stem cell transplantation at that time, but because his wound was in a bad condition, he was not able to undergo transplantation at other institutions. Thus, he was admitted to our hospital for

![Fig. 1. Strawberry milk sign.](image-url)

Wound condition showing a mix of whitish necrotic tissues and granulation is known as “Strawberry milk sign.”
Fig. 2. Strawberry sherbet sign.
Wound condition with almost no necrotic tissues and good granulation is known as “Strawberry sherbet sign.”

Fig. 3. Clinical course of case 1.
Proper debridement at the proper time contributed to the success of this treatment.
local active treatment of the wound. Under the strict control of diabetes, PGE1 injection and LDL apheresis were carried out for Buerger disease. Ulcer with bone exposure was apparent in the left MP junctions of his first and fifth toes. There was an infection with necrotic tissues attached to the surface of the ulcer with poor vascularity. The pain in his foot was extreme with difficulty in measuring SPP, and he was on narcotic drugs. Femoral/sciatic nerve block was also used during the treatment due to ischemic pain. The TIME evaluation was as follows: T – slough, necrotic tissues, and biofilms present, I – inflammation leading to infection, M – exudate was well balanced, E – dermal pocket was present with chronic condition in the wound borders. Thus, closure of the wound seemed impossible. Therefore, debridement of necrotic tissues to alleviate infection was necessary. Maintenance debridement, where frequent debridement does not affect vascularity, was performed. Cleansing and wet-to-dry dressing was performed to purify the wound. When the strawberry milk sign become apparent, trafermin spray was used with continuous maintenance debridement. With the appearance of the strawberry sherbet sign, we began NPWT. The dressing change with NPWT was done once a week, and maintenance debridement with trafermin spray was performed during the change. We were able to attain good WBP with granulation treatment, where frequent debridement does not affect vascularity, was performed. Cleansing and wet-to-dry dressing was performed to purify the wound. When the strawberry milk sign become apparent, trafermin spray was used with continuous maintenance debridement. With the appearance of the strawberry sherbet sign, we began NPWT. The dressing change with NPWT was done once a week, and maintenance debridement with trafermin spray was performed during the change. We were able to attain good WBP with granulation

**Conflict of interest**

All authors declare no conflicts of interest.

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The study sponsors had no involvement.

**Ethical approval**

We made an effort to preserve patient’s privacy in our figures. Additionally, we obtained informed consent from the patient. The patient read and agreed with the submitted version of the paper.

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