

# Wound bed preparation of difficult wounds: an evolution of the principles of TIME

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## ABSTRACT

In the last few years, considerable progress has been made in the treatment of chronic ulcers, thanks to new therapy methods. Wound bed preparation is a modern approach for the removal of local barriers to healing by optimising debridement, reduction of bioburden and exudate management through the TIME principles, which have been introduced by the International Advisory Board on Wound Bed Preparation. However, this protocol does not evaluate the state of the repair process and therefore does not suggest the ideal therapeutic choice for each single patient. The revised TIME-H concept considers also the supposed healing time, H, and gives a score that correlates the wound condition with the incidental concomitance with medical pathologies related to the therapeutic measures, thus guiding the clinician towards a practical and systematic approach in the treatment. By applying this scheme to our situation, the average healing time was considerably reduced. The formulation of the new protocol TIME-H for a critical assessment of treatment scheme, which also includes the general conditions of the patient, represents a more rational and adequate approach for an accurate prognosis and therefore for a more suitable therapeutic choice in the treatment of difficult wounds.

**Key words:** Difficult wounds • TIME • TIME-H • Wound bed preparation

## INTRODUCTION

Patients with chronic ulcers demand a treatment that is burdensome in socioeconomic terms due to the costs related to hospitalisation, medications and surgical operations, prosthesis aids and rehabilitation, nursing time and loss of working days both for patients and their relatives.

In Western Europe, about 6 million people suffer from difficult wounds or ulcers, with an average cost of \$1000 per patient. In Italy, about 800 000 people each year present with this condition, but this number is constantly rising due to the life span prolongation; the management of these patients absorbs 60% of

the activity of the trained nurses working in the districts.

Consequently, in the last few years, we have been interested in evaluating strategies in order to accelerate healing and recovery. Thanks to new therapy methods aiming at creating ideal conditions for the formation of granulation and epithelial tissue, considerable progress has been made.

## Wound bed preparation

Wound bed preparation (WBP) is a modern therapy strategy for management of cutaneous ulcers based on an interdisciplinary, overall and dynamic analysis of the problem 'wound', which allows the definition of a protocol for adequate therapy and follow up (1).

The concept of WBP neither strictly represents the healing of the ulcer nor implies the mere removal of necrotic tissue, but it rather defines a therapeutic course combining different elements of the clinical practice in wound care by considering the management of exudates and

## Key Points

- the concept of wound bed preparation defines a therapeutic course combining different elements of the clinical practice in wound care by considering the management of exudates and reduction of bioburden as essential steps for the removal of local barriers to healing

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### Key Points

- the acronym TIME was introduced as a systemic approach aiming at properly organizing the principles of WBP in order to identify the necessary elements for and optimal WBP
- the possible developments that TIME may experience in the next years lie in some key points, including precise evaluation of the pathology, correct control timing, use of a protocol as personal as possible and treatment of correlated systemic pathologies

reduction of bioburden as essential steps for the removal of local barriers to healing.

This new approach originates from the identification of the pathological and physiological abnormalities of chronic ulcers that impede and delay healing, as well as the ways to correct them. In fact, the harmful effects of an excessive quantity of exudates are well known at present: it destroys the extracellular matrix and ruins the effectiveness of new therapeutic measures such as the use of growth factors and engineered tissues. Moreover, the importance of the adjustment of the biological microenvironment of the wound has been demonstrated, that is the existence of a cellular load characterised by phenotypically abnormal cell populations and altered elements of the matrix that must be removed or 'corrected'. Last, the value of an efficient and extended phase of debridement, as well as the use of antibiotics in order to accelerate the healing of chronic cutaneous wounds, is unquestionable.

In summary, the therapy for chronic cutaneous wounds through the concepts of WBP is defined as 'the overall coordinated management of a wound in order to accelerate the endogenous healing or facilitate the effectiveness of other therapeutic measures' (2).

### The TIME concepts

In order to apply this idea into clinic practice effectively, the acronym TIME was introduced by the International Advisory Board on Wound Bed Preparation (3) and presented as a systematic approach aiming at properly organising the principles of WBP in order to identify the necessary elements for an optimal WBP, such as necrotic bioburden treatment, inflammation and infection control, humidity balance and stimulation of the epithelial wound edges.

TIME scheme wants to correlate the pathogenetic abnormalities in difficult-to-heal wounds through the use of modern therapies and procedures, as summarised in Table 1.

According to Falanga (1), tissue-repair key steps schematised in TIME represent the

starting point for a proper interpretation of the WBP concept: they outline a dynamic, non linear structure that, by assessing different types of chronic ulcers, enables to determine the evolution towards healing.

This matrix reported in Table 1 was received and further developed by the European Wound Management Association in order to spread the use and to increase its value.

### Aim of the study

TIME is a useful approach as a generic protocol in difficult wound treatment, but it does not define a prognosis and, consequently, a therapy for every single patient, who often presents with concomitant pathologies or pathologies responsible for the ulcer.

In short, it cannot anticipate the wound healing time, H (healing), and it does not show a protocol that can be personalised according to any clinical variation the cutaneous ulcer may present.

While treating chronic cutaneous ulcers, it is important to consider the rate of the wound healing process and to identify, possibly within the fourth week of a standard treatment, whether the ulcer is not responding to treatment in order to provide the patient with the greatest benefit from alternative therapeutic strategies. Therefore, important questions arise, such as how is it possible to determine the prognosis of a difficult wound? How is it possible to predict and accelerate wound healing time? Which protocol clinicians should refer to for the standardisation of therapies, and then suggest also to general practitioners and nurses?

The answer to these questions represents one of the possible developments that TIME may experience in the next years, and it lies in some key points, including precise evaluation of the pathology, correct control timing, use of a protocol as personal as possible and treatment of correlated systemic pathologies.

## MATERIALS AND METHODS

### Revised TIME-H protocol

The principles of TIME-H have been formulated to remind the most important aspects of chronic wounds and to lead the clinician towards a practical and systematic treatment approach, giving a score that allows to connect the seriousness of the wound condition and the

**Table 1** TIME: the principles of wound bed preparation (3)

T	Non vital or insufficient tissue
I	Infection or inflammation
M	Maceration or dryness: fluid imbalance
E	Epidermis: non proliferating or undermined borders

incidental concomitance with medical pathologies correlated to the therapeutic measures necessary to reach the expected clinical results.

### Local conditions

A difficult and non healing wound can be identified either in a very early phase or in case healing does not occur within 60 days of treatment; if the lesion does not heal within this time frame, it is nosologically considered as a cutaneous ulcer classifiable according to its stage and different assessing scales.

The real size of the wound is an objective parameter, and although other factors difficult to identify may exist, there are variables that can be quantitatively and qualitatively evaluated, such as the wound colour and size (4).

It is important for the clinician to dispose of wound classification systems able to guide him/her in the therapeutic approach, both in the starting phases and in the ongoing evaluation of the effectiveness of the treatment (5).

The measurement of the wound-area changes enables the clinician to make more rational decision on any appropriate interventions the treatment regime may require; therefore, it is essential to adopt a wound assessment that it is precise, quick, simple, accurate and objective (6,7).

In the last few years, a lot of evaluation methods have been developed (8,9), as we can see in Tables 2 and 3, but only through the development of systems and techniques that provide a clear and continuous suggestion of the evolution of the parameters, it has been possible to monitor the healing process (10,11).

Falanga (1) developed a classification where two indications, referred to the appearance of the wound and the quantity of the exudate, are combined (Table 4). According to that scheme, a score to the wound appearance is given depending on the granulation tissue extension, fibrinous state and eschar presence (range from A to D), and the score to the state of the exudate is based on its amount and the

**Table 2** Classification of the wound according to National Pressure Ulcer Advisory Board (8)

Stage I	Erythema and oedema
Stage II	Deep cutis with or without derma involvement
Stage III	Subcutis destruction, not extending beyond the fascia
Stage IV	Deep necrosis

**Table 3** The Sessing scale (9)

0	Normal cutis, but at risk
1	Integral cutis, but hyperpigmented
2	Subcutis destruction not extending beyond the fascia
3	Ulcer basis and border with granulation, modest exudates and smell
4	Modest granulation tissue, initial and modest necrotic tissue, exudates and moderate smell
5	Presence of abundant exudates, evil-smelling, eschar; reddened border and ischaemia
6	Further ulceration around primary ulcer, purulent exudates, intense smell, necrotic issue, sepsis

frequency of dressing changes (range from 0 to 3): the wound stage comes from the combination of the letter and the number.

Some preliminary data would suggest that the system is valid for prediction as to the potentiality of wound healing, even though some clinical questions (e.g. if score A2 is better than B1 for prognosis and vice versa) need further investigation and analysis (12).

In order to introduce an assessing instrument that goes beyond the limitations of the current systems of classification and in order to make it corresponding to the clinicians' operative needs, we have experimented a simple mnemonic grid (similar to the one for the staging of neoplasias – TNM) that enables us to codify and measure a wound on the basis of some objective parameters (minimum score: 0, maximum score: 3 as exemplified in Table 5), proving a useful aid for the evaluation of a chronic ulcer.

In the scheme of Table 5, the parameters used can assume the values included in the intervals of variability reported in Table 6.

Letter 'E' in TIME represents the key to healing and will be regarded as the parameter whose variations, in relation to the recovery of the epithelial integrity and of the cutaneous integrity functionality compared with the previous data obtained from the weekly controls, will make it possible to establish whether the ulcer is going to heal (it is known that, for venous and diabetic lesions, an advancement of the epithelial margins >0.7 cm per week is a predictor of wound healing).

It is very difficult to typify the appearance of the margins (epidermis repair) of a chronic wound whose assessment allows to point out a progression in the healing (no surprise if

### Key Points

- the principles of TIME-H have been formulated to remind the most important aspects of chronic wounds and to lead the clinician towards a practical and systematic treatment approach, giving a score that allows to connect the seriousness of the wound condition and the incidental concomitance with medical pathologies correlated to the therapeutic measures necessary to reach the expected clinical results
- a difficult and non healing wound can be identified either in a very early phase or in case healing does not occur within 60 days of treatment

**Key Points**

- clear evidence shows that the calculation of the reduction of the wound size over time is a valid prognostic sign
- H healing time must not be more than 2 months and it is necessary to think critically on the reason of the failure

**Table 4** System of classification for wound diagnosis and ongoing evaluation and healing power (1)

Wound appearance				
Score	Tissue			State of exudate in the wound
	Granulation	Fibrinous state	Eschar	
A	100%	–	–	1. Under total control; no or little quantity; no need of absorbing dressing; if admitted, dressing changes once a week
B	50–100%	+	–	2. Under partial control; moderate quantity; dressing two or three times a week
C	<50%	+	–	3. No control; heavily exuding wound; dressing once or more a day
D	Any quantity	+	+	

**Table 5** Classification of difficult wounds according to the seriousness of the wound

Score	0	1	2	3
T	0%	<30%	<60%	<90%
I	Absent	Contamination	Colonization	Infection
M	Absent	Little exudate	Much exudate	Evil-smelling exudate
E	0	>30%	>60%	>90%

the assessment of a wound progression is based only on a subjective evaluation, such as 'it seems to go better'); as a matter of fact, this evaluation influences the therapeutic decisions.

Clear evidence shows that the calculation of the reduction of the wound size over time is a valid prognostic sign. The graph obtained from these measurements allows to determine a 'healing curve' that represents an important prognostic healing indicator; in the last few years, some interesting data have raised from the prediction of the wound healing, thanks to the data collected during the first 4 weeks of healing.

In fact, if after the application of the principles of TIME-H, the factors above listed prevail, and if at least one of the first four parameters has not changed positively, a critic reassessing of the treatment plan is important, and some advanced therapies might be necessary at cellular level to restore the epithelium reconstruction/repair.

**Table 6** Parameters of the intervals of variability

T =	0	>90%
I =	Absent	Infection
M =	Absent	Evil-smelling exudate
E =	Absent	>90%

H, healing time, must not be more than 2 months; in fact, if H is >60 days, TIME-H has not reached its aim. It is necessary to think critically on the reason of the failure: the causes could represent answers to the following questions that must be asked in case of this eventuality.

T: presence of necrotic tissue?

I: presence of inflammation/infection?

M: presence of maceration?

E: no presence of epidermis construction?

H: healing has not been achieved.

In its turn, such a therapeutic failure might depend on various factors, such as wrong timing >1–2 weeks for clinic control, inaccuracy of assessing criteria (too generic?), incorrect therapeutic line (according to a generic and not personalised assessing logic of the different possible treatments), poor and inaccurate transmission of clinical communications among health operators and poor pursuit of H, healing time.

H prolongation determines super infection, more pain, general and progressive functional deficit, psychodepressive state, worse standard of life and higher social cost.

To shorten healing and hospitalisation time and therefore to accelerate healing as much as possible, we must consider the classification

according to TIME-H and the application of personalised therapeutic protocol.

### General conditions

The modification to Falanga's protocol we suggest assesses healing time once a week and makes a further update in the score possible, if complications and correlated pathologies coexist.

Global assessment of general conditions of a patient suffering from chronic cutaneous ulcers should include an accurate anamnesis (important systemic diseases), including nutritional conditions, self-sufficiency conditions, motility conditions, presence of pain, presence of temperature, psychic conditions and logistic familiar conditions.

Having to assess the general conditions potentially tending to failure of a therapeutic strategy, we decided to take into account the possibility of assessing the evaluation scales in force and widely used in the clinical practice (13).

For pressure ulcers, the first and most widely used assessing scale was produced by Norton *et al.* (14), followed by other scales in the following years. Norton's assessing scale is reported in Table 7.

Instead, other authors, identifying the problem of the objectivity for the variables, immediately have defined and adopted their own scale of variables with respective scores (Norton Stotts, Norton Exton – Smith, Gosnell, Braden, Hospital of Utrecht); we report in Table 8, an overall vision of the various indicators provided by the different scales (14–22).

More precise information is necessary: any assessing scale is adopted, it will never say if the person will develop a wound in the future, but it can indicate that a person is more likely at risk for cutaneous lesions than another, so that one can use his resources in a better way (17).

Comparing the different scales, we noticed that they all take into account self-sufficiency (activity, mobility, incontinence, etc.); therefore,

it is unanimously accepted as a primary risk element for the rise of cutaneous ulcers (23). Basing on this, we have worked out a simple grid that examines mental conditions, self-sufficiency, nutrition, age and predisposing diseases. The parameter of general conditions can have a score ranging from 0 to 5, which is represented by parameter GC and can assume the values reported in Table 9.

Obviously, the protocols of treatment are approximate because a range of many clinical possibilities and therapeutic consequences exist (24–27).

The final classification of difficult wounds of TIME-H reported in Table 10 considers the score on the basis of their local appearance and the general score and besides, it contributes to determine a prognosis and a therapeutic line.

For example, a cutaneous ulcer with T0, I0, M0, E0 and GC0 could be a wound characterised by the absence of necrotic tissue (T0), absence of contamination (I0), absence of exudate (M0), granulation tissue >90% (E0) and good general conditions (GC0); an ulcer with T3, I3, M3, E3 and GC4 would be characterised by the presence of necrotic tissue >90% (T3), evident infection (shown by biopsy, I3), evil-smelling hyperexudation (M3), absent granulation tissue (E3) and poor general conditions (GC4).

Now it is possible to determine the most suitable therapeutic line to reduce H, as it can be seen in Table 11.

### Adopted therapeutic protocol

Therefore, the therapeutic protocol was studied after an accurate analysis of the pathology and of the objective possibilities of therapy, being able to use advanced combined medications, associable with Vacuum Assisted Closure (VAC) timing, debridement and surgery without neglecting the patient's general conditions.

### Case studies

At our centre for serious wound treatment of the Department of Plastic Surgery in Asti, we

### Key Points

- having to assess the general conditions potentially tending to failure of a therapeutic strategy, we decided to take into account the possibility of assessing the evaluation scaled in force and widely used in the clinical practice
- obviously, the protocols of treatment are approximate because a range of many clinical possibilities and therapeutic consequences exist
- the therapeutic protocol was studied after an accurate analysis of the pathology and of the objective possibilities of therapy, using advanced combined medications, associable with VAC timing, debridement and surgery without neglecting the patient's general conditions

**Table 7** Assessing scale according Norton *et al.* (14). Patients are at risk if total score = 14

General conditions	Mental state	Deambulation	Mobility	Incontinence
4, good	4, lucid	4, normal	4, full	4, absent
3, quite good	3, apathetic	3, limited	3, walk with help	3, limited
2, poor	2, confused	2, chair bound	2, very limited	2, usual (urine)
1, very poor	1, astonished	1, bed bound	1, immobile	1, double

**Table 8** Comparison among the indicators of different scales

Variable indexes	Norton (14)	Gosnell (15,16)	Knoll (17)	Andersen (18)	Norton plus (19)	Waterlow (20)	Braden (21,22)
General conditions	Yes		Yes	Yes	Yes	Yes	
Mental conditions	Yes	Yes	Yes	Yes	Yes		Yes
Activities	Yes	Yes	Yes		Yes		Yes
Mobility	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Incontinence	Yes	Yes	Yes	Yes	Yes	Yes	
Urinary incontinence.							
Faecal incontinence							
Temperature					Yes		
Haematocrit					Yes		
Therapy					Yes	Yes	
Nutrition		Yes	Yes			Yes	Yes
Age				Yes		Yes	
Hydration			Yes	Yes			
Cutis condition				Yes		Yes	
Diabetes					Yes		
Hypertension					Yes		
Albuminemia					Yes		
Moderate mental state					Yes		
Constitution						Yes	
Predisposing diseases			Yes				
Neurological deficit						Yes	Yes
Major operations, surgical traumas						Yes	
Sex						Yes	
Pain							
Humidity							Yes
Sliding or friction							Yes
Need to breathe							
Need to drink and eat							
Need to expel							
Need to move							
Need to sleep							
Need to dress							
Need to wash							
Need to walk							
Need to learn							

compared the results of different strategies by evaluating 52 patients suffering from ulcers of different aetiology, 36 of whom were treated

according to TIME protocol and 16 according to the revised TIME-H scheme.

## RESULTS

The result is a remarkable reduction of the average and total stay in hospital for patients

**Table 9** Assessing scale of complications or comorbidity of cutaneous ulcers

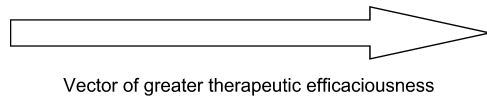
	0	1
General conditions		
Mental conditions	Good	Poor
Self-sufficiency	Good	Very poor
Nutrition	Good	Poor
Age (years)	<70	>70
Predisposing diseases	Absent	Present

**Table 10** Scale of TIME-H total scores

Pathology	Score
Certain healing wound	0–6
Uncertain healing wound	6–12
Difficult healing wound	12–18

**Table 11** Analysis of therapeutic treatments

T	Autolysis osmotic larval enzymatic	Ultrasonic mechanical debridement	Waterjet (Versajet) mechanical debridement	Surgical debridement
I	Detergents	Disinfectant solutions; advanced medications; ag	Disinfectants + systemic antibiotics + advanced medications; Ag	Mechanical or surgical debridement; VAC
M	Alginates	Hydrofibres	Polyurethane	VAC
E	Collagen; hyaluronic acid; hydrocolloid; growth factors	VAC	Artificial derma; new cultivated grafting	Skin autologous grafting



**Key Points**

- there is a remarkable reduction of the average and total stay in hospital with patients who benefitted from the approach according to the TIME-H scheme
- H was reduced which was important for many reasons, including the reduction of super infections, reduction of patient's haemodynamic and functional alterations, reduction of pain, improvement of the patient's compliance and psychic condition and reduction of socioeconomic cost of pathology
- if all the elements of TIME algorithm will be considered and properly applied, the wound healing possibilities will increase

who benefited from the approach according to the revised TIME-H scheme, as it can be seen in Table 12.

In short, H was reduced, which is important for many reasons, including the reduction of super infections, reduction of the patient's haemodynamic and functional alterations, reduction of pain, improvement of the patient's compliance and psychic condition and reduction of socioeconomic cost of the pathology.

**DISCUSSION**

**TIME versus TIME-H**

WBP and TIME must not be meant exclusively as a proposal that is an end in itself, but rather it must be placed in a global approach to the patient suffering from cutaneous wounds, an approach that takes into account also the patient's psychosocial needs and the underlying pathologies (28,29).

If the WBP represents a challenge for clinicians in effectively managing wounds, TIME-H provides a systematic approach for the achievement of this aim in order to 'help'

the wound healing by using the most suitable therapies (ultra sounds, VAC, hypercaloric diet, blood transfusions, hyperbaric therapy, laser, vascular surgical operations, surgical debridement, bioengineering and advanced and combined medications, etc.).

This enables us to more properly assess the ulcer and, as a consequence, to adopt a more accurate and systematic therapeutic strategy, which can be examined weekly and modified, if necessary, in case of any changes in the patient's pathology (30,31).

In conclusion, we believe that a more complete organisation of any clinical features of the systemic pathologies, correlated and possible, as well as a more dynamic idea of the TIME paradigm, may allow to formulate a new, more accurate and incisive protocol (TIME-H), which, considering both the clinical and the cellular components to be taken into account in wound healing, can help determine a prognosis and therefore a more correct therapeutic choice (32,33).

Last but not least, through the new paradigm of TIME-H, it is possible to codify the ulcer anatomic features correlated to incidental systematic pathologies, which can further worsen the total score.

In the light of this criterion, if all the elements of TIME algorithm will be considered and properly applied, the wound healing probabilities will increase (34,35).

Such a precise and synthetic scale can be communicated to other health professionals and staff, who will be able quickly to turn the score into symptoms, prognosis and therapeutic strategies so as to speed treatment time and increase healing possibility (36,37).

**Table 12** Case studies in 2005. Department of Plastic Surgery, C. Massaia Hospital of A.S.L. 19, Asti

Patients treated	N	Time for healing (days)	
		Minimum	Maximum
Patients according to TIME scheme	36	60	300
Patients treated according to TIME-H	16	15	90
Total of patients	52		

### Key Points

- TIME-H is suitable for a critical assessment of the treatment plan for its variability in the therapy, and it represents a more rational approach as to the methodology to the wound management that takes into account the treatment of the causes of the chronic wounds, without forgetting the patient his/her conditions and possible concomitant pathologies

Inside this multidisciplinary perspective, in the light of the most recent acquisitions, TIME-H delineates a new strategy of global and dynamic approach to the patient, essential in order to guide the clinician's therapeutic choices, to be successfully applied to particular clinical situations, to provide clinicians with confidence in using new treatments and to make a good outcome more certain, even in the case of wounds requiring intensive and specialised treatment (38,39).

To conclude, TIME-H is suitable for a critical assessment of the treatment plan and for its variability in the therapy, and it represents a more rational approach as to the methodology to the wound management that takes into account the treatment of the causes of the chronic wounds, without forgetting the patient, his/her conditions and possible concomitant pathologies.

All this could sensibly reduce healing time and cost (not only economic, but also social) of cutaneous ulcer treatment, with real advantages for the patients, thanks to the treatments currently available; this is similar to what has happened in the field of oncological surgery, where the TNM paradigm has considerably reduced the number of women who have undergone mastectomy according to Halsted, or colon-rectum resection according to Miles, thus providing not only a reduction of healing time but also a better quality of life for the patient (40,41).

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