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ORIGINAL ARTICLE

Predicting complex acute wound healing in patients from a wound expertise centre registry: a prognostic study

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Abstract

It is important for caregivers and patients to know which wounds are at risk of prolonged wound healing to enable timely communication and treatment. Available prognostic models predict wound healing in chronic ulcers, but not in acute wounds, that is, originating after trauma or surgery. We developed a model to detect which factors can predict (prolonged) healing of complex acute wounds in patients treated in a large wound expertise centre (WEC). Using Cox and linear regression analyses, we determined which patient- and wound-related characteristics best predict time to complete wound healing and derived a prediction formula to estimate how long this may take. We selected 563 patients with acute wounds, documented in the WEC registry between 2007 and 2012. Wounds had existed for a median of 19 days (range 6–46 days). The majority of these were located on the leg (52%). Five significant independent predictors of prolonged wound healing were identified: wound location on the trunk [hazard ratio (HR) 0·565, 95% confidence interval (CI) 0·405–0·788; $P = 0·001$], wound infection (HR 0·728, 95% CI 0·534–0·991; $P = 0·044$), wound size (HR 0·993, 95% CI 0·988–0·997; $P = 0·001$), wound duration (HR 0·998, 95% CI 0·996–0·999; $P = 0·005$) and patient's age (HR 1·009, 95% CI 1·001–1·018; $P = 0·020$), but not diabetes. Awareness of the five factors predicting the healing of complex acute wounds, particularly wound infection and location on the trunk, may help caregivers to predict wound healing time and to detect, refer and focus on patients who need additional attention.

Introduction

Some wounds heal quickly and uneventfully, whereas others take much longer and require more effort to heal. Wound healing may be prolonged in the presence of chronic diseases such as diabetes, arterial or venous insufficiency or pressure ulcers. Also, wounds with an acute aetiology, that is, after trauma or surgery, may be prone to delayed wound healing and may therefore need advanced professional care to achieve closure (1). Nowadays, these so-called complex acute wounds are increasingly treated by teams of specialised physicians and

Key Messages

- knowing which wounds will heal poorly helps determining the wounds that need special attention and care
- for chronic wounds several factors have been shown to predict (impaired) wound healing, but not for acute wounds, originating after trauma or surgery
- in this study, wound size, duration, infection, location on the trunk and the patient's age predicted (impaired)

healing of acute wounds treated in a wound expertise centre
- with these predicting factors the time to complete healing can be estimated, based on our prediction formula
- this may help timely detection and referral of acute wounds that need extra attention to promote wound healing

nurses, sometimes concentrated in a wound expertise centre (WEC) (2). The idea behind these WECs is that a more concerted and dedicated care would bundle available expertise and evidence as to wound care and, thus, improve quality and efficiency in the chain of clinical, outpatient and home wound care (3). Furthermore, WECs would counteract unwanted variation due to the huge number of wound products on the market and inter-professional variation among caregivers (4,5), despite available evidence regarding the treatment of a wide range of wound types (6). In the Netherlands, more than 20 WECs within and outside hospitals have now been launched, based on referral and care agreements among general practitioners, clinical specialists and wound care or home care nurses.

To appreciate which patients with wounds need advanced professional care, it would be helpful to know beforehand which wounds may heal poorly. To date, health care professionals, policymakers and researchers use prognostic models to identify variables that are influential in predicting patients at risk and for clinical decision making (7). Evidence from such prognostic models can help health care professionals to better advise their patients and to evaluate new prognostic variables in the context of existing knowledge (8).

In wound care, prognostic models have been developed to predict wound healing in chronic ulcers (9–13), but not yet for acute, complex wounds. This is desirable because acute wounds occur more frequently than chronic wounds (14). Furthermore, even though most of these acute wounds heal without difficulty, many of these wounds can be subjected to factors that impede healing, for example, due to infection, damage to the vasculature or concomitant systemic disorders. This makes it hard to apply chronic wound models to acute wounds. Hence, it is important to know the factors that may predict a compromised healing of complex wounds, such as those treated in a WEC. This predictive modelling requires a comprehensive registry, which is kept by most WECs.

Therefore, the aim of this study was to investigate which factors best predict time to wound healing, regardless of the dressing materials or treatments used, in patients with complex acute wounds treated in a WEC. This may help caregivers to better inform and treat their wound patients, and to give input for the development of better wound treatments, in particular for those who are likely to have a protracted wound healing.

Methods

We based the description of our methods and results on the Quality in Prognosis Studies (QUIPS) tool (15). Our institutional medical ethics committee waived the need for approval for this study as it had no impact on the patients and their treatment, and data collection and analysis were performed anonymously.

For the purpose of this study, we employed the registry of the Mitralis Expertise Centre for Wound care in Heerlen, the Netherlands. This is an independent, nurse-led, outpatient expertise centre run by 20 nurse practitioners and specialised wound care nurses. These nurses followed postgraduate education in wound care on bachelor or master levels. This WEC treats about 1400 patients with refractory wounds yearly, referred from regional hospitals and general practitioners.

Their registry (Woundmonitor®, SoftwarePartners Zuid BV, Heerlen, the Netherlands) was developed as an electronic patient data management system. This online software program contains data on patient characteristics, wound characteristics and documentation of wound care regimens, applied during the wound treatment period in the WEC. The registry is populated routinely by the nurses during the first patient visit. Factors related to wound healing were also assessed and entered at the first consultation. Data have been collected since the inception of the WEC in 2007.

Our dataset was extracted from this registry and contained data from patients treated between November 2007 and April 2012. We included patients with any type of wound with an acute aetiology, that is, after trauma or surgery. We excluded wounds due to arterial or venous insufficiency, pressure sores or malignancy, and diabetic foot ulcers. From patients with more than one wound, we randomly selected only one wound, under the condition that the baseline data were complete. Patients with a recorded treatment period of less than 7 days, that is, in which no meaningful treatment could have been given in the WEC, or without recorded baseline characteristics were excluded. Primary outcome was the time to complete wound healing after first assessment in the WEC.

The choice of potentially prognostic factors was based on data from the literature (10,11,16) and suggestions made by a national expert panel, consisting of 16 specialised wound care nurses and 1 physician-'woundologist' in the Netherlands. The expert panel completed an online questionnaire, using a commercially available online survey tool (http://www.surveymonkey.com), about which factors they rated as most predictive of wound healing.

Data analysis

Data coding and analysis were performed using IBM SPSS statistics software (version 20.0.0.1, IBM, Armonk, NY). Possible predictive factors as proposed by the literature and the expert panel were analysed for their association with wound healing. Continuous factors were not categorised or dichotomised. To determine which of these factors best predict time to complete wound healing, a Cox proportional hazards regression analysis was chosen (17). Potentially predictive factors were entered into the model only if at least ten events were recorded per factor (18).

First, we checked the proportional hazards assumption for the possible predictive factors using log-minus-log plots. If a factor seemed non-proportional, we tested whether the factor had different effects in different groups, and whether an interaction existed between the time variable and the factor.

We detected significant independent prognostic factors through a multiple backward Cox regression analysis. Possible prognostic factors were removed one by one in order of the weakness of their multivariable association with the time to complete wound healing. Some prognostic factors (i.e. diabetic mellitus) were considered commonly accepted predictors and were therefore kept in the model. The impact of a prognostic value was expressed as a hazard ratio (HR), that is, change in the odds (hazard) of wound healing in relation to the size of the factor. Values larger than one indicate a beneficial effect of the factor on wound healing, whereas values below 1 indicate a detrimental effect. The significance level was set at 0·05.

As a measure of the predictive power of the regression model as to eventual wound healing, we calculated Harrell's C-parameter. This parameter expresses the error rate, that is, the percentage of healed wounds with a higher risk profile to heal according to the model than the wounds that did not heal (19).

Finally, we performed a linear regression analysis after log transformation of the healing time as dependent factor to generate a formula to calculate the expected time to wound healing using the predicting factors as derived from the Cox regression analysis.

Results

The database contained 1660 wounds in unique patients, recorded during the study period. Of these, 766 records were either non-acute wounds ($n = 103$) or had insufficient data ($n = 663$) on the duration and time to healing of the wound and were therefore excluded. The baseline data had not been entered for 248 wound patients and a further 83 wounds had not received any treatment in the WEC. Hence, these were also excluded, leaving a total of 563 wounds for analysis in the final database.

Demographics of included patients and wounds are summarised in Table 1. The patients' wounds existed for a mean of 7 weeks before referral to the WEC. Most wounds were located on the leg (52%) or on the trunk (39%). During the study period, 455 (81%) wounds had healed.

The final set of most important potential prognostic factors derived from the literature and group of experts is shown in Table 2. These factors comprised 15 patient characteristics and 7 wound characteristics, of which 4 were not available in the registry. Univariable regression analysis showed eight significant factors, as shown in Table 2. All available factors were entered in a multivariable Cox regression analysis, for which 368 of 563 patients were available owing to missing values for one or more variables for some patients. The PUSH-tool was excluded from this analysis as it combines several wound characteristics already present in the model. No time-dependent factors were introduced as covariate.

Table 3 shows the final model with six independent prognostic factors for the time to complete wound healing: the patient's age, the location, duration and size of the wound, and the presence of more than one sign of a wound infection. Wound characteristics had the greatest impact on wound healing. In contrast, diabetic patients did not seem to have a significantly longer wound healing time. Wounds located on the trunk had a significantly lower chance of healing (HR 0·565) than head or neck wounds. This means that, at any given time point, the chance of healing of a trunk wound is 0·565 times lower than a wound in another area. The vast majority of these trunk wounds comprised larger, open abdominal wounds after surgery, 10% of which were drained intra-abdominal abscesses or fistulae. For continuous outcomes like wound size, the HR of 0·993 indicates that each additional square centimetre in size decreases the chance of wound healing with 0·7%.

The error rate of the model, based on Harrell's C-parameter, was intermediate, 41%. Using the total wound healing time rather than the treatment period in the WEC until wound healing did not yield different predictive factors.

Linear regression analysis showed an R^2 of 0·33, that is, 33% of the variation in wound healing time could be explained by this model. The following formula could be derived to calculate time to complete wound healing for acute wounds, in which 'e' is the base of the natural logarithm, with a value of approximately 2·72.

$$\begin{aligned} e^{\text{wound healing}}\ (\text{in days}) &= 4{\cdot}12 - 0{\cdot}005 * \text{age} \\ &+ 0{\cdot}003 * \text{wound size}\ \left(\text{in cm}^2\right) \\ &+ 0{\cdot}001 * (\text{wound duration in days}) \\ &+ 0{\cdot}41\ \ (\text{if wound located on trunk}) \\ &+ 0{\cdot}17\ \ (\text{if infection present}). \end{aligned}$$

For example, a patient aged 50 with an acute, infected wound of 50 cm^2 on the trunk, which already existed for 5 days before treatment, has a predicted time to complete wound healing of:

$$e^{4{\cdot}12-0{\cdot}25+0{\cdot}15+0{\cdot}005+0{\cdot}41+0{\cdot}17} = e^{4{\cdot}605} = 100 \text{ days}.$$

Discussion

This study shows that delayed healing of complex acute wounds treated in a WEC, as well as time to complete wound healing, can be predicted using simple patient and wound characteristics, available when the patients first present themselves at a WEC. The factors with the highest impact on wound healing were wound characteristics, among which the location on the trunk was the most significant, as well as clinical signs of wound infection. This suggests more attention and effort should be spent on an early treatment and prevention of wound infections, for which various options are available (20–23). Furthermore, large abdominal wounds may benefit from earlier referral to specialised wound care, for example, in a WEC. The clinical importance of age was, albeit significant, limited, as its hazard ratio was close to 1, and cannot be influenced. The effect of having diabetes on the healing of these wounds was insignificant.

Previous research mainly focused on predictive models for chronic wounds. In pressure, venous and diabetic ulcers, ulcer size reduction was found to predict wound healing (24–26), but this could not be assessed until after 2 or 4 weeks of observation. In venous leg and diabetic foot ulcers, the size

Table 1 Patient and wound characteristics at admission

Characteristics	*N* (%)	Mean (SD)	Median (IQR)	Range
Patient characteristics				
Male gender	223 (40)			
Age		66·3 (17·4)	69·0 (56·0–80·0)	6–98
BMI		27·4 (6·5)	26·4 (23·4–29·9)	14–66
Smoking	059 (11)			
Alcohol abuse	12 (2)			
Drug addiction	1 (0·2)			
Mobility				
Independent	267 (59)			
Walking aid	139 (31)			
(Wheel) chair	42 (9)			
Bedridden	3 (1)			
General reasons for referral				
(Complex) acute wound treatment	425 (66)			
Negative pressure wound therapy	138 (22)			
Diabetes mellitus	113 (20)			
Cardiovascular disease	218 (39)			
Kidney disease	15 (3)			
Use of corticosteroids	31 (6)			
Nutritional status (unwanted >5% weight loss, abnormal BMI or seriously ill)	32 (6)			
Wound characteristics				
Location				
Leg	230 (52)			
Trunk, armpit, groin	172 (39)			
Arm, hand	22 (5)			
Head, neck	22 (5)			
Duration at admission (days)		49·9 (93·8)	19 (6–46)	0–740
Duration until healed (days)		67·2 (91·0)	45 (21–77)	7–1200
Size (cm^2)		17·9 (32·1)	6·0 (1·8–19·4)	0·1–277
Depth (cm)		0·8 (2·0)	0·0 (0·0–0·5)	0·1–12
PUSH-tool score*		8·5 (2·9)	8·0 (7·0–10·0)	3–16
More than one sign of infection†	98 (17)			
Pain score (more than 4 on 10-point VAS)	17 (3)			
Foul smell	69 (13)			
Exudate (moderate or much)	300 (54)			

BMI, body mass index; VAS, visual analogue scale.
*PUSH-tool score is based on wound surface area, amount of exudate and wound appearance (30).
†Based on the Celsian signs: calor, rubor, dolor, tumor and function loss.

and duration of the wound were also predictive of an earlier wound healing (11,12), which is similar to our findings.

We did not find an association between the presence of diabetes and delayed wound healing, which is a longstanding tenet (27). Apparently in acute wounds, particularly the abdominal wounds that usually have a better blood perfusion than leg wounds, this disorder has less impact on wound healing, as opposed to wounds with a chronic aetiology. Another reason could be that the patient population we investigated may have had an overall well-controlled glycaemia. The number of smokers in this study was relatively low, which may explain why we did not find an association with poor wound healing, although this is an acknowledged relationship (28).

Some limitations of this study need to be mentioned. First, in our patient sample, the more complex wounds may have been overrepresented owing to selection of patients referred to this WEC. This might have biased the outcomes of this prognostic study. On the other hand, it may have increased the prevalence of otherwise infrequent predictive factors. Second, the validity of this retrospective study depends on the accuracy of the WEC's registry and the completeness and uniformity of the data the personnel collects. The software program used by the WEC facilitates this and undergoes regular improvement updates. However, the registry was not primarily designed for research purposes. On the basis of our findings during this study, we suggested several improvements for this registry to allow more robust wound research in the future. Third, study validity was also influenced by the missing values in our model, but it is unlikely that missing values occurred more often in either quicker or slower healing wounds. Rather, these omissions probably occurred in the initial, learning phase of the registry or in times of higher workload, and therefore did not bias our results substantially. Fourth, not all potentially relevant data could be retrieved or analysed. The aetiology of the wound and previous treatments were not always clear, while the types of treatment and dressings used by the WEC and medication during the wound healing process changed irregularly. On the other hand, treatment regimens were according to best local practice and are therefore not likely to impede wound healing. These four limitations may

Table 2 Potentially prognostic factors based on literature and questionnaire and univariable regression analysis

Factor	Univariable Cox regression *P*-value	HR for wound healing	95% CI
Patient characteristics			
Age	0·016	1·008	1·001–1·014
Gender	0·390	1·087	0·898–1·316
Race	n.a.		
Mobility	0·427	1·046	0·938–1·167
Nutritional status			
BMI	0·026	0·983	0·968–0·998
Nutritional score	0·367	1·119	0·877–1·428
Smoking	0·781	0·958	0·707–1·297
Alcohol abuse	0·938	1·027	0·530–1·988
Drug addiction	*		
Use of corticosteroids	0·336	0·823	0·554–1·224
Diabetes mellitus	0·328	0·888	0·701–1·126
Cardiovascular diseases	0·115	1·165	0·963–1·410
Kidney disease	0·646	0·874	0·492–1·552
Seriously ill patient	*		
ICU stay	n.a.		
Incontinence	n.a.		
Wound characteristics			
Duration of the wound (from inception to presentation at WEC)	0·001	0·998	0·997–0·999
Location			
Head/neck versus leg	0·613	1·144	0·679–1·925
Arm versus leg	0·188	0·705	0·419–1·187
Trunk versus leg	<0·001	1·692	1·375–2·082
Size	<0·001	0·992	0·987–0·996
Depth	<0·001	0·912	0·872–0·955
More than one sign of infection†	0·004	0·689	0·535–0·887
PUSH-tool (30)	<0·001	0·907	0·877–0·938
Percentage change in wound area over time	n.a.		

BMI, body mass index; CI, confidence interval; HR, hazard ratio; ICU, intensive care unit; n.a., not available data; WEC, wound expertise centre.
*Not included because less than ten events were recorded per factor.
†Based on the Celsian signs: redness, swelling, pain, warmth and function loss.

Table 3 Final model with significant independent predictive factors for wound healing derived from the multivariable Cox regression analysis

							95% CI for Exp(*B*)	
	B	SE	Wald	df	*P*-value*	Exp(*B*)†	Lower	Upper
Age	0·009	0·004	5·420	1	**0·020**	1·009	1·001	1·018
Diabetes	0·142	0·158	0·814	1	0·367	1·153	0·847	1·570
Wound duration	−0·002	0·001	8·023	1	**0·005**	0·998	0·996	0·999
Wound size	−0·007	0·002	10·143	1	**0·001**	0·993	0·988	0·997
Wound infection	−0·318	0·158	4·057	1	**0·044**	0·728	0·534	0·991
Wound location								
Leg versus head/neck	−0·162	0·159	1·033	1	0·310	0·851	0·623	1·162
Trunk versus head/neck	−0·571	0·170	11·316	1	**0·001**	0·565	0·405	0·788
Arm versus head/neck	0·132	0·403	0·107	1	0·743	1·141	0·518	2·514

CI, confidence interval.
†Exp(*B*) = hazard ratio; values above 1 indicate a beneficial effect of the factor on wound healing, whereas values below 1 indicate a detrimental effect.
**P*-values of significant factors are shown in bold.

have caused the relatively high error rate of the model. Lastly, external validation of our study results is needed to appreciate the implications for wound care on a larger scale, as the study was performed in a specific cohort of patients treated in a WEC. Hence, these results are not necessarily the same for settings other than a WEC. A prospective study that predefines the factors and outcomes of interest may give more insight in the general applicability of our results.

The purported advantage of treating (complex) wounds in a WEC is still under debate. In a previous study, wound treatment in a WEC was not found to be a prognostic factor for wound healing (11,29). On the other hand, the multidisciplinary, evidence-based treatment of complex wounds is likely to counteract practice variation and improve quality of wound care. In the Netherlands, a national set of criteria and indicators has been formulated for current or starting WECs to warrant the quality of their care. Also, if the registry of a WEC is accurate, this may help detect prognostic factors and timely treatments for (impaired) wound healing of more or less complex acute wounds.

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