Hard-to-heal wounds: a holistic approach

Wound complexity and healing

Psychosocial factors and delayed healing

Economic burden of hard-to-heal wounds
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Even with increasing knowledge and the development of more sophisticated interventions, many clinicians will encounter wounds that are 'hard-to-heal' where, despite best efforts, wound healing is prolonged or never achieved. This often causes increased psychological stress and anxiety for all involved and creates a considerable financial burden for already hard-pressed healthcare systems.

While some attention has been placed on understanding the biological factors influencing delayed healing, relatively little has been placed on the psychosocial factors involved. This document aims to redress this balance and looks at how all of these factors may have an impact on healing and affect a patient’s life.

In the first paper, *Wound complexity and healing*, Vowden, Apelqvist and Moffatt identify issues that affect wound healing. They bring together the practical aspects of dealing with wounds and the increasing scientific data that demonstrate why some wounds fail to heal. The authors describe how physical, bacteriological and biochemical wound- and patient-related factors can be used to give an indication of risk for delayed healing. The paper sets out a framework showing how the patient, the patient’s wound, the skills and knowledge of the healthcare professional, and resource availability interact to define wound complexity, and how this relates to potential problems with healing.

The paper also introduces the importance of psychosocial factors and their impact on healing. In particular, a short patient commentary gives an insight into the psychosocial impact of a large non-healing wound and how the introduction of an advanced portable dressing system enabled the patient to return quickly to normal living and employment.

This theme continues in the second article *Psychosocial factors and delayed healing* by Moffatt, Vowden, Price and Vowden, which explores the close interrelationship between anxiety and depression, sleep deprivation, socioeconomic status, wounding and non-healing.

Although the main focus of both papers is the patient, it is important to recognise that non-healing also impacts directly on healthcare professionals who are under increasing pressure to justify their actions in terms of cost-effectiveness and clinical outcomes.

The third paper, *Economic burden of hard-to-heal wounds* by Romanelli, Vuerstaek, Rogers, Armstrong and Apelqvist, examines the potential cost implications of hard-to-heal wounds in different countries. The significant economic burden of these complex wounds relates mainly to extended time to healing and to associated complications. Management of wounds should therefore focus on identifying problems early and using appropriate strategies and interventions to facilitate healing and to avoid complications. This may, however, require the use of apparently more expensive interventions. Clinicians will need to adopt a broad view of total resource use, rather than focusing on acquisition costs alone, in order to present robust economic arguments to fund holders. However, a problem in evaluating the cost of disease states is the wide variation in the cost criteria used by different studies.

Although the themes covered in this document are equally relevant to all practitioners, problems specific to wound complexity and delayed healing will be greatly influenced by individual circumstances such as product availability, the reimbursement system and the care setting.

The challenge for clinicians is to recognise and take the appropriate measures to simplify or downgrage the complexity of the wound so that it can heal in the least invasive setting, in the shortest time possible and without negatively impacting on the patient’s quality of life. Early recognition of a wound that is slow to heal is very important and should trigger a reappraisal of the treatment plan. Professionals may need to look for alternative treatment strategies. In some situations, the goal of treatment may change to effective symptom control, ensuring the patient has the best possible quality of life despite the presence of a wound.
INTRODUCTION

Over the past 20 years there have been major advances in our understanding of the biology of wound healing. This means that it is now possible to predict the likely sequence of events in the healing trajectory and to forecast the approximate time it will take for a wound to close completely. However, despite our increasing knowledge and the development of many interactive wound care products, healthcare professionals will encounter wounds where healing is prolonged or never achieved. This paper suggests that the key to appropriate and effective management lies in recognising the complex combination of factors, both within and outside the wound, that are involved in the process of healing. Management can then focus on initiating appropriate measures to address any that are causing problems. The challenge is to identify as early as possible when a wound is slow to heal.

PREDICTING HEALING PROGRESSION

The importance of regular wound assessment and wound size measurement in identifying potentially hard-to-heal wounds has been reviewed by Troxler et al. Recognising early wound size reduction by measuring advancement of the wound edge (epithelial advancement) – the so-called ‘wound edge effect’ – has been shown to be a useful general measure of healing outcome in different wound types. Phillips et al., looking at percentage reduction in venous ulcer area, found that in approximately 77% of cases, healing outcomes could be predicted based on a wound size reduction of more than 44% at three weeks. Zimny and Pfohl have shown that weekly wound radius reduction could be used to predict healing in a group of patients with diabetic foot ulceration. Margolis et al. have successfully demonstrated that a simple scoring system for venous leg ulcers, based on ulcer size and duration, can give a good indication of the likely outcome at 24 weeks.

Epithelial advancement is, however, only one component of the healing process. Falanga et al. incorporated measurement of epithelial advancement into a scoring system that correlates with the healing of venous leg ulcers. This system also examines other characteristics including the extent of periwound dermatitis, the presence of eschar, periwound callus and/or fibrosis, a pink/red wound bed and the amount of exudate and oedema.

WOUND COMPLEXITY AND HEALING PROGRESSION

The above predictors offer a useful guide and help to alert healthcare professionals to healing difficulties (i.e., that the wound is not progressing according to the projected timelines with standard therapy). However, the variability of healing rates among individuals and the many factors affecting this must also be recognised. Wound complexity will have a major impact on healing progression and the factors involved can be broadly categorised into four key groups:

- patient-related factors
- wound-related factors
- skill and knowledge of the healthcare professional
- resources and treatment-related factors.

Only by appreciating and understanding the interaction of these factors and their impact on healing (Figure 1) can clinicians develop effective and appropriate strategies to improve patient outcomes. The following sections discuss each of these categories in detail and explore how the factors involved may influence healing progress.

KEY POINTS

1. Clinicians should be encouraged to recognise, understand and address the factors that contribute to wound complexity as these may impact on healing progression.
2. It is important to identify as early as possible when a wound is likely to be slow and/or hard to heal.
3. Interventions should be targeted at reducing all aspects of complexity, including those related to the patient, the wound, the healthcare professional and available resources.
HARD-TO-HEAL WOUNDS: A HOLISTIC APPROACH

The environment in which an individual patient’s wound exists is affected by a number of physical (such as underlying pathology, comorbidities, etc), psychological and social factors.

It has been shown that physical factors, such as diabetes mellitus, obesity, malnutrition, old age (over 60), decreased perfusion, peripheral vascular disease, malignancy, organ failure, sepsis, and even restrictions in mobility, have an impact on healing'. Correcting, where possible, the underlying wound pathology and any comorbidities is, therefore, a central feature of wound management. If the underlying disease cannot be corrected or is difficult to manage, wound healing can be delayed.

Marston et al found that improved glycaemic control positively influences wound outcome in diabetic foot wounds, particularly when dermal substitutes are used. Similarly, it has long been recognised that restoration of pulsatile blood flow, by either surgery or angioplasty, markedly improves the outcome in ischaemic lower limb ulceration. This is in contrast to the situation in venous ulceration, where early surgical correction of superficial venous reflux has proved to be no more beneficial than high compression bandaging. The benefit of surgery here, as was demonstrated in the ESCHAR study, is in the reduction of ulcer recurrence in both the short- and the long-term.

Diseases and treatments that directly affect the immune system have a major impact on wound healing and often increase the complexity of the wound. The inflammatory process is an integral part of acute wound healing, and derangement of this process is recognised as one of the primary causes of wound chronicity. Immunodeficiency states, the use of immunosuppressant drugs such as corticosteroids, azathioprine or methotrexate, or the presence of diseases (such as diabetes mellitus) that are known to affect the immuno-inflammatory response, all adversely affect healing and increase the risk of wound sepsis.
In addition, other patient-related factors, such as the wound care product used previously or drug sensitivity/allergy, may determine the complexity of the wound and the treatment outcome by restricting the range of suitable treatments (see Figure 1, page 3).

Psychosocial factors, such as social isolation, gender, economic status, pain experience, have also been found to influence healing (see Moffatt et al, pages 10–14). Recognition of the impact of these factors is seen as being particularly relevant when dealing with recalcitrant venous ulcers in an elderly population. It is therefore important that appropriate referral is made (eg to social workers) so that the problems can be addressed effectively.

Stress and depression have been linked to changes in immune function, and may therefore adversely influence a broad range of physiological processes, including wound healing. In a human experimental model, it was found that stress and depression had a possible role in the modulation of matrix metalloproteinases (MMPs) and in the expression of tissue inhibitors of metalloproteinases (TIMPs). In a hostile marital environment, pro-inflammatory cytokines were found to be elevated and wound healing was delayed.

Patients with a chronic, non-healing wound will attempt to develop coping strategies. The nature of their response will be determined by a variety of psychological factors: these include personality type (pessimistic or optimistic, for example), previous experience and psychological disorders such as depression, phobias and obsessive compulsive disorder.

**Patient beliefs**

Salaman and Harding investigated a group of 45 hospital patients with venous ulceration, 16 (36%) of whom were considered to be failing to make satisfactory progress. Only half of these 16 patients claimed to have received any explanation about the cause of their ulcer and the method of its treatment. Seventy-five per cent of the total group appeared to understand the importance of compression in ulcer healing, but 62% felt that it was not proving effective in healing their ulcer. Seven of the 16 patients with non-healing wounds (44%) believed their ulcer would heal.

Although the study was very small and focused on a mixed group of patients, 36% of whom were highly refractory, it raised important issues about the impact on wound healing of the patients’ beliefs and their confidence in treatment. Further research is needed to understand patients’ ability to tolerate and adhere to treatment modalities when they do not believe they will help them.

**Concordance**

Despite some patients feeling that they have no control over their situation, many do make attempts to ensure that the care they receive meets their own needs (Box 1, page 5). Some patients become experts in their own condition, often using the Internet to access information and frequently developing routines to ensure that their treatment plan matches their expectations. In addition, patients may constantly take note of how their care is provided. Such patients use a form of coping called ‘monitoring’.

Another form of coping is called ‘blunting’; this is where patients appear unconcerned about their treatment and may not be greatly interested in their progress. Although blunting has been shown to be a useful coping strategy in acute situations, for patients with long-term conditions, it may lead to poor adherence to therapy and a refusal to engage in treatment. Further research is required to confirm the long-term effects of blunting in patients with chronic wounds.
WOUND-RELATED FACTORS
In a study by Margolis et al, specific wound characteristics were shown to correlate with healing. Patients with a large wound area, an ulcer of long duration, a reduced ankle-brachial pressure index or a visual estimate of fibrin on more than 50% of the wound surface had delayed venous ulcer wound healing at 24 weeks. Other wound characteristics such as the condition of the wound bed and anatomical location may also impact on complexity and healing.

Wound duration and senescence
Wound duration is a recognised indicator for potentially delayed healing in a variety of wound types. This may relate to the development of a senescent cell population (ie a population of cells that is unable to replicate) in the wound. Henderson has reviewed the potential effect of fibroblast senescence on chronic wound healing, looking at the interrelationship of oxidative stress, pro-inflammatory cytokine generation and accelerated telomere degradation. The author concludes that although the chronic wound environment promotes senescence, not all cells are uniformly affected. The ratio of senescent to non-senescent fibroblasts has been linked to healing outcome: an accumulation of greater than 15% senescent fibroblasts has been described as a threshold beyond which wounds become hard to heal.

Size and depth
While studying venous leg ulcers, Margolis et al observed the importance of wound size and depth in determining healing outcomes for different wound types. After using pooled data from almost 30,000 patients with diabetic foot ulcers, Margolis et al concluded in a series of papers that ulcer size (>2cm²), duration (>two months) and ulcer depth (penetration through to exposed tendon, ligament, bone or joint) were the three most important factors for predicting outcome. Patients with all three factors had only a 22% chance of healing by 20 weeks.

Several classification systems for diabetic foot ulceration have been devised to allow risk stratification. One such validated system is the S(AD) SAD classification system – Size (Area and Depth), Sepsis, Arteriopathy and Denervation – which identifies ulcer size and the presence of arteriopathy as the most important factors associated with ulcer healing. In this system, lower grading is associated with more rapid healing. Kramer and Kearney have also shown that the size and depth of pressure ulcers are good predictors for healing, ie the lower the ulcer grade the greater the chance of healing.

Owing to the physical nature of the healing process, it is inevitable that large wounds will take longer to heal than small ones. Furthermore, the longer a wound is open the greater the risk of complications such as infection. Treatments that reduce wound size and the risk of wound infection therefore offer potential benefits.

Wound bed condition
The presence of necrotic tissue in a wound has long been recognised as a barrier to assessment, as well as a potential factor for delayed healing and a locus for infection. The importance of regular debridement when managing diabetic foot ulceration was demonstrated by Steed – a chance to reduce wound size and the risk of wound infection therefore offer potential benefits.

BOX 1. One patient’s experience
I served for 25 years in the Royal Navy but had to leave after my entire colon was removed as a curative procedure. The resultant stoma, which affected my self image and resulted in a loss of income, proved a huge psychological shock.

One day I woke up with what I thought was a blocked stoma. After two operations, I was left with a very large wound. It was about 25cm long, 20cm wide and 6cm deep; you could see my intestines moving in the bottom of this hole and I could easily have put both my hands in it with room to spare. To cap it all, my diabetes became unstable and I was converted on the spot to an insulin injecting diabetic.

When I first saw my wound I almost passed out. For the next three or four dressing changes I held a towel over my eyes to stop myself looking at the gaping hole in my stomach.

A dressing system (V.A.C. Therapy) was used, which seemed to reduce the size of the wound quite rapidly. I was given a portable version of this dressing system (V.A.C. Freedom), which allowed me to go home just six weeks after the second operation to pick up the pieces of my life and my business. This was very important to me as I am self-employed, although I did have to persuade my GP to fund my treatment at home.

I see training in the use of advanced dressing technology as essential. Fortunately, on one occasion at 5am in accident and emergency, when the nursing staff lacked the necessary experience with this new technology, my partner was able to do a very good job of cleaning the wound out, cutting a new sponge and reapplying the dressing.

Commander N Westwood

Note: This case demonstrates the impact of living with a complex wound. The early introduction of an effective advanced therapy aided recovery and allowed the patient to return home and continue working while the wound healed. It is important to recognise the need for additional training and education when new technologies are introduced.
finding while conducting a trial of platelet-derived growth factor in diabetic foot ulcers30. Studies with skin substitutes have also demonstrated the importance of effective debridement and offloading in the management of diabetic foot wounds31,32. Other factors relating to the wound bed condition and surrounding tissues can also affect outcome; for example, the presence of dystrophic calcification (calcinsosis) can result in the failure of a leg ulcer to heal33.

**Ischaemia**

According to Mogford and Mustoe34, wound ischaemia is, arguably, the most common cause of a wound failing to heal. Poor perfusion deprives tissue of effective gas and metabolic exchange and leads to increased vascular permeability, leukocyte trapping and the production and release of free oxygen radicals and proteolytic enzymes. Wound healing in the foot has been directly related to both tissue oxygen (TcPO2) levels35 and perfusion pressures (absolute ankle and toe systolic pressures and brachial pressure ratios)36.

It has been demonstrated that wound healing following surgery is compromised by poor patient hydration and reduced body temperature, resulting in reduced tissue perfusion and poor oxygenation37. In addition to the pro-inflammatory effect of poor tissue perfusion, hypoxia affects cellular function in the key cell types involved in wound healing38,39.

In chronic wounds, there is a tendency for the inflammatory response (an important element in the initial wounding response) to become exaggerated. This results in increased production of pro-inflammatory cytokines, reactive oxygen species and proteolytic enzymes (such as certain MMPs, elastase and plasmin). This activity is combined with reduced inhibitor release of, for example, TIMPs40,41 and is enhanced by alterations in wound bed pH42. Excessive activity of these enzymes causes not only deleterious extracellular matrix destruction, but also growth factor inactivation40,43-45. The chronic wound environment therefore shows sustained inflammation with matrix degradation, reduced growth factor bioavailability and increased fibroblast senescence, all of which combine to reduce tissue repair, cellular proliferation and angiogenesis.

**Infection**

There is a close relationship between infection, ischaemia and inflammation, and all have a detrimental effect on wound healing. Chronic wounds are characterised by a high bacterial content, the presence of more than one bacterial strain, an increased tendency to harbour drug-resistant organisms and the presence of biofilms (highly organised microbial communities living within a protective bacteria-derived extracellular matrix)46. The presence of bacteria in the tissue of a chronic wound may act as a major factor in delaying healing by stimulating chronic inflammation47. Davies et al48 found a significant link between wound swab bacterial diversity and density and time to healing.

Biofilms may be more commonly present in wounds than is normally assumed: Ngo et al found them in debrided tissue from seven of 12 chronic wounds tested49. The potential significance of biofilms has been indicated by an in vitro study. This showed that bacteria in a biofilm are protected from the action of silver antimicrobials50. This led Bjarnsholt et al51 to suggest that a far higher concentration of silver may be required than is currently provided in antimicrobial dressings if treatment is to be effective.

The presence of specific bacterial species in a wound has also been linked to healing outcomes. For example, the presence of Pseudomonas aeruginosa in venous leg ulcers can delay healing52. It has also been suggested that anaerobic cocci may have a potential role in delayed wound healing53,54.
When a wound is situated on a pressure-bearing surface or a mobile area such as around a joint, the dressing material and the method of fixing chosen are critical. These can help to preserve limb function, dressing performance, and avoid secondary pressure-related problems. Safely applying a dressing to a neuropathic foot ulcer can be particularly challenging, as the patient frequently lacks a protective pain response. In addition, offloading is a vital part of the management of both diabetic foot and pressure ulcers, and alternative dressing methods may be required, such as protective bridging techniques for topical negative pressure therapy (V.A.C.® Therapy) or a windowed cast for pressure redistribution. The diabetic foot is a particularly difficult location for complex wound management. Blume et al have recently demonstrated an advantage for topical negative pressure therapy over other advanced dressing products in this situation.

Although traditional beliefs suggest that diabetic heel ulcers do not heal, both Apelqvist et al and Oyibo et al found that the site of foot ulceration did not influence outcome. Chipchase et al did find, however, that while the overall healing rates of foot ulcers were similar, heel ulcers tended to heal more slowly. The authors concluded that the outcome was generally favourable, with 65.6% of heel ulcers healed in a median of 200 days.

It is well documented that the initial response to treatment can be a reliable predictor of subsequent healing time. Response to treatment can also be an indicator of tissue viability and healing potential. It has been suggested, for example, that a reduction in wound area of around 15% within one to two weeks of topical negative pressure therapy use is an indication that the wound is likely to continue to make good progress, and that this observation can be used as a justification to continue treatment. Using these parameters it is possible to identify non-responsive wounds with an accuracy of 75%; such outcomes are, however, dependent upon the accuracy and consistency of wound measurement. When a patient's wound does not heal in an expected timeframe with 'standard therapy', it is essential to reassess the patient and alter the treatment regimen accordingly.

The skills, knowledge and attitudes of healthcare professionals can have a major impact on their ability to assess the complexity of a wound, control a patient's symptoms and manage associated problems. However, the issues surrounding non-healing have generally been studied from a patient perspective, with little attention placed on the impact of a non-healing wound on healthcare professionals. Over the past decade, improvements in assessment and treatment have led to heightened expectations of healing: healing rates are considered to be the most important endpoint of wound management. As a result, healthcare professionals who are unable to secure the healing of a patient's wound frequently feel impotent, and may become anxious when confronted with the increasing expectations of patients, their families and the healthcare system. Perceived professional failure, such as that manifested by a non-healing wound, may lead to defensive behaviour in staff. Recent research has explored patient and professional reactions to wounds that fail to heal. This revealed that professionals were often emotionally overwhelmed by the reality of not being able to heal a wound – a feeling that was compounded if patients' suffering was not controlled or if they were considered difficult to manage. There is evidence to suggest that this feeling of helplessness on the part of healthcare staff can lead to their resorting to social defences such as withdrawing visits, avoiding providing continuity of care, labelling, blaming, and blunting of emotional responses to patient suffering. Although these defensive strategies may help to protect the professional, they can have an extremely negative effect on the patient. Box 2 provides strategies that may help the clinician to focus on the patient's needs.
An expanding range of physical and biochemical characteristics within and around areas of ulceration have been, and continue to be, defined\(^6\),\(^8\). These characteristics – such as protease activity, oxidative stress and bioburden – are increasingly being linked to outcome and are being used to target treatments and develop new therapeutic strategies. In the future, access to data on these characteristics (see Future markers below) will play a major role in the clinician’s ability to recognise and treat complex wounds earlier and more effectively.

The patient’s experience described in Box 1 on page 5 illustrates how the early use of an appropriate advanced intervention reduced the complexity of a patient’s wound. This allowed healing progression at a rate that enabled the patient to return quickly to a normal lifestyle and employment. Gaining access to this technology, however, raised issues regarding resources and education.

Several authors\(^7\),\(^8\) have emphasised the importance of educating staff so that they have the knowledge and skills to initiate appropriate therapy and to develop wound care protocols and formularies. Too often, however, therapy is based on tradition and habit, and decisions are made on subjective information, which is neither standardised nor appropriate\(^7\).

Many biochemical characteristics are being investigated as indicators of healing status. Protease levels for example may be potential markers for healing\(^6\). It is most likely that data on combinations of markers, rather than a single marker, will be required to predict outcome in individual patients\(^6\). In addition, gene expression profiling is likely to have a role. Chronic ulcers contain distinct sub-populations of cells that have different capacities to heal and gene expression profiling can be used to identify them\(^9\). Such techniques may, in the future, allow detailed assessment of healing potential and treatment targeting.

Wound healing normally occurs in a predictable sequence, but for some wounds healing is prolonged or never achieved. The healing process is the result of a complex interaction between patient- and wound-related factors, the treatment used, and the skills and knowledge of healthcare professionals. Only with careful initial assessment and repeated evaluation of therapy can the factors contributing to wound complexity be recognised and the potential status of wounds assessed. The challenge for healthcare professionals is to initiate effective therapeutic strategies in a timely and cost-effective way so as to reduce wound complexity, manage the patient’s symptoms and expectations, and, where possible, achieve healing.

Future markers

Wound healing is normally occurs in a predictable sequence, but for some wounds healing is prolonged or never achieved. The healing process is the result of a complex interaction between patient- and wound-related factors, the treatment used, and the skills and knowledge of healthcare professionals. Only with careful initial assessment and repeated evaluation of therapy can the factors contributing to wound complexity be recognised and the potential status of wounds assessed. The challenge for healthcare professionals is to initiate effective therapeutic strategies in a timely and cost-effective way so as to reduce wound complexity, manage the patient’s symptoms and expectations, and, where possible, achieve healing.

CONCLUSION

References

HARD-TO-HEAL WOUNDS: A HOLISTIC APPROACH


It is now recognised that psychosocial factors – anxiety and depression, social isolation, low economic status and pain, for example – are associated with delayed healing of wounds. However, little research has been undertaken to examine how these factors may not only be a consequence of delayed healing, but may also play an important role in delaying healing. It is suggested that an evaluation of a patient’s psychosocial status should therefore be included as part of a general wound assessment.

Patients who have a chronic, non-healing wound are affected by a complex interaction of factors that influence their psychological response and ability to cope with the situation. These include the patients’ previous experiences, together with their individual circumstances, preferences and values. The impact on quality of life of these factors is far-reaching and often extends beyond the local management of an open wound.

In 1997, Chase et al introduced the concept of ‘forever healing’. It is not unusual for patients with chronic, recurring wounds who experience long episodes of slow or delayed healing, with unremitting symptoms such as pain, to believe that they are in a permanent state of ‘wounding’. Briggs and Flemming continued this theme when they emphasised that chronic wounds should receive the same focus of care as other chronic conditions such as diabetes and arthritis, and that there should be an emphasis on learning to live with and to manage the condition. There is much literature from the field of oncology to suggest that patents ‘re-calibrate’ their views on quality of life in accordance with their shifting priorities as they progress along their illness and treatment journey.

In 2003, van Korlaar et al defined health-related quality of life (HRQoL) as ‘the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient’. Clinicians often use HRQoL to measure the effect chronic illness has on a patient to understand better how it interferes with that person’s day-to-day life. HRQoL is a measure distinct from overall quality of life, which takes into account many different factors that are not necessarily related to an individual’s health – economic status, for instance. It can be measured using physical, social and psychological factors, among others. Research has shown that chronic wounds are associated with a severe deficit in HRQoL.

Hopkins carried out an in-depth assessment of patients with leg ulcers, based on semi-structured interviews. The study examined the impact of leg ulcers on daily living and provided valuable qualitative data. It was found that while patients accepted leg ulcers as ‘part and parcel’ of their lives, they struggled with the social exclusion that ulcers brought. Using a generic assessment tool (Nottingham Health Profile – available from www.cebp.nl/media/m83.pdf [accessed March 2008]), Franks and Moffatt demonstrated that large leg ulcers were associated with pain, emotional problems and social isolation, and pain and isolation were significantly associated with long ulcer duration.

When examining current life situation and function in elderly people with and without leg ulceration, Wissing et al concluded that people with leg ulceration are more vulnerable and have a poorer quality of life. Persoon et al also reviewed the overall effect of leg ulceration.

**KEY POINTS**

1. Anxiety, depression, social isolation, economic hardship and pain are key psychosocial factors associated with delayed healing.
2. It is important to recognise that psychosocial factors may not only be a consequence of delayed healing, but may also play an important role in delaying healing.
3. The future needs to focus on raising awareness of the significance of these factors and developing effective strategies to manage them.
ulceration on daily living and indicated that issues such as pain, reduced mobility, odour and poor social interaction had a negative impact on patients’ lives. A similar association has been made in patients with diabetic foot ulceration and in pressure ulcer populations. Interestingly there is relatively little research focusing on the impact of pressure ulcers on a patient’s quality of life.

**Socioeconomic Status**

Socioeconomic status is recognized as a powerful predictor of health outcome in the general population, with lower occupational status being associated with poorer healing. This is supported by the work of Franks et al., who also found that low social class, lack of central heating and being single were significantly associated with delayed healing. It has been shown that venous ulcers occur mainly in low income populations and that these ulcers are present for long periods and are recurrent. This can have a significant impact on patients’ ability to work, with the potential to reduce further their economic status.

**Social Isolation**

Social isolation has been defined as a lack of or low level of social contact and/or communication with family, friends, neighbours, community and social sources. It can be a consequence of geographic, physical, economic, personal and social barriers, and appears to affect many patients living with a chronic wound. Moffatt et al. showed that patients often have very low levels of perceived social support and small social networks. This may result from a number of issues: lack of mobility, curtailment of social activities and embarrassment, for example. Odour is recognized as a particularly distressing symptom of chronic wounds and can cause embarrassment and social withdrawal. Problems of social isolation and restriction were also apparent in an analysis of venous ulceration in intravenous drug users.

The perceived level of social support in patients with leg ulceration has been shown to be significantly lower than in age/gender matched controls, while patients with larger social networks have an increased likelihood of wound healing. It must be noted that confounding was not analysed in this study. Patients who are socially isolated and who lack friends or family support, may be at increased risk of psychological problems such as depression and anxiety.

**Psychosocial Impact of Wound-Related Symptoms**

Sleep deprivation, anxiety and depression, pain and the perception of pain, are all intimately linked and share a common pathway, probably through a neuroendocrine response that influences inflammatory responses, host resistance and vasoreactivity. Inadequate management of these factors may lead to an adverse wound response and delayed healing.

The chronic illness literature shows that the intrusion of wound-related problems such as pain, exudate and odour may cause patients to make lifestyle changes. Patients’ beliefs and attitudes about their condition, coupled with uncontrolled symptoms, are perhaps among the most important factors to influence their ability to adhere to treatment, and may increase the risk of delayed healing and development of psychological problems such as depression and anxiety.

**Sleep deprivation/disturbance**

Interference with sleep is a common problem in patients with chronic wounds and is often associated with uncontrolled pain. It is likely that loss of sleep is one of the most important factors to interfere with a patient’s sense of wellbeing. Despite this, it has been given very little attention by health professionals.

Research from the chronic illness literature has shown the profound effect sleep disturbance has on daily living. Exhaustion may prevent patients from being able to socialise and, as sleep schedules become more irregular, patients are often forced to sleep during the day.
Interference with sleep may also affect personal relationships. For example, patients who suffer from disturbed sleep may have to sleep in a separate room to avoid disturbing a partner. This may further exacerbate their feelings of isolation and affect family relationships within the home. Partners may also be anxious about sharing a bed with and/or having a sexual relationship with a person with a chronic wound, fearing they will inadvertently cause pain or trauma. Furthermore, uncontrolled odour from the wound may lead to repulsion by loved ones, who may choose to sleep separately.

Sleep deprivation may interfere with normal immune responses, which, in turn, may affect healing and host defences. Mostaghimi et al found that sleep deprivation did not appear to have a significant impact on wound healing in a rat model, while Gumustekin et al found that sleep deprivation in combination with nicotine administration adversely affected healing in a similar rat model. These changes may be linked to cortisol levels, with elevated morning cortisol levels being found to be associated with delayed healing in a human volunteer model. In addition, Wright et al demonstrated a blunting of the cortical secretion response following sleep deprivation. This work needs repeating in a chronic wound population before we can truly ascertain its relevance.

Pain is the most significant predictor of depression in leg ulceration and interferes with individuals’ ability to cope with their situation. Research has shown that anxiety and depression may be associated with delayed healing in leg ulceration. This study found that 15 out of 16 patients diagnosed with anxiety (using an anxiety and depression scale) experienced delayed wound healing, while wounds were slow to heal in all 13 patients who had depression. Kiecolt-Glaser et al demonstrated that delayed healing of acute wounds occurred in patients experiencing high levels of anxiety when compared to normal controls. However, further research is needed to clarify the relationship between healing and clinically significant anxiety and depression.

It is unclear whether depression is a consequence of non-healing or whether it is caused by other interrelated factors such as sleep deprivation, low economic status and social isolation. In addition, the question about whether psychological distress may affect healing by influencing the endocrine and neuro-endocrine systems must be further addressed.

Broadbent et al concluded that psychological stress can lead to an impaired inflammatory response and matrix degradation after surgery and that it may result in delayed healing. Similarly, Marucha et al found more rapid healing of mucosal wounds in non-anxious subjects. Anxiety has also been associated with delayed skin barrier function recovery, and symptoms of depression have been linked to delayed mucosal wound healing. Furthermore, pain has been shown to play an important role in post-surgery wound healing. Because of the potential for pain to impact on healing, the literature now demands that clinicians recognise that persistent pain can dominate patients’ lives and that, as such, it requires effective management.

Wound healing is associated with a reduction in pain intensity. Although the mechanisms for this remain poorly understood, it is thought to be due to reduction in the levels of inflammatory cytokines as healing progresses. Improvement in pain can also occur in those who fail to heal, although often to a lesser degree. The improvement may be due to effective management of other factors, such as oedema, and reduction in bacterial burden and exudate.

Many chronic, non-healing wounds produce copious amounts of exudate, which can cause considerable patient distress. However, Jones et al found that pain and odour, rather than exudate, were associated with anxiety and depression. Patients fear that people may notice or comment on the odour, and this may cause them to become socially isolated from family and
friends. Such fears may have a profound effect on the development of personal relationships. Control of exudate levels can contribute to a reduction in odour\textsuperscript{44}. This may involve assessing the wound, reducing the bacterial burden, choosing wound management products that are designed to manage exudate, and correcting the underlying problem\textsuperscript{44}.

**Infection**

Clinical experience shows that recurrent wound infections may cause severe patient anxiety and depression. During episodes of infection, patients may experience unpleasant systemic symptoms and also notice a deterioration in their wounds – a visible reminder of their illness and of their vulnerability.

Media attention on problems such as hospital hygiene and MRSA (methicillin-resistant \textit{Staphylococcus aureus}) has highlighted issues surrounding infection risk. Although little attempt has been made to understand how this publicity might affect patients psychologically, anecdotal reports suggest that they are often extremely anxious about developing resistant or hospital-acquired infections. As a consequence, some patients may not wish to be referred to a hospital for specialist advice because they fear that infection may cause further problems, including possible death.

**Lifestyle issues**

Many patients with chronic, non-healing wounds are forced to make considerable changes to their lifestyle\textsuperscript{45}. In a phenomenological study involving 14 patients with painful venous leg ulcers, it was found that a number of them felt frustrated with many aspects of their lives\textsuperscript{45}. Some had to make major life changes, such as retirement, because they realised that their ulcer was not healing as a consequence of their current lifestyle. Patients experienced considerable guilt when they were faced with making a choice between following their healthcare providers’ advice and continuing with an activity such as work, which they felt was of greater importance. In such situations, the professionals frequently used blaming behaviour, which increased the emotional distress felt by patients, particularly if their wounds were not healing\textsuperscript{45}. There is evidence, however, that many patients do adjust to their condition and in many cases this will be facilitated by access to appropriate treatment strategies that help patients to return to a normal lifestyle (see Box 1, page 5).

**MEASURING PSYCHOSOCIAL IMPACT**

There are a number of different ways of assessing HRQoL, each with advantages and disadvantages. Generic measures of HRQoL have been designed to look at the impact of a given disorder on everyday living and compare any given group of patients with age and sex-matched norms established for the healthy population. These tools allow for comparisons to be made across a variety of conditions or diseases, such that the impact of a chronic, non-healing wound could be compared with the impact of HRQoL on having a hip replaced. However, the questions used in these tools may not focus adequately on the specific issues related to living with chronic wounds. Condition-specific tools are more responsive to items of particular interest to patients, as the questions relate directly to the condition being investigated. Experts recommend using both a generic and a condition-specific tool when using HRQoL as an outcome in clinical trials\textsuperscript{46}. Some examples of condition-specific tools used in wound care are shown in Box 1 (see page 12). The ideal HRQoL questionnaire is user-friendly and easy for the clinician to integrate into everyday practice. It will have sufficient discrimination and sensitivity to detect change in HRQoL over time and to take into account cross-cultural issues\textsuperscript{52}.

**CONCLUSION**

The key to managing quality-of-life issues in the small but important group of patients with chronic wounds that do not heal as expected lies in identifying problems early. Professionals must give priority to helping patients have the very best quality of life despite living with a chronic wound. The emphasis must be on good symptom control, with the elimination of pain a priority for all patients, whatever the underlying condition or prognosis. Goals of treatment should move towards comfort and patient tolerance. This will require a
reappraisal of the treatment plan, with referral to appropriate members of the multidisciplinary team, eg psychologists, pain specialists and social workers. It also requires recognition that patients are partners in their care.

Research has shown that living with a hard-to-heal wound often means being faced with a number of intimately linked psychosocial issues, which, if not adequately addressed and managed, may lead to an adverse response and further healing problems. The future needs to focus on raising the profile of these issues and on developing sensitive, reliable and user-friendly tools that detect and assess their impact on the patient.

References

Economic burden of hard-to-heal wounds

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INTRODUCTION

Hard-to-heal wounds are associated with long duration and a high incidence of complications, often resulting in considerable financial burden. To gain an understanding of the cost issues involved in various types of hard-to-heal wounds, this paper draws on the experiences of a number of authors from different countries.

PRESSURE ULCERS

A multiplicity of factors can influence total cost of care for pressure ulcers (Box 1) and reliable data related specifically to the costs of hard-to-heal pressure ulcers is limited. However, a study by Bennett et al estimated the cost of healing a grade 4 pressure ulcer to be about ten times that of healing a grade 1 ulcer¹. These authors also estimated that in 2000 the cost of healing a hard-to-heal (eg infected) grade 4 pressure ulcer was £9,670 versus £7,750 for a grade 4 ulcer that healed without complication within the expected timeframe¹.

An Italian perspective

Italy has a largely decentralised public health service (Servizio Sanitario Nazionale) with healthcare spending decisions made mainly at a local or regional level. In 1994, the overall prevalence of pressure ulcers in 2,144 hospital-based patients in Italy was 13.2%³.

Venous Leg Ulcers

The prevalence of venous leg ulcers is approximately 1% in the whole population; this increases with age⁷. It is accepted that where appropriate research-based treatment protocols are in place, about 50% of ulcers will heal within four months, 20% do not heal within two years and about 8% do not heal even after five years⁷. In 1991, the national cost of leg ulcer treatment in the USA was estimated to be between US $775 million and US $1 billion annually⁷. In the UK, the total cost of treating venous leg ulcers for 2005/6 has been estimated as at least £168–198 million⁷. The factors that correlate positively with increasing cost are duration of active therapy, ulcer size and the presence of at least one comorbidity⁷.

Note on currency:
To prevent inaccuracies, currencies have been retained as in the original source.
A recent study by Tennval et al confirmed that leg ulcers with an area of 10 cm² or more and of longer duration (ie six months or more) are the most expensive to treat. The yearly cost, for example, of treating a venous leg ulcer of < six months' duration in Sweden was estimated as 1,827 euros versus 2,585 euros for an ulcer of > six months' duration.

Product costs are often considered to be synonymous with the cost of care. However, the purchase price of dressings (including compression bandages), rarely forms a significant portion of the actual cost of care. Dressing costs are often negligible in comparison with other factors such as costs associated with frequency of dressing changes, nursing time, time-to-heal, quality of healing (avoidance of ulcer recurrence), ability to return to paid employment and the cost of the care setting. Cost-cutting exercises that focus on the use of less costly dressings might in fact result in higher overall costs if the dressing change frequency is increased (necessitating increased nursing time) and time-to-heal is extended.

When analysed by care setting, home healthcare accounted for the largest proportion (48%) of the total cost of treating venous leg ulcers in the USA. A study in the UK calculated that the cost per patient could be substantially reduced by treating patients in a leg ulcer clinic rather than in the community. These findings suggest that wider provision of high quality care based in outpatient clinics may help to improve cost efficiency.

DIABETIC FOOT ULCERS

BOX 2. Measures to reduce DFU

- Better organised multidisciplinary foot care
- Extra depth or custom moulded shoes
- Home monitoring of foot temperatures

NB: If combined or adopted in part, the above measures may prevent 48–73% of DFUs and LEAs, saving the USA healthcare system up to US $21.8 billion annually.

CURRENT RESEARCH

Factors influencing cost/ resource use

Few studies in wound care provide full cost-effectiveness analysis. Comparisons are further complicated by differences in study design. These include whether the study is prospective or retrospective, patient inclusion criteria, wound type, healthcare setting studied (eg primary or secondary care), treatment practices, period of investigation, reimbursement system and countries included. Most studies focus on the estimated direct medical costs of treating wounds, but not the indirect costs relating to loss of productivity, individual patient and family costs, and loss of quality of life. Therefore cost estimates are often falsely low.

Using the model of hard-to-heal DFUs, the most significant factors related to high cost have been identified as number of surgical procedures, inpatient hospital stay and time to healing.

The cost of a minor LEA (ie foot level) in Sweden has been estimated as SEK 258,320. For major lower extremity amputation (ie above ankle) the figure is SEK 390,150, of which 77% of the cost occurred after surgery. Amputation was regarded as costly as a result of its consequences, such as the need for additional nursing and institutional care. This is why cost analysis studies should follow up patients until a specific endpoint (eg complete healing or completion of successful rehabilitation). Although many of the new technologies and dressings used to treat hard-to-heal wounds are more expensive than the compared...
treatment, their use may be more cost-effective if they result in more effective or faster healing\textsuperscript{20,21,23,24}. Therefore, when assessing use of resources, it is important not to focus on unit costs such as dressings or procedures, but to adopt a broader view of total resource use. It is crucial to be aware that a specific treatment could be more cost-effective in one group of patients or for one type of wound than in others, or in one setting or country than another.

In a study comparing resource use associated with diabetic foot infection in three European countries, substantial differences were identified in the rate and duration of inpatient stay and in the use of antibiotics and vascular surgery\textsuperscript{27}. The authors conclude that these differences could largely be explained by variations in access to inpatient and outpatient facilities, selection bias of patients, patients’ characteristics, reimbursement and healthcare systems. The same observations could be made from the recently presented Eurodiale study\textsuperscript{28}.

In a comparison of diabetes-related foot lesions in patients in the Netherlands and California, the duration of hospital stay was substantially longer in the Netherlands, whereas the incidence of lower extremity major amputation was higher in the USA\textsuperscript{29}. This has an important implication in the drive to cut costs by early discharge. These variations might be explained by differences in access to healthcare, financing and reimbursement systems\textsuperscript{25}. It is unfortunate that reimbursement systems in some countries appear to favour amputation because of shorter hospital stays and reduced length of time to healing.

A major problem with analyses of cost of disease states is the wide variation in cost criteria used. Difficulties in comparing cost analyses are compounded by variations in care protocols and the economic status of different countries, eg variations in rates of pay to healthcare staff. Significant efforts will be required to standardize criteria for cost analyses that can be used to further identify the most economically effective ways to treat hard-to-heal wounds and to aid useful comparisons between different care protocols and healthcare systems.

\textbf{CONCLUSION}

References

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