



Pressure ulcers in the chronically critically ill patient

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Chronically critically ill (CCI) patients are almost universally at high risk for developing pressure ulcers. They typically have multiple comorbid illnesses (eg, malnutrition, diabetes, renal failure, sepsis), and are ventilator-dependent and immobile for an extended period of time. With such strong predispositions, CCI patients may develop pressure ulcers despite preventive care and continuous monitoring. Some patients bring to the chronic phase of critical illness pressure ulcers that developed during the acute period in the ICU. Others may develop new ulcers or experience a worsening of pressure ulcers during chronic critical illness, even with careful treatment. Although multiple risk factors increase the challenge of pressure ulcer care for the CCI population, steps can be taken to reduce risk and to improve the healing process. This article outlines some of these steps and describes the pressure ulcer surveillance and treatment paradigm developed at Mount Sinai Hospital in New York City. Although there is no conclusive data with respect to the efficacy of some of the treatment and preventive measures described in this paper, our recommendations are informed by both prior research and our extensive clinical experience.

Previous reports have emphasized the risks of pressure ulcers [1–8]. The importance of continuous surveillance and prompt intervention is emphasized to achieve diagnosis and definitive treatment of pressure ulcers at the earliest possible time. Daily examination of “danger areas,” such as the pelvic region and heels, followed by immediate treatment can be expected to reduce the high costs (human and financial), as well as the morbidity and mortality associated

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with pressure ulcers. Treatment goals and appropriate care plans will vary among patients.

We recommend the approach presented in Table 1, which has been effective in our clinical experience. Selected components of this approach are discussed.

The impact of pressure ulcers

Pressure ulcers are associated with pain and discomfort, various other important morbidities, lost productivity, poor utilization outcomes of health care, and huge financial expenditures. These ulcers are highly prevalent in the hospitalized elderly, who comprise the largest proportion of patients with chronic critical illness. The prevalence of pressure ulcers (see Table 2 for staging) is estimated to be at least 10% of hospitalized patients [1,9–11] greater than 20% among patients in nursing homes [1], and 20–30% among patients with spinal cord injury and those in rehabilitation units. Pressure ulcers are also associated with increased mortality, especially if they do not heal [2,3]; even for Stage II ulcers, which extend only into the dermis, the healing rate has been as low as 26% at 6 months [12].

In assessing the total cost of pressure ulcers, the costs of nontreatment should be considered. For example, a small ulcer in a critically ill patient may not be considered a significant clinical problem. However, an untreated small ulcer can progress to the level of bone, thereby becoming a source of extreme morbidity and mortality. As a wound progresses to Stage IV, it becomes increasingly difficult and costly to treat, and is also likely to cause greater pain and discomfort for the patient.

We retrospectively analyzed the charges for a small cohort ($n = 11$) of patients who developed pressure ulcers in the hospital [13], calculating only those charges

Table 1

Treatment goals and care plans for pressure ulcers

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1. Recognition that every patient with chronic critical illness is at great risk for pressure ulcer development.
 2. Aggressive nutritional support with objective parameters of improvement.
 3. Daily assessment of the skin around the ischial, sacral, buttock, and heel areas.
 4. Initiation of a treatment protocol immediately upon recognizing a break in the skin (ie., the emergence of a new wound or presence of an existing pressure ulcer).
 5. Objective measurement by photography (with ruler in the photographic field) of every wound (at minimum, weekly) and thorough, systematic, ongoing documentation of its status.
 6. Establishment of a moist wound-healing environment.
 7. Relief of pressure from the wound.
 8. Debridement of all nonviable tissue.
 9. Elimination of all drainage and cellulitis.
 10. Consideration of biological therapies for patients with wounds that are not healing rapidly after initial treatment.
 11. Physical therapy.
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Table 2
Staging for pressure ulcers

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- Stage I: nonblanchable erythema of intact skin; the heralding lesion of skin ulceration. In individuals with darker skin, discoloration of the skin, warmth, edema, induration, or hardness may also be indicators.
 - Stage II: partial-thickness skin loss involving epidermis or dermis or both. The ulcer is superficial and presents clinically as an abrasion, blister, or shallow crater.
 - Stage III: full-thickness skin loss involving damage or necrosis of subcutaneous tissue, which may extend down to but not through underlying fascia. The ulcer presents clinically as a deep crater with or without undermining of adjacent tissue.
 - Stage IV: full-thickness skin loss with extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures (such as tendon and joint capsule). Undermining and sinus tracts also may be associated with stage IV pressure ulcers.
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Pressure ulcers as staged above, represent the National Pressure Advisory Panel guidelines, published by the Agency for Health Care Policy and Research, Rockville, Md. *Adapted from* Maklebust J. Pressure ulcer assessment. *Clin Geriatr Med* 1997;13:455–473.

that were directly attributable to consequences and complications of nonhealing pressure ulcers. All of the patients were chronically critically ill during the hospitalization. In our sample, hospital-acquired pressure ulcers were associated with an average charge of \$225,615 per patient (one admission per patient). One of the highest costs associated with these pressure ulcers was that of dialysis replacement therapy, necessitated by renal failure due to sepsis attributable to the wound. Morbidities and costs did not appear to be associated with the patients' initial diagnosis (eg, pneumonia), suggesting that these resulted mainly from care required by the wound and independent of the primary illness. Although appropriate early treatment of pressure ulcers involves its own financial costs, we think that it will reduce both long-term financial costs and other complications of pressure ulcers (see Table 3). As always, appropriate treatment will vary with individual patients' care goals.

Although prevention of pressure ulcers is the ideal, prevention is not always possible in the CCI population, many of whom have already developed pressure ulcers in the acute stage of their illness. We postulate, however, that aggressive, ongoing surveillance and early intervention in the context of a comprehensive treatment paradigm will help to halt the progression of pressure ulcers and

Table 3
Costs related to the treatment and management of pressure ulcers

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1. Wound dressings
 2. Management of bacterial colonization and systemic infection (eg, blood cultures)
 3. Care by health professionals
 4. Diagnostic procedure (eg, X-rays)
 5. Therapeutic procedure
 6. Medications (analgesics, antibiotics)
 7. Treatment of secondary infections: eg, renal failure, pneumonia, sepsis
 8. Fees for legal representation in pressure ulcer-related litigation, which is increasingly prevalent
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Delayed treatment of chronic wounds results in morbidity and mortality, prolongs hospitalization, and increases the cost of care.

promote healing, even in the CCI population. Many of the same techniques are successful in both prevention and treatment of pressure ulcers.

Pathogenesis of pressure ulcers: chronic wounds

Wounds can be categorized as either acute or chronic. The healing of acute wounds, such as surgical incisions, occurs sequentially, in a timely fashion [14], and without definitive intervention. Platelets enter the wound and secrete growth factors that subsequently recruit macrophages. Macrophages also release growth factors [15] that cause endothelial cells to migrate and proliferate in the wound, thereby stimulating angiogenesis and collagen synthesis [16]. The orderly and timely reparative process characteristic of acute wounds results in a sustained restoration of anatomic and functional integrity [14]. Chronic wounds, by contrast, may not heal at all if left untreated. Because of an underlying physiologic impairment, chronic wounds fail to heal in an orderly manner, with consequent compromise of anatomic and functional integrity [17]. All pressure ulcers are chronic wounds.

Although observational evidence indicates that the inability to move in response to pressure correlates with the development of pressure ulcers, other factors also contribute. Among these, intriguing evidence indicates that “pressure” ulcers reflect an underlying physiologic impairment of vascular flow and angiogenesis. For example, Auerbach and colleagues established experimentally that angiogenic response is dependent on anatomical location. Experimentally, the angiogenic (new blood vessel growth) response is significantly less in the lower dorsum than in the upper dorsum [18–20]. This might help explain the distribution of nonhealing wounds in the lower back (eg, the sacrum) compared to the upper back over bony prominences. Evidence also exists that wound healing is slowed in the lumbosacral area [21]. In addition to an inability to move in response to pressure, chronically critically ill patients may also have impaired blood flow or impaired angiogenic responses in areas where pressure ulcers commonly develop.

Although clinicians may be unable to change underlying physiology, we propose that aggressive surveillance for and early treatment of pressure ulcers can help avoid their occurrence or reduce their intensity and duration. This paper will now describe a strategy seeking to prevent the formation and progression of pressure ulcers in a CCI patient. Because many prophylactic strategies may also be effective in curing or halting the progression of existing ulcers, preventive and curative treatments are discussed together. Not all of the techniques described below are appropriate for every patient with pressure ulcers. Clinicians (including the wound-healing specialist, primary physician, intensivist, nurse), families, and patients should work together to determine the best care plan in accordance with each individual patient’s realistic care goals. The risks of treatment and nontreatment and the risks and benefits of all available treatment options should be clearly identified, articulated, and understood by everyone involved.

Prevention and treatment strategies

Assessment

Preventive measures for pressure ulcers are standards of ICU care. If an ulcer develops despite these preventive measures, it must be discovered immediately, so that treatment can begin rapidly. Every chronically critically ill patient should have the skin around the pelvic, sacral, and heel areas examined every day; we consider this to be an obligation of physicians as well as of nursing staff. Any break in the skin is an emergent situation, requiring consultation with a clinician having expertise in wound management to initiate a comprehensive treatment plan.

Objective wound measurement

Daily examination of the wound and documentation of the findings in the medical record should be mandatory. Every ulcer should be measured (length, width, and depth) every week. The simple recording of pressure ulcer measurements may suffice, but we have used planimetry to reduce the error that may result from qualitative assessment and notation. Specifically, we photograph the wound, trace its margins in a computer-based program, and calculate the wound area. The ambiguous, but commonly heard phrase “a wound looks good” does not reflect adequate wound assessment, because a wound that “looks good” may nevertheless be failing to contract, epithelialize, and close in a timely manner, and may even be progressing towards osteomyelitis or already be a source of fever or sepsis.

Pressure relief

The goal of tissue load management is to develop an environment that enhances the viability of the soft tissues and promotes healing. In addition to the vigilant use of proper positioning techniques, we have found that support surfaces designed to decrease pressure, friction, and shear while providing levels of moisture and temperature to support tissue health and growth are useful.

Turning

Turning and positioning remain the standard nursing mandate for preventing and treating pressure ulcers in seriously ill and immobile patients. The accepted standard is to reposition immobile and bed-bound patients every 2 hours [22]. The goal of frequent turning is to limit tissue exposure to ischemia or altered blood flow by limiting the time in which tissue is exposed to pressure [23]. There are no randomized controlled trials analyzing the efficacy of frequent turning, which is supported by animal experimental evidence and historically controlled observational study of patients. There is recent indirect and observational evidence suggesting limitations of the efficacy of turning [22], and CCI patients have so many risk factors for developing pressure ulcers that they often develop them despite the most meticulous nursing care and frequent turning schedules.

Based on existing observational evidence, clinical experience, and practice guidelines, frequent turning is part of our clinical protocol for treatment of patients with chronic critical illness, but we recognize that the relationship between turning, pressure relief, and pressure ulcers deserves further study.

Bed therapy

The diversity and supply of pressure-relieving beds have recently proliferated. There is no definitive evidence, however, about which type of bed is best for prevention or treatment of pressure ulcers [23]. Two important factors to be considered are pressure relief and blood flow. In choosing a bed, potential benefits for the patient should be balanced against the equipment cost. Despite initial high cost, pressure relief beds may help reduce overall costs by preventing ulcers from progressing; in the long term, such beds may be most practical and cost-effective for patients with early-stage ulcers. The outcome of cost-benefit decisions about bed therapy will vary among different patients and institutions. Although the evidence is still under consideration, in our clinical experience, alternating air therapy, which appears to promote blood flow and decrease pressure, has been of value in halting progression and accelerating healing of pressure ulcers [24,25].

Direct care of existing wounds

As already discussed, care of existing wounds should be planned within the context of appropriate and realistic overall care goals for the patient. Potential symptom burden associated with treatment, and the “big picture” of prognosis for functional recovery, must always be considered in clinical decision making. For some patients (eg, multiorgan failure or palliative care), the likelihood of poor outcome is extremely high despite even with aggressive treatment to promote pressure ulcer healing; in such cases treatment is not prudent except to the extent it relieves distressing symptoms, as the burdens will exceed the potential benefits. These issues require full discussion among all members of the clinical team and the patient or surrogate decision makers. Aggressive symptom management should be integrated into any treatment plan.

Wound bed preparation

The goal of wound bed preparation is to have well-vascularized granulation tissue without any signs of local infection (including drainage, cellulitis, and odor). Efficacy, defined by contraction, epithelialization, and accelerated closure, is the primary objective in evaluating the various options. Successful treatment should include the removal of all nonviable tissue as part of mandatory wound bed preparation (see Table 4). Proper debridement will simultaneously prepare the wound bed and begin the healing process. Maximal wound bed preparation stimulates the formation of granulation tissue (ie, new collagen formation and angiogenesis) and decreases bacterial burden.

Table 4
Mandatory wound bed preparation for pressure ulcers

Steps

- Removal of nonviable tissue
- Evaluation of pathology; eg, granulation tissue, scar, gangrene, infection, and tumor
- Evaluation and treatment of deep culture; goal to decrease bacteria count
- Pressure relief and stimulation of blood flow (alternating air therapy)

Goals

- Absence of cellulitis and elimination of odor
 - Absence of drainage
 - Stimulation of angiogenesis
 - Stimulation of new collagen formation
 - Stimulation of epithelialization
 - Initiation of closure and contraction
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Debridement

For most wounds, debridement, the simple sharp excision of the superficial tissue, nonviable scar, and infected tissue, will accelerate skin closure. This can be achieved via a variety of methods, but in our clinical experience, mechanical debridement with a scalpel is both the most effective and practical method if maximal healing is the primary care goal. To determine viability (eg, scar versus granulation tissue), the superficial tissue is sent for pathologic analysis. Under sterile conditions, the remaining deep tissue is also sent for pathology and culture. Viable tissue should not be excised, and the wound margins should not be extended more than 1 or 2 mm. If the deep tissue contains scar, necrosis, or bacteria, and the wound is not healing (ie, not contracting), then further intervention is required. This generally entails additional debridement and/or antimicrobial therapy.

Ulcers that penetrate to the level of bone represent osteomyelitis by definition. These require surgical debridement if wound healing is a realistic care goal, although they may not heal even with debridement if the comorbid conditions precipitating the development of the ulcer persist. In our experience, antibiotics should not generally be used for osteomyelitis, because debridement often results in removal of the source of sepsis, and antimicrobial treatment thereafter may have little incremental benefit while promoting drug resistance. However, antibiotics are appropriate if the bone culture is positive and the patient has a persistently high white blood cell count, fever, or a noncontracting wound.

Sepsis is a common and often fatal complication of chronic critical illness, with multiple potential sources. A pressure ulcer may be implicated among other possible foci of infection. We generally regard the ulcer as the main focus if others have been carefully and systematically excluded and close, expert examination of the ulcer confirms its severity. In these cases, aggressive intervention including surgical debridement is indicated if life-prolonging therapy continues to be appropriate in the overall context of the patient's illness. We caution, however, that 1-year mortality remains exceptionally high

for the chronically critically ill patient with a Stage IV ulcer, even with skilled, aggressive treatment.

Moist healing environment

Wound bed preparation can only be considered adequate when there is debridement to the level at which scar and infection are removed or treated. It should also be directed toward creating a moist wound healing environment while facilitating granulation tissue formation. Wounds heal faster when they are kept moist [26,27]. A variety of dressings may be used to maintain a moist wound environment, including hydrocolloid occlusive dressings, semipermeable foam dressings, and polyurethane film. Definitive data to guide selection among these is not available at present. In the past, it was common to change dressings as often as three times a day; today, however, there are many slow-release dressings (eg, cadexomer iodine or silver) that need to be changed only every other day or at most, every day. This may reduce wound exposure to the external environment, decrease the overall time required to perform dressing changes, and locally stimulate the wound bed by decreasing bacterial count. Each local or topical therapy should address the underlying pathology. We have used a combination of topical antimicrobial and collagenase therapies in the successful treatment of pressure ulcers in chronically critically ill patients.

Topical antibiotics

The advantage of topical antibiotics in wounds with local bacterial colonization is well established for burn wounds [28,29]. Because the types of bacteria found in burn wounds are similar to the bacteria found in pressure ulcers, the lessons learned from burn wounds may be transferable to pressure ulcers. However, there are no randomized controlled trials that have provided evidence on the efficacy of topical antibiotics as a treatment for pressure ulcers.

Collagenase

Collagenase is an endogenous protein that maintains a critical role in the formation of new blood vessels. Collagenase-1 (mammalian metalloproteinase-1) is regulated by the angiogenic inducer Cyr61 gene, which stimulates endothelial chemotaxis and proliferation [30]. Agents that inhibit collagenase also inhibit angiogenesis (eg, minocycline) [31–35]. Additionally, α -interferon inhibits angiogenesis, downregulating transcription and protein production of collagenase-IV [36]. Specific angiogenic growth factors may work in part by stimulating endogenous collagenase (eg, expression of acidic fibroblast growth factor may stimulate angiogenesis by mediating mammalian metalloproteinase-1) [37]. There is also decreased collagenase in “aged” endothelial cells, which explains in part why some findings suggest a decreased angiogenic response in elderly patients [38].

Collagenase is used as a topical chemical debridement agent, and is one of several compounds that might indirectly stimulate angiogenesis, a prerequisite for wound healing. The collagenase that can be used at the bedside is not necessarily identical to the form of collagenase studied in the experimental research summarized above. We have observed, however, that application of collagenase to pressure ulcers in chronically critically ill and other patients may be associated with the development of well-vascularized granulation tissue, which appears to prevent fibrous necrosis from recurring and to facilitate contraction and closure.

Wound closure: investigational therapies

Drugs

The field of wound healing has expanded with approval by the Food and Drug Administration of new drugs to accelerate the closure of nonhealing wounds. These include platelet-derived growth factor-BB, also known as becaplermin [39,40], and human skin equivalent [25,41–47], which consists of cultured keratinocytes and fibroblasts. We emphasize again that, based on our clinical experience, the wound bed should be prepared correctly before any therapy (biological or other) is used.

One type of human skin equivalent is a bilayered living skin construct containing an outer layer of live allogeneic human keratinocytes and a second layer of live allogeneic fibroblasts on type-1 collagen dispersed in a dermal layer matrix.

Both cell layers are grown from infant foreskin. The product looks and feels like human skin, but its biologic activity is distinct from that of an autologous skin graft in that it appears to stimulate wound healing (whereas a skin graft is intended only to be a permanent covering). Human skin equivalent has potential value in the treatment of pressure ulcers because it may add additional cells and growth factors to the wound-healing environment [25], where these elements are insufficient due to either deficient synthesis or function. Human skin equivalent has been used with success in the healing of venous stasis ulcers of greater than 1-year duration [42,44], diabetic foot ulcers [25,48], and pressure ulcers [25]. In the absence of local infection, one or two applications of human skin equivalent after proper preparation of the wound bed has been associated with accelerated healing of pressure ulcers we have treated in chronically critically ill patients.

Summary

All chronically critically ill patients are at high risk for development and progression of pressure ulcers. Constant surveillance including daily examination

of the skin must be part of the care protocol. All pressure ulcers are chronic wounds that have an inherent, physiologic impairment to healing. As soon as a pressure ulcer develops, intervention should begin immediately, and a treatment plan should be determined. We believe that early intervention and appropriate treatment, guided by the paradigm we have described, can retard progression and promote healing [49]. Treatment decisions should be made within the context of the patient's overall care goals.

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