Necrotizing soft tissue infections

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Objective: **To provide a contemporary review of the diagnosis and management of necrotizing soft tissue infections.**

Data Sources: **Scientific literature and internet sources.**

Study Selection: **Major articles of importance in this area.**

Conclusions: **The mortality for necrotizing soft tissue infections appears to be decreasing, possibly due to improved recognition and earlier delivery of more effective therapy. Establishing a diagnosis and initiating treatment as soon as possible provides the best opportunity for a good outcome. (Crit Care Med 2011; 39: 000–000)**

KEY WORDS: diagnosis; necrotizing soft tissue infection; outcome; treatment

The earliest report of a necrotizing soft tissue infection (NSTI) dates back to Hippocrates' description of a complication of erysipelas in the 5th century BC. At that time, he wrote "many were attacked by the erysipelas all over the body when the exciting cause was a trivial accident . . . the erysipelas would quickly spread widely in all directions. Flesh, sinews, and bones fell away in large quantities . . . fever was sometimes present and sometimes absent . . . they were many deaths. In the course of the disease was the same to whatever part of the body it spread" (1).

The first recorded modern description of NSTI in the United States was by Joseph Jones, a Confederate Army surgeon, who reported 2,642 cases of "hospital gangrene" with a mortality approaching 50% (2). The French physician, Jean Alfred Fournier, described necrosis of the perineum in five men in 1883, and perineal NSTIs continue to bear the eponym of Fournier's gangrene (3). Brewer and Meleney (4) noted an association between hemolytic streptococcal infection and fascial gangrene, and proposed that the synergistic effects of various bacteria involved in these infections was responsible for their rapid progression. The term "necrotizing fasciitis" was proposed by Wilson (5) in 1952, and depicts the most common feature of these infections, that is, fascial necrosis. More recently, the term "necrotizing soft tissue infection" (NSTI) has been proposed for this collection of infectious diseases since it encompasses all forms of this disease process regardless of anatomical location or depth of infection.

Epidemiology

The Centers for Disease Control and Prevention reports that there are 500 to 1,000 new cases of necrotizing fasciitis reported yearly in the United States (6). A population-based study from the United States estimates that group A streptococcal necrotizing fasciitis has an incidence of 0.4 per 1,000 persons per year (7), while Kaul et al (8) report a similar incidence based on a population-based study in Ontario, Canada. This can be a misleading statistic since only NSTIs due to group A streptococcal infections are enumerated. Clinical experience suggests that the total number of NSTIs greatly exceeds that estimate and may be increasing (9).

The actual incidence of NSTI is difficult to determine in part due to the multiple terms used to describe this clinical entity. Some classify NSTI based on anatomical region, depth of invasion, or the microbial source of infection. It is more appropriate to recognize these different conditions as part of a clinical spectrum of diseases that share common traits and have a similar clinical course. Regardless of its cause or incidence, NSTI is a highly lethal condition that requires early aggressive treatment to optimize survival and avoid complications.

Demographics

The predilection to develop NSTI increases with age (8, 9). Most series report an association of NSTI with a chronic systemic disease, diabetes mellitus, obesity, peripheral vascular disease, alcohol, or intravenous drug use (10–12).

Pathophysiology

In general, any untreated infection can result in local necrosis. NSTIs tend to spread rapidly along tissue planes involving the skin and subcutaneous tissues, fascia, or muscle, causing vascular occlusion, ischemia, and tissue necrosis (13). The specific pathophysiologic mechanisms for necrosis depend on the specific properties of the byproducts produced by the bacteria involved in the infection and are discussed in further detail below. Necrosis can be directly mediated by toxins or occur secondary to vascular involvement.

Classification

NSTIs can be classified according to depth of tissue involvement, severity of infection, or microbiology. Each system has its advantages. The Food and Drug Administration classifies infections of skin and soft tissues as either complicated or uncomplicated. An uncomplicated infection responds to a simple course of antibiotics or incision and drainage. Complicated infections involve deeper tissues and generally require surgical intervention (14, 15). Understanding these definitions is important, especially when interpreting data from clinical trials. However, the utility of the Food and Drug Administration classifica-

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tion is limited by the exclusion of necrotizing infections.

When necrotizing infections are categorized by the microbes involved, there are three types. Each type has its unique epidemiology, pathology, microbial composition, and prognosis. Knowing the type of infection facilitates clinical decision making, including antibiotic selection.

Type I Infections. Type I infections are the most common type of NSTI and are responsible for 80% or more of infections. On average, four or more organisms are isolated from Type I infections, and usually include a mix of aerobic and anaerobic bacteria. The most common aerobic species isolated from these infections are streptococci, however, staphylococci, enterococci, and the family of Gram-negative rods are also found. Bacteroides species are the most common anaerobes involved and are found in more than half of cases, while peptostreptococci are isolated from approximately one-third of patients (16, 17).

The involvement of multiple organisms in Type I infections is likely due to the presence of multiple pathogenic organisms at the nidus of infection and also may represent an underlying failure of the host immune system. Diabetes mellitus, obesity, peripheral vascular disease, chronic kidney disease, and alcohol abuse are commonly found in this group of patients (18, 19).

Several Type I infections are named based on their anatomical location. Fournier's gangrene is a necrotizing infection involving the perineum or genital areas. The preponderance of cases occurs in men. These infections can arise from a genitourinary, colorectal, or dermatologic source, including perirectal abscess, chronic urethral strictures, and Bartholin gland abscesses (20, 21). Ludwig's angina is a polymicrobial infection involving the submandibular space that can extend into the fascial planes of the neck and mediastinum. The latter condition is also known as cervical necrotizing fasciitis. Ludwig's angina and cervical necrotizing fasciitis have several unique features. Stridor and airway obstruction are common complications. Most of the cases have an odontogenic etiology. The microbiology is different from the other Type I infections in that fewer organisms are isolated (2.2 on average) and oral anaerobes, such as fusobacteria and peptostreptococci, are more common (22, 23). In 40% of the cases, infection extends to the mediastinum, which markedly increases mortality (24).

Type II Infections. Type II infections were originally thought to be caused only by β-hemolytic streptococcal species. These infections account for 10% to 15% of NSTIs (25, 26). *Staphylococcus aureus*, especially methicillin-resistant species, is increasingly associated with Type II NSTIs, either as a single isolate or in conjunction with streptococci (27, 28). Typically, these infections originate from an apparent minor injury that provides a portal of entry for the bacteria or creates an environment where hematogenously transported bacteria can thrive. These infections have been associated with nonsteroidal anti-inflammatory drug use in some smaller studies (29).

β-hemolytic streptococci are highly potent and can cause a wide array of diseases, including pharyngitis, erysipelas, glomerulonephritis, and rheumatic fever, in addition to necrotizing infections. These organisms produce a variety of virulent factors, including M protein, Protein F, streptococcal inhibitor of complement, streptolysins, hyaluronidases, streptokinase, cell envelope proteinases, and pyrogenic exotoxins. The capsule of these streptococci resists phagocytosis (30, 31). M proteins also have this property and inhibit the binding of antibodies and opsonins (32). Protein F enhances adherence to epithelial cells while the streptococcal inhibitors of complement inactivate membrane attack complexes (33). Streptolysin O lyses cells; however, the mechanism of toxicity for streptolysin S is unknown (34, 35). Hyaluronidase facilitates spread through the surrounding tissues. Streptokinase is a well-known fibrinolysin and cell envelope proteinases cleave interleukin-8, which prevents polymorphonuclear leukocyte recruitment (36). Finally, these bacteria produce pyrogenic exotoxins, which are a family of superantigens that directly activate T cells resulting in massive cytokine release (37).

S. aureus has fewer but still a potent array of toxins. Panton-Valentine leukocidin causes leukocyte destruction and tissue necrosis. It is produced by the methicillin-resistant *S. aureus* strain USA300 (38, 39). This organism also produces an α-hemolysin that creates pores in host cells (40), and phenol-soluble modulins, which attract and lyse polymorphonuclear leukocytes (41).

Type III Infections. Clostridial myonecrosis is the prototypical Type III infection. These are the least common NSTI, accounting for <5% of all infections. Clostridia are ubiquitous, Gram-positive, anaerobic, spore-forming bacilli found in soil. They are not strict anaerobes, but nonetheless need to be inoculated deeply into tissues in an environment of low oxygen tension to be pathogenic. These infections typically occur as a result of a deeply penetrating wound or a crush injury that is accompanied by local devascularization (42–44). Clostridial myonecrosis has also been reported following intestinal surgery, black tar heroin injection (skin popping) (45), and in association with obstetrical complications, such as retained placenta, prolonged rupture of membranes, and spontaneous abortion (46, 47). *Clostridium perfringens* is the most common pathogen of this species. Spontaneous clostridial myonecrosis also can be due to *C. septicum* and occurs in association with a gastrointestinal or hematogenous malignancy in 80% of patients (48). In contrast to patients with traumatic myonecrosis, those with spontaneous infections are often immunosuppressed or have a malignancy (49).

Type III infections are highlighted by rapid progression, which can measure up to 2 cm/hour. This feature is related to an impressively muted host response (50) and an elaborate set of bacterial toxins (48). The α-toxin has phospholipase C activity and is lytic to many cell lines, including red blood cells, myocytes, fibroblasts, platelets, and leukocytes. This toxin may also decrease inotropy, release histamine, and cause platelet aggregation (51–54). The θ-toxin, like the staphylococcal α-hemolysin, forms pores in host cells and causes direct vascular injury as well as hemolysis and destruction of white blood cells (55). The clostridial κ-toxin has collagenase properties (56), and γ-toxin is a hyaluronidase (57).

Other Infections. Several water-borne bacterial infections can cause NSTI and are not readily classified by the abovementioned system. Necrotizing infections following exposure to a water-borne agent are almost always attributable to either *Vibrio vulnificus* or *Aeromonas hydrophilia*. *Vibrio* is a Gram-negative bacterium that occurs in marine and estuarial environments (58, 59). The majority of infections related to *Vibrio* occur after handling seafood, often during a recreational water activity (60, 61). Most patients who develop these infections have underlying liver disease, such as alcoholic cirrhosis, chronic hepatitis, or hemochromatosis (62). Virulence is related to a toxin that produces a reactive

oxygen species (63). *Aeromonas hydrophilia*, formerly considered part of the *Vibrio* family, is a Gram-negative bacillus that is primarily a freshwater organism. Infections can occur in immunocompetent hosts, as demonstrated by the high rates of wound isolates after the 2004 Indian Ocean tsunami (64). The exact complement of toxins produced by these bacteria is unknown.

Rarely, NSTI can be due to fungi. The three most common human pathogens are *Rhizopus*, *Mucor*, and *Rhizomucor* (65). Rhino-orbital-cerebral and cutaneous involvement typifies these unusual NSTIs.

Mucormycete spores are ubiquitous and can migrate to susceptible soft tissues by inhalation or ingestion, or can be directly inoculated into wounds. The intact immune system handles routine fungal exposure easily (66); however, a high degree of contamination or depressed immune system can result in infection. Conditions predisposing to these infections include diabetes mellitus, hematologic malignancies, organ transplantation, steroid use, acquired immunodeficiency syndrome, treatment with desferoxamine, and iron overload (65, 67, 68). *Rhizopus* contains a ketone reductase, which allows the fungus to grow in the glucose-rich, acidic environment frequently found in patients with diabetic ketoacidosis (69). The growth and pathogenicity of *Rhizopus* is also increased by chelated iron, which explains why the iron chelator desferoxamine as well as iron overload facilitates infection (70). Of interest, statins inhibit these fungi *in vitro*, which may in part explain the decline in these infections in the United States over the last two decades (71).

Hyphae from these organisms directly invade the vasculature, causing infarction and necrosis (72). The rhino-orbital-cerebral syndrome is initiated with the implantation of fungal spores in the paranasal sinuses, which then spread throughout other sinuses. Contiguous structures become involved rapidly with a resultant classic black eschar of necrotic tissue spreading to the face, orbits, cavernous sinus, and carotid canal. Cutaneous mucormycosis spreads rapidly as the vasculature becomes involved and thromboses (66, 73, 74). Disseminated fungemia is rare (65, 75).

Presentation

The initial presentation of the various forms of NSTIs is similar. As the disease progresses, the presentation becomes characterized by the specific type of infection described above. The initial symptom is usually pain at the site of infection. Typically, the degree of pain is disproportionate to the local physical findings (76). The initial appearance of the skin can be deceptive. Edema and minimal erythema are common early in the course of these infections. During this phase of infection, systemic signs are often limited to low grade fever, tachycardia, and mild tachypnea. As the infection progresses, pain at the advancing front can be intense, while areas of necrosis become insensate. Blistering, crepitus, bullae, or hemorrhagic blebs will eventually develop. Ulceration, a bronze discoloration of the skin, and a foul odor are common (11, 77). As with other anaerobic infections, the putrid odor can be intense (78). Toxic shock syndrome and skin desquamation can occur. The toxin-mediated suppression of polymorphonuclear leukocytes produces a bland "dishwater pus." Mucormycotic infections form a black eschar, which is initially noted in the nasal mucosa and palate and can eventually involve cranial nerves resulting in blindness, loss of extraocular movements, and facial numbness (74). Systemic inflammatory response, sepsis, and profound shock with multisystem organ failure are common sequelae of all forms of necrotizing infections.

Diagnosis

The diagnosis of NSTI is obvious when patients present with skin changes indicative of necrosis. The challenge for clinicians is to distinguish necrotizing infections from the much more common nonnecrotizing variety early in the course of disease when pathognomonic physical findings are absent. Various adjunctive methods have been investigated, including radiographic studies, laboratory scoring systems, and pathologic examination.

Plain radiographs can be helpful if gas is demonstrated in the soft tissues; however, this only occurs in one-third of patients with NSTI (12, 79). Computed tomography has a sensitivity of approximately 80% for the presence of soft tissue gas and inflammatory changes, but computed tomography is not very specific for NSTI (80, 81). A recent report by Zacharias et al (82) suggests that newer scanners have improved specificity (81% in their study) with a negative predictive value of 100%. However, not all patients in their study underwent operation so the actual disease-free population was imprecisely defined. At very least, this study suggests that computed tomography may have a role in the diagnosis of NSTIs, although further corroboration about its precision is needed. Magnetic resonance imaging can differentiate some necrotizing from non-necrotizing infections; however, its low sensitivity (80%–90%) and specificity (50%–55%), and the time required to complete a magnetic resonance imaging study tend to limit its usefulness (11, 83, 84).

Multiple scoring systems have been suggested to aid in the diagnosis of NSTI. The scoring system that has been most extensively evaluated is the Laboratory Risk Indicator for Necrotizing Fasciitis (85). Points are assigned based on the levels of C-reactive protein, white blood cell count, hemoglobin, and serum sodium, creatinine, and glucose. While the positive and negative predictive values in the initial publication were promising, subsequent analyses have failed to confirm the initial results and it is no longer used extensively (78, 86, 87).

Majeski and John (78) have described a technique of bedside tissue biopsy with immediate frozen-section evaluation. While their results were promising, the logistics of performing the frozen section during the night are challenging. Furthermore, there seems to be little benefit in doing a biopsy at the bedside rather than taking the patient to the operating room where exploration of deeper tissues can be done.

In summary, adjunctive diagnostic studies and scoring systems have limited utility for the diagnosis of NSTI. Direct examination of the involved tissues is usually required to make the diagnosis. Given the potential lethality and morbidity associated with delays in diagnosis and treatment of these infections, there should be a very low threshold for operative exploration if the diagnosis is under consideration.

Treatment

There are four important principles that are critical for the immediate treatment of NSTI. These are: 1) fluid resuscitation and correction of electrolyte and acid-base abnormalities; 2) initiation of antimicrobial therapy; 3) immediate debridement of necrotic tissues; and 4) support of failing organ systems. Although all of these tasks are important, early surgical debridement is the single parameter that is most associated with survival; however, the other components of care

Table 1. Recommended antimicrobial regimens for the treatment of necrotizing soft tissue infections (97, 101)

Drug Regimen by Type of Infection	Adult Dose (Intravenous)
Type I Infections (Mixed)[a]	
Piperacillin-tazobactam	3.375 gm q6h
Plus	
Clindamycin	600–900 mg q6–8h
Plus	
Ciprofloxacin	400 mg q12h
Imipenem-cilastatin	500–1000 mg q6h
Meropenem	1 gm q8h
Type II Infections	
Clindamycin	600–900 mg q6–8h
Plus	
Penicillin	2–4 million units q4–6h
Or	
Linezolid (if allergic to penicillin)	600 mg q12h
Or	
Vancomycin (if allergic to penicillin)	30 mg/kg/day in 2 divided doses
Type III Infections	
Clindamycin	600–900 mg q6–8h
Plus	
Penicillin	2–4 million units q4–6h
Vibrio or *Aeromonas* Infections	
Doxycycline	1 gm q12h

must be implemented rapidly to reduce the likelihood of an adverse event or delay of operation (12–14).

Fluid Resuscitation and Correction of Electrolyte and Acid-base Abnormalities. The major goal of fluid resuscitation is to restore intravascular volume, which is always depleted among patients with NSTI due to the fluid shifts associated with the response to infection. Optimizing blood and intravascular volume also improves organ and tissue perfusion and will help reduce the incidence of later organ system failure. Additionally, restoration of intravascular volume helps avoid hypotension during operation. Excision of necrotic tissues frequently leaves a large body surface area that leaves the patient subject to additional absorptive fluid loss after the procedure.

Crystalloid fluids are first-line treatments and lactated Ringer's solution is the preferable solution since these patients usually have acidemia. Colloid solutions can be useful for patients who are malnourished, have liver disease, or do not have a satisfactory response to large volumes of crystalloid. Blood should be given when there is anemia, which sometimes may occur due to hemolysis caused by toxins produced by some of the infecting organisms. Fresh frozen plasma and platelet transfusions are reserved for patients who have coagulopathy and thrombocytopenia, respectively.

The most common electrolyte disturbances among patients with NSTI are mild hyponatremia and hypocalcemia, the latter due to precipitation of calcium in necrotic subcutaneous fat. Lactated Ringer's solution or 0.9% normal saline used for resuscitation will usually correct the mild hyponatremia that is common in NSTI patients while calcium gluconate can be given to correct hypocalcemia. Hyperglycemia should be treated with insulin. Because low serum albumin can result in decreased serum calcium, ionized calcium should be used to guide calcium replacement. The adequacy of fluid replacement therapy should be assessed by measuring central venous pressure and urine output in addition to reassessing vital signs.

Initiation of Antimicrobial Therapy. Prompt initiation of antimicrobial therapy is an important component of the treatment of NSTI. Although adjunctive to debridement, antibiotics are necessary to ameliorate or prevent the systemic manifestations of infection, including sepsis syndrome and septic shock. Antibiotics do not penetrate necrotic tissue, so they should not be considered a replacement for operation.

The choices for antimicrobial therapy are listed in Table 1. In general, it is best to initiate treatment with a combination of broad-spectrum agents in all but the most minor infections. The treatment choice should be refined later based on culture results and patient response. The increased prevalence of methicillin-resistant *S. aureus* in both the community and hospital environments mandates empirical treatment for these strains (88). Clindamycin has been demonstrated to possess the unique property of suppressing toxin production by *S. aureus*, hemolytic streptococci, and clostridia and should be included when these organisms are present or suspected and for all patients with hypotension, coagulopathy, or organ system failure (89). Vancomycin or linezolid can be used for clindamycin-allergic patients, but these agents do not possess the same toxin-suppressing properties.

Because of the increased prevalence of resistant Gram-positive organisms, combination therapy is used for most patients with NSTI, particularly if the fascia is involved. Suggested regimens are outlined in Table 2. Doxycycline or a related tetracycline should be added when infection is thought to be due to *Vibrio* or *Aeromonas*. Patients with renal or hepatic failure may need to have dosage adjustments. As with other infections, it is important to refine the choice of antimicrobial treatment based on the results of blood cultures and the antimicrobial sensitivities of the organisms isolated from cultures of the tissue obtained during debridement.

Operative Debridement. Early and complete operative debridement of necrotic tissue is the mainstay for treatment of NSTI (10, 11). Inadequate debridement has been associated with a seven-fold increase in death from this disease (90), and delay in operation has been associated with a nine times greater likelihood of death (17). The area of necrosis often extends beyond what is anticipated based on external appearance of the skin due to thrombosis of the dermal capillary beds that precedes skin necrosis. All obviously necrotic skin, subcutaneous tissue, fascia, and muscle must be excised. When there is crepitance present over an area of normal appearing skin, an exploratory incision should be made throughout the involved area to determine whether the underlying tissues are viable. The presence of soft tissue gas does not mandate excision as long as the underlying tissues are viable. This crepitance often resolves after the necrotic tissue is removed.

Amputation should be reserved for situations when the affected limb either is not viable or is not expected to be functional following debridement (91). Amputation also may be necessary to control infection when there is extensive limb

involvement, which is more common among patients with diabetes mellitus or intravenous drug abuse. The need for amputation has been reported to range from 25% to 50% of patients with extremity-based infections. Amputation is more likely when lower extremities are involved (10, 91). A diverting colostomy may be needed to avoid soiling of the perineum. This is usually necessary when there is contiguous involvement of the perianal area and the patient is incontinent of stool (10). Orchiectomy is rarely needed when Fournier's gangrene is present, since the blood supply to the testicles is usually preserved (20).

The debrided area should be covered with a layer of 0.9% normal saline-soaked gauze and an absorbent dressing such as an ABD or burn pad. It is recommended that these patients be re-explored in the operating room under an anesthetic within 24 hrs, which usually allows for completion of resuscitation and attendance to any abnormal medical conditions. Since it is common to find additional areas of necrosis that need to be debrided, evaluation in the operating room is more comfortable for the patient and allows for more thorough exploration of the involved areas. Subsequently, dressings should be changed two to three times daily. Dilute sodium hypochlorite (Dakin's solution) can be substituted for normal saline if excessive local bacterial contamination develops later. The use of a vacuum-assisted closure system can accelerate wound contraction and time to closure, but this should not be initiated until the necrosis and infection are controlled and granulation tissue has appeared (92). The exposed area should not be covered with skin grafts before the acute infection has resolved.

Support of Failing Organ Systems. Patients who are hypotensive after appropriate fluid resuscitation should receive vasopressors and should be monitored in an intensive care unit (77). Norepinephrine (0.02–0.08 μg/kg/min), vasopressin (0.1–0.4 IU/min), or dopamine (5–10 μg/kg/min) can be used to improve perfusion. Monitoring of arterial and central venous pressures as well as urinary output should be done. Often, the best way to support organ systems is by rapidly controlling the infectious process, which then allows the physiologic environment to return to normal.

Other Adjunctive Measures. Intravenous immunoglobulin (IVIG) has been advocated for the treatment of NSTI due to streptococci and staphylococci (93). Supporters of its use believe that IVIG provides antibodies that can neutralize circulating exotoxins produced by these organisms and may modulate the systemic inflammatory response induced by cytokine stimulation. These actions would potentially reduce the detrimental effects of exotoxins on tissue necrosis and negate the effects of cytokines on failing organ systems. The evidence supporting the use of IVIG for treatment of NSTI is controversial, although there are retrospective as well as prospective studies that have demonstrated some benefit (93). If IVIG is used, it should be given selectively to patients with severe sepsis due to either staphylococcal or streptococcal infections. Plasma exchange therapies have not been demonstrated to be beneficial to patients with NSTI.

Hyperbaric oxygen (HBO) therapy also has been proposed for the treatment of NSTI. HBO results in greater oxygen tensions in perfused body tissues (94). Recommendations for its use are based on experimental and human studies that show inhibition of exotoxin production by clostridia (95). The results of human studies are conflicting and most prospective studies fail to show a benefit for HBO in these circumstances. Its use is further limited by delays in definitive care when transferring a patient to a facility that has HBO therapy available. A recent retrospective comparison of outcomes of NSTI at two hospitals failed to demonstrate a survival advantage to HBO and there were actually a greater number of operative debridements done in patients who received HBO (96). The low mortality in both HBO-treated and untreated groups suggests that patients at high risk for death were not included.

Both IVIG and HBO therapy may be effective in certain situations; however, operative debridement should not be delayed to initiate these therapies. Most patients with NSTI have polymicrobial infections, and culture results are usually unavailable for at least 48 hrs.

Later Treatments. Nutritional support should be initiated after the infection and septic response are controlled. Enteral feeding is preferred; however, parenteral nutrition can be used when the enteral route is not possible or practical. Appropriate vitamins (vitamin A, C, and D) and minerals such as zinc should be provided since these can promote wound healing.

Split-thickness skin grafts and various flaps are useful to restore epithelial continuity to the debrided areas. Coverage should not be done until after the septic response has abated, the patient is recovering, and there are early signs of healing over debrided areas. As mentioned above, the use of vacuum-assisted closure systems can reduce the area that will need coverage.

Mortality

The mortality for NSTI has declined from historical reports of 33% to 40%. A review of >3,000 patients reported between 1980 and 2008 demonstrated an overall mortality of 23.5%, with mortality <22% since 1999 (97). A recent presentation of NSTI from the National Surgical Quality Improvement Program reported a mortality rate of only 12% (ref). The single most common factor associated with increased mortality was delay to operative debridement (10, 11, 91, 98). Other parameters that have been associated with worse mortality in large series of patients include age >50 yrs, greater extent of body surface area involved, lactic acidosis, organ dysfunction at admission, hypotension, immune compromise, and a white blood cell count >30,000/mm^3 (10, 11, 91, 92, 98, 99).

Long-Term Outcomes

Light et al (100) have reported a large consecutive single-institution series of long-term outcomes of patients with NSTI compared to population-based mortality rates. Among patients who survived at least 30 days after initial hospitalization, 25% died over a mean follow-up period of 3.3 yrs. Median survival was 10.0 yrs. The major reasons for late death included cardiopulmonary diseases, diabetes mellitus, malignancies, and infectious causes. Deaths related to infection among these survivors of NSTI were considerably greater than those predicted for the population at large, suggesting that patients who suffer NSTI may have an inherent defect in host defenses.

CONCLUSION

The mortality for NSTIs appears to be decreasing over recent years, possibly due to improved recognition and earlier delivery of more effective therapy. Establishing the diagnosis and initiating treatment as soon as possible provides the best opportunity for a good outcome. Continued improvements in the education of

healthcare practitioners about the subtle presenting signs and symptoms of this disease process and advancements in the management of these critically ill patients should result in improved outcomes in the future.

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