Development of a Computed Tomography-Based Scoring System for Necrotizing Soft-Tissue Infections

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Background: Necrotizing soft-tissue infections (NSTIs) are associated with significant morbidity and mortality, but a definitive nonsurgical diagnostic test remains elusive. Despite the widespread use of computed tomography (CT) as a diagnostic adjunct, there is little data that definitively correlate CT findings with the presence of NSTI. Our goal was the development of a CT-based scoring system to discriminate non-NSTI from NSTI.

Methods: Patients older than 17 years undergoing CT for evaluation of soft-tissue infection at a tertiary care medical center over a 10-year period (2000–2009) were included. Abstracted data included comorbidities and social history, physical examination, laboratory findings, and operative and pathologic findings. NSTI was defined as soft-tissue necrosis in the dictated operative note or the accompanying pathology report. CT scans were reviewed by a radiologist blinded to clinical and laboratory data. A scoring system was developed and the area under the receiver operating characteristic curve was calculated.

Results: During the study period, 305 patients underwent CT scanning (57% men; mean age, 47.4 years). Forty-four patients (14.4%) evaluated had an NSTI. A scoring system was retrospectively developed (table). A score >6 points was 86.3% sensitive and 91.5% specific for the diagnosis of NSTI (positive predictive value, 63.3%; negative predictive value, 85.5%). The area under the receiver operating characteristic curve was 0.928 (95% confidence interval, 0.893–0.964). The mean score of the non-NSTI group was 2.74.

Conclusions: We have developed a CT scoring system that is both sensitive and specific for the diagnosis of NSTIs. This system may allow clinicians to more accurately diagnose NSTIs. Prospective validation of this scoring system is planned.

Key Words: Necrotizing soft-tissue infection, Necrotizing fasciitis, Computed tomography, Debridement of soft-tissue infections.

(*J Trauma.* 2011;70: 894–899)

Necrotizing soft-tissue infections (NSTI) represent a spectrum of surgical emergencies associated with significant morbidity and mortality. NSTI is a broad term that encompasses anatomic diagnoses, depth of tissue involvement, and microbial pathogens.[1] Although NSTI is a relatively infrequent diagnosis, a high index of suspicion is required as morbidity and mortality are directly proportional to time to intervention.[2,3] The recommendation of early debridement for NSTI has been entrenched in the medical literature since World War I.[4,5]

Because securing the diagnose of NSTI may be difficult based on physical examination alone,[6] laboratory and radiographic studies are often used to facilitate early intervention. Although laboratory analysis is helpful,[7,8] computed tomography (CT) is a useful diagnostic tool for patients in whom the diagnosis and the need for operative management is not clear. NSTI has classically been associated with the presence of air in the soft tissue on plain radiography or CT.[9] However, the presence of soft-tissue gas may be limited to infections with anaerobic organisms or late stages of disease presentation.[10] With recent advancements in the quality and versatility of cross-sectional imaging and reformatting of those images, it is likely that radiographic criteria can be identified in a reproducible fashion to assist clinicians in diagnosing NSTI.[11]

The prototypical patient with NSTI is no longer a soldier with a puncture wound, but often an immunocompromised individual with a polymicrobial infection. As such, guidelines for diagnosis and treatment of NSTI must be re-examined in the context of new technology, more widespread intravenous (IV) drug abuse, and the increase in the immunosuppressed populations (diabetics, patient receiving chemotherapy, transplant recipients, etc.). Our hypothesis is that a CT-based scoring system could be developed to assist clinicians in establishing the diagnosis of NSTI.

PATIENTS AND METHODS

Patient Selection

After obtaining approval from the Yale University Human Investigations Committee, the Yale New Haven Hospital patient registry was queried. Through International Classification of Diseases—9th Revision (ICD-9) codes, we identified patients admitted to the hospital between January 1, 2000, and December 21, 2009, with the diagnoses of necrotizing fasciitis (ICD-9 code 728.86), or cellulitis, and abscess (ICD-9 code 682.00–682.99). We narrowed our search to include only patients older than 17 years undergoing CT to aid in the diagnosis of NSTI. Basic demographics (gender, age), comorbidities (obesity, diabetes, peripheral vascular

Submitted for publication October 7, 2010.
Accepted for publication January 31, 2011.

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Presented as a poster at the 69th Annual Meeting of the American Association for the Surgery of Trauma, September 22–25, 2010, Boston, Massachusetts.
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DOI: 10.1097/TA.0b013e3182134a76

disease, human immunodeficiency virus [HIV]), history (organ transplant, trauma at the affected site, history of chemotherapy or radiation therapy), and social history (ethanol or IV drug use) were abstracted. Physical examination findings (temperature, heart rate, and systolic blood pressure on presentation; and presence of tissue erythema, tenderness, crepitance, necrosis, and bullae) and laboratory findings (white blood cell count, hemoglobin, serum sodium, bicarbonate, creatinine, lactic acid, and glucose) were also abstracted. Timing and details of surgical debridement (number of debridements, use of vacuum assisted closure devices, and split-thickness skin grafts) and antibiotic therapy, as well as wound microbiology, were noted. NSTI was defined as soft-tissue necrosis in the dictated operative note or the final surgical pathology report. Outcomes, including length of stay, in-hospital mortality, and discharge status (home, extended care facility, or against medical advice) were recorded for all patients.

Computed Tomography

Images were obtained over a 10-year period (January 2000–December 2009), which included upgrades from a 4- to 16-slice scanner (January 2004) and 16- to 64-slice scanner (October 2007). Images were reviewed by a single radiologist blinded to all patient data. The CT scan date, prescription, and use of IV contrast material (contrast was nonionic, isosmolar, and administered in standard volumes) were recorded. If a CT scan was performed without IV contrast, the rationale (allergy, acute or chronic renal insufficiency, or prior contrast administration within 24 hours) was recorded. The radiologist reviewed the depth of inflammation on CT and the following variables, which were treated dichotomously: vessel thrombosis, fluid tracking, perifascial air, skin thickening, lymphadenopathy, abscess, muscle edema, and fat stranding.

Statistical Analysis

All information was entered and maintained in an Excel (Microsoft Office 2007, Microsoft Corp, Redmond, WA) spreadsheet. SPSS version 16 (SPSS, Chicago, IL) was used for statistical analysis. Univariate analysis was performed with χ^2 and the Student's t test, or logistic regression analysis was performed whenever appropriate. Normally distributed data are reported as mean values (with SD), and non-normally distributed data are reported as the median value. A p value <0.05 was considered statistically significant. Based on the disparate incidence of CT scan findings in the NSTI and non-NSTI groups, a scoring system was developed and the area under the receiver operating characteristic (ROC) curve was optimized.

RESULTS

A total of 715 patients were identified by ICD-9 codes. CT scans were performed on 305 patients to aid in the diagnosis of NSTI (in the group that did not undergo CT [n = 410]: 22 patients underwent immediate surgical debridement for NSTI; 141 patients underwent surgical therapy for a non-NSTI; and 247 patients were treated with antibiotics alone). Based on the criteria identified above, 44 of the 305 patients undergoing CT were assigned to the NSTI group and 261 of the 305 patients were assigned to the non-NSTI group (Fig. 1). The median length of stay for the

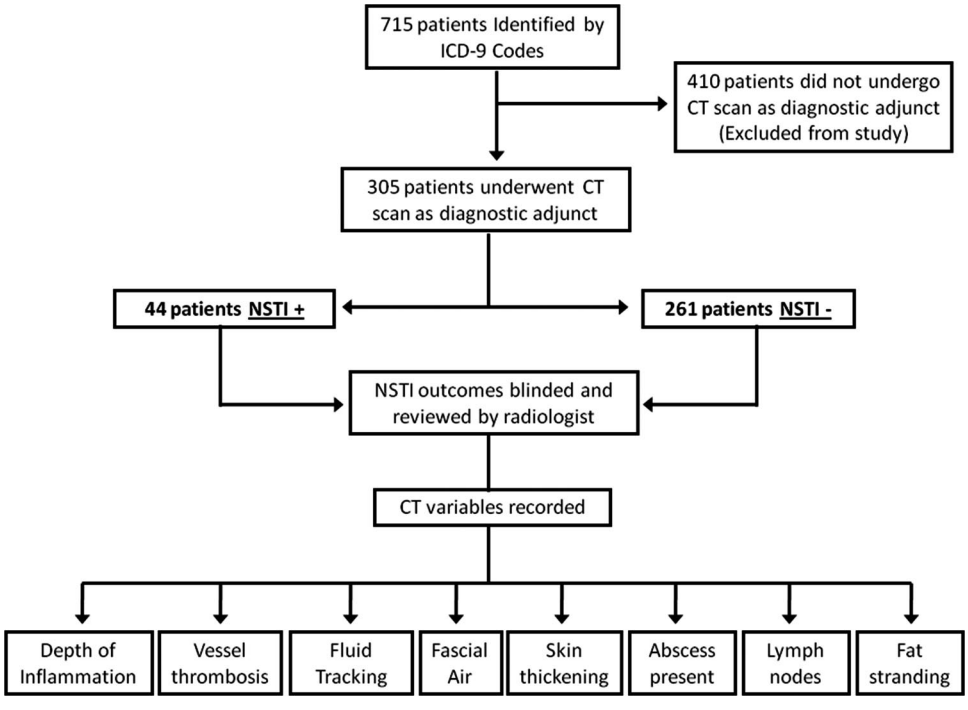

Figure 1. Study design including radiographic variables reviewed.

non-NSTI and NSTI groups was 6 days and 23 days, respectively ($p < 0.001$).

There was no statistically significant difference between the NSTI and non-NSTI groups in terms of gender (NSTI, 50% men; non-NSTI, 58% men), mean age (NSTI, 47.1 ± 10.2; non-NSTI, 48.1 ± 12.2), incidence of obesity (body mass index > 30 kg/m^2; 29.5% NSTI, 21.2% non-NSTI), or hemodynamic instability at presentation (systolic blood pressure < 90 mm Hg, or heart rate > 110 beats/min; 20.4% NSTI, 14.9% non-NSTI). The incidence of immunosuppression (diabetes, HIV, chemotherapy or radiation therapy, organ transplant, or a history of prior trauma at the site of infection) was higher in the NSTI group than the non-NSTI group (Fig. 2). On physical examination, necrosis (45.4% NSTI, 4.9% non-NSTI, $p < 0.001$) and bullae (27.2% NSTI, 3.8% non-NSTI, $p < 0.001$) were noted more frequently in the NSTI group, whereas there was no difference in the presence of crepitance, erythema, and tenderness. NSTI was associated with pronounced leukocytosis, anemia, hyponatremia, metabolic acidosis, and acute kidney injury (Table 1).

In the NSTI group, parenteral antibiotics were initiated in all 44 patients within 12 hours of arrival at the emergency department (mean 4.2 hours ± 1.2 hours from emergency department registration to antibiotic administration). These 44 patients underwent a mean of 3.1 (±1.8) debridements under general anesthesia; with a mean time of 15.1hours (±7.5 hours; range, 2–72 hours) from initial log in to the emergency department until debridement (5 patients were debrided >24 hours from initial presentation). The anatomic distribution and final microbiological cultures and sensitivities varied (Fig. 3). Eleven of the 44 patients (25%) had a polymicrobial infection. Negative pressure wound therapy and split-thickness skin grafts were used for wound coverage in 11 (25%) and 9 (20.4%) patients, respectively. Mortality in the NSTI group was 3 of the 44 (6.8%); 15 of the 44 (34.1%) patients required discharge to a skilled nursing facility secondary to physical deconditioning and wound management requirements.

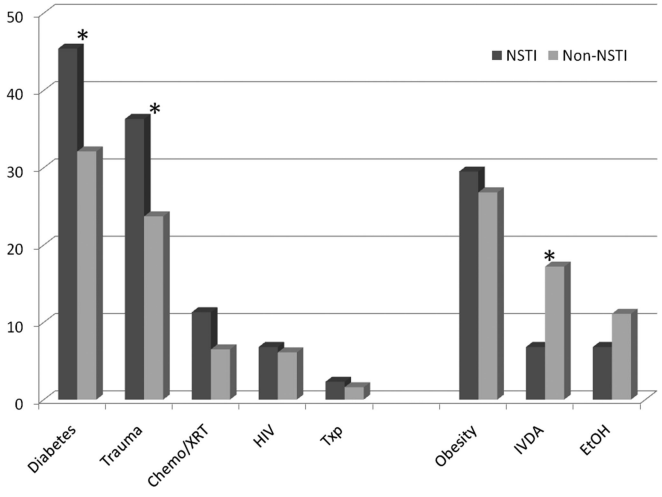

Figure 2. Presenting comorbidities and social habits in the NSTI and non-NSTI groups. An asterisk denotes a p value < 0.05. XRT, radiation therapy; TXP, solid organ transplant; IVDA, intravenous drug abuse; EtOH, alcohol abuse.

The CT scans of 305 patients (44 in NSTI group and 261 patients in the non-NSTI group) were reviewed by a single blinded radiologist (Fig. 1). IV contrast was used in 220 of the 305 studies (72.1%); the most frequent rationale for a noncontrast study was an evidence of acute kidney injury or chronic renal insufficiency. The incidence of muscle or fascial involvement (86.3% NSTI, 13.7% non-NSTI; $p < 0.001$), fluid tracking in subcutaneous tissues (38.6% NSTI, 13.0% non-NSTI; $p < 0.001$), perifascial gas (43.1% NSTI, 1.9% non-NSTI; $p < 0.001$), lymphadenopathy (45.4% NSTI, 26.8% non-NSTI; $p = 0.03$), and subcutaneous edema (100% NSTI, 88.5% non-NSTI; $p = 0.04$) were higher in the NSTI group. There was no difference in the frequency of abscess formation, fat stranding, or vessel thrombosis (vessel thrombosis was unable to be assessed, however, in 56.7% of studies; Table 2).

Given the increased frequency of perifascial air, muscle/fascial edema, fluid tracking, lymphadenopathy, and subcutaneous edema in the NSTI group, a numerical CT scoring system was developed (Table 3) with more points assigned to those findings associated with higher odds ratios. Validation parameters for a score of >6 points included sensitivity (86.3%), specificity (91.5%), negative predictive value (NPV) (85.5%), and positive predictive value (PPV) (63.3%). Validation parameters for fascial air alone yielded a sensitivity of 44.1%, specificity 61.1%, NPV 35.2%, and PPV 58.9%. The mean scores of the NSTI and non-NSTI group were 8.57 (±1.22) and 2.74 (±0.65),

TABLE 1. Laboratory Values, at Presentation, for the NSTI and Non-NSTI Groups

	NSTI (n = 44)	Non-NSTI (n = 261)	*p*
Mean WBC (×10^3; nl range, 4–10)	18.7 (±4.4)	12.8 (±3.3)	<0.001
Mean HgB (mg/dL; nl range, 12–16)	11.8 (±1.6)	12.6 (±1.5)	0.02
Mean serum sodium (mm/L; nl range, 135–145)	132.1 (±4.4)	134.2 (±5.1)	0.13
Mean serum creatinine (mg/dL)	1.89 (±0.44)	1.11 (±0.22)	<0.001
Mean serum bicarbonate (mEq/L; nl range, 22.5–25)	21.1 (±4.1)	23.2 (±3.1)	0.007
Mean serum glucose (mg/dL)	254.5 (±66.2)	152.8 (±44.2)	<0.001
Mean serum glucose (non-diabetic patients) (mg/dL)	112 (±31.4)	108 (±21.1)	0.67
Mean serum lactate (mmol/L; nl <2.2)	2.8 (±1.9) (n = 21)	2.1 (±1.0) (n = 53)	0.54

WBC, white blood cell; HgB, hemoglobin.

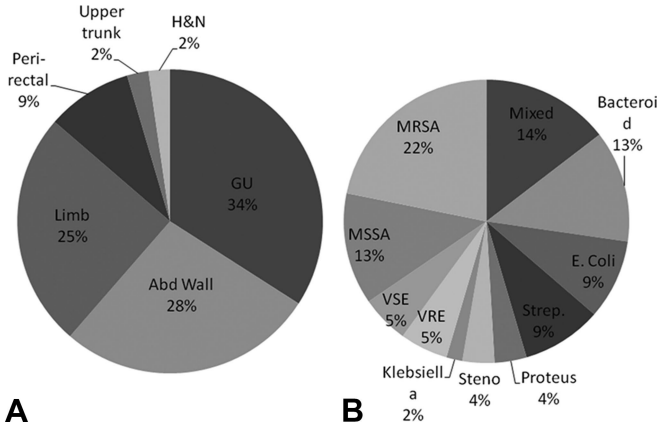

Figure 3. Anatomic distribution of NSTI *(A)*, with final microbiological results *(B)*. H&N, head and neck; GU, genitourinary; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; VRE, vancomycin resistant enterococcus sp.; VSE, vancomycin-sensitive enterococcus sp.; Steno, *Stenotrophomonas maltophilia*.

TABLE 2. CT Scan Findings in the NSTI and Non-NSTI Groups

	NSTI (n = 44)	Non-NSTI (n = 261)	*p*	Odds Ratio
Fascial air	43.1	1.9	<0.001	22.6
Muscle/fascial edema	86.3	13.7	<0.001	6.3
Fluid tracking	38.4	14.7	<0.001	2.6
Lymphadenopathy	45.4	26.8	0.03	1.7
Subcutaneous edema	100	88.5	0.04	1.1
Thrombosis	7.7	8.4	0.88	—
Abscess	27.9	35.3	0.55	—
Fat stranding	97.7	91.2	0.91	—

TABLE 3. NSTI Scoring System

Variable	Points
Fascial air	5
Muscle/fascial edema	4
Fluid tracking	3
Lymphadenopathy	2
Subcutaneous edema	1

respectively. In subset analysis, the mean score for patients in the NSTI group who did not have fascial gas present on CT was 7.19 (±1.1). An ROC curve was generated for our scoring system and the area under the ROC curve was determined (Fig. 4). The area under the ROC curve was 0.928 (95% confidence interval 0.893–0.964).

DISCUSSION

NSTIs are associated with significant in-hospital morbidity and mortality[12,13] and limitations in functional status after hospital discharge.[14] Given that early diagnosis and treatment are paramount, investigators have often

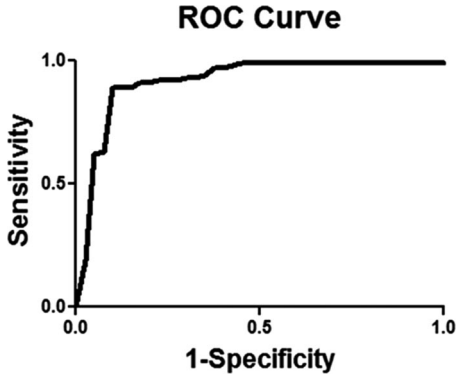

Figure 4. ROC curve for the CT-based scoring system.

focused on aspects of patient presentation that may be pathognomonic for NSTI. Immune function is an important factor to consider in the diagnosis of NSTI, and it should be noted that immunocompromise applies not only to traditional populations (i.e., patients with HIV or those status after solid organ transplant) but also to patients with decreased barrier function (trauma), poor nutritional status (EtOH misusers), and poor granulocyte function (diabetics).[15] In addition to immune status, there has been a historical link of NSTI to the physical examination findings of crepitance and gray wound drainage; however, these findings are unreliable and laboratory and radiographic findings are routinely completed in at-risk populations.[6,16] Wong et al. proposed the laboratory risk indicator for necrotizing fasciitis (LRINEC). Using total white cell count, hemoglobin, sodium, glucose, serum creatinine, and C-reactive protein, the authors created a scoring system with reasonable PPV and NPV.[8] Although this scoring system is useful in patients for whom clinicians have either high or low suspicion for NSTI, it is likely that radiographic studies will be pursued in the group of patients who are at moderate risk.

Cross-sectional imaging has rapidly evolved, and clinicians are no longer required to rely on gas in soft tissues on plain films as the sole radiographic indicator of NSTI. This may be viewed as a positive development, as soft-tissue gas is often a result of long-standing infection with anaerobic organisms. Furthermore, in patients with recent injury or those who underwent previous wound instrumentation, soft-tissue gas may be incidental rather than pathologic. CT is preferable to plain radiography because CT offers high-resolution analysis of compartmental structures. Although magnetic resonance imaging also offers high-resolution images of subcutaneous compartments, CT is timelier, widely available in U.S. centers, and more amenable to rapid interpretation by nonradiologists.[17,18] Although CT imaging of soft-tissue infections has been examined in detail,[10,19,20] currently, there is a dearth of simple scoring systems that would aid in the diagnosis of NSTI.

Of 715 patients initially identified in this study, 305 patients underwent CT scans to aid in the diagnosis of NSTI. It is likely that these 305 patients represent the middle of the soft-tissue infection spectrum; patients at the end of the spectrum (i.e., patients with soft-tissue infections obviously

requiring debridement or non-toxic appearing patients with relatively benign soft-tissue infections) generally do not routinely undergo cross-sectional imaging. Not surprisingly, the 44 patients who met the criteria for NSTI were more likely to be immunocompromised compared with the non-NSTI cohort. Diabetes seemed to be a prominent risk factor for NSTI. The average serum glucose was 100 mg/dL higher in the NSTI group than the non-NSTI group. The average time elapsed from emergency department registration to operative debridement was 15 hours, a delay that is concerning and may reflect waiting room time and/or delay in obtaining surgical consultation. Because our institution has an attending radiologist, responsible for interpreting emergency department studies, available in-house 24 hours per day, we do not think that there is a significant time lag in obtaining and interpreting CTs in patients with soft-tissue infections. Furthermore, as soft-tissue infections are predominantly managed by in-house trauma and emergency general surgeons, it is unlikely that there was a delay to operative intervention once the diagnosis of NSTI was made.

Operative therapy for NSTI consists of surgical debridement with a low threshold for re-exploration.[13,21,22] Although these tenets have not changed recently, vacuum-assisted wound closure (11 of 44) and split-thickness skin grafts (9 of the 44) were used with our NSTI population to manage large soft-tissue defects. Although hyperbaric oxygen therapy and IV immunoglobulin for NSTI have been described,[3,23] these were not used for the patients in this study. Of note, the mortality and long-term morbidity of NSTI in these 44 patients is testament to a need for early diagnosis and therapy, and our data correlate favorably with rates reported in the literature.

It is likely that patient characteristics and the diagnostic algorithm for soft-tissue infection in this study are similar to most North American tertiary centers. Thus, a CT scoring system that consists of rapidly identifiable variables may be a valuable tool in the clinician's armamentarium. Our CT-based scoring system, relying partially but not exclusively on the presence of soft-tissue gas, is statistically robust for a cutoff score of >6. Although IV contrast is preferred for imaging soft-tissue infections, using this scoring system, it is not necessary. This is of relevance as many patients with comorbidities that predispose to soft-tissue infections have coincident acute or chronic renal injury and IV contrast may be contraindicated. Finally, this imaging-based scoring system may be used in conjunction with existing laboratory-based scoring systems[24,25] to strengthen diagnostic confidence for soft-tissue infections.

Despite yielding clinically relevant results, the limitations of this retrospective study must be acknowledged. Despite the adherence to basic surgical and critical care principles with regard to the diagnosis and treatment of NSTI, the care of each patient may have been influenced by local practice patterns as well as individual clinician's preferences. Additionally, diagnostic imaging technology advances rapidly, and the CT scanner used was upgraded twice during the study period. As CT system upgrades affect image quality and resolution, this has the potential to confound our data. Finally, it would have been advantageous to apply the LRINEC to the NSTI and non-NSTI groups to determine whether a combined laboratory-radiographic tool could be developed; however, C-reactive protein, a component of LRINEC analysis, was not routinely measured at our intuition during the study period. Finally, a single, blinded radiologist reviewed the CT scans in this study. As these CT variables are somewhat subjective, inter-rater variability should be assessed before prospective validation of this scoring system.

Overall, this study has broad implications with regard to caring for patients with a challenging clinical entity. As the number of patients with NSTI risk factor increases, the number of soft-tissue infections seen in U.S. emergency departments will increase. Use of this CT-based scoring system for soft-tissue infections, along with laboratory analysis and a high clinical suspicion, may improve diagnostic accuracy in patients with soft-tissue infections of indeterminate severity. Prospective validation of this scoring system is planned.

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