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Early surgical intervention and its impact on patients presenting with necrotizing soft tissue infections: A single academic center experience

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Abstract

Objectives:

Early diagnosis and emergent surgical debridement of necrotizing soft tissue infections (NSTIs) remains the cornerstone of care. We aimed to study the effect of early surgery on patients' outcomes and, in particular, on hospital length of stay (LOS) and Intensive Care Unit (ICU) LOS.

Materials and Methods:

Over a 6-year period (January 2003 through December 2008), we analyzed the records of patients with NSTIs. We divided patients into two groups based on the time of surgery (i.e., the interval from being diagnosed and surgical intervention): Early (<6 h) and late (≥6 h) intervention groups. For these two groups, we compared baseline demographic characteristics, symptoms, and outcomes. For our statistical analysis, we used the Student's *t*-test and Pearson Chi-square (χ^2) test. To evaluate the clinical predictors of early diagnosis of NSTIs, we performed multivariate logistic regression analysis.

Results:

In the study population (n = 87; 62% males and 38% females), age, gender, wound locations, and comorbidities were comparable in the two groups. Except for higher proportion of crepitus, the clinical presentations showed no significant differences between the two groups. There were significantly shorter hospital LOS and ICU LOS in the early than late intervention group. The overall mortality rate in our study patients with NSTIs was 12.5%, but early intervention group had a mortality of 7.5%, but this did not reach statistical significance.

Conclusions:

Our findings show that early surgery, within the first 6 h after being diagnosed, improves in-hospital outcomes in patients with NSTIs.

Keywords: Early surgery, necrotizing fasciitis, necrotizing soft tissue infections, necrotizing fasciitis, and early surgery

INTRODUCTION

Necrotizing soft tissue infections (NSTIs) are rare but highly lethal with a reported mortality rate of up to 76%.[1,2,3,4,5,6,7,8] Poor outcomes can be partially explained by the frequent delays in diagnosing NSTIs. Prior reports have identified prompt treatment (defined by surgical debridement within 8–24 h after the patient arrives at the emergency department) as leading to decreased mortality rates.[2,5,6,7,8] The general agreement among surgeons is that the sooner one operates and debrides the necrotic tissue, the better the outcome. However, how early is early enough has not been well-defined. In our practice, we have noticed that the earlier we operate, the better the outcome. Most of our patients with NSTIs undergo an operation within the first 2–4 h after their arrival or diagnosis. However, we could not find any large study that reported operations in the first 2–4 h, probably because some patients need aggressive resuscitation before the operation. We sought to examine the effect of early surgery on patients' outcomes and, in particular, on hospital length of stay (LOS) and Intensive Care Unit (ICU) LOS. Our hypothesis was that operating within the first 6 h after diagnosis of NSTIs would improve outcomes.

MATERIALS AND METHODS

The University of Arizona Institutional Review Board approved this as a single institution observational retrospective study, which we conducted in our urban academic Level I trauma center. Our trauma acute care surgery team and our orthopedic service treated all patients. We analyzed the records of those who underwent an operation for NSTIs (defined by necrotizing fasciitis, gas gangrene, and Fournier gangrene) over a 6-year period (January 2003 through December 2008). In our computer-generated search of our medical database, we used the International Classification of Diseases Version 9 codes (ICD-9) discharge codes for NSTIs for necrotizing fasciitis (728.86), gas gangrene (040.0), and Fournier gangrene (608.83). The study group included only patients whose diagnosis was confirmed by operative findings revealed by analysis of the electronic medical record. Patients were categorized into two groups by time of surgery (i.e., the interval from being diagnosed by the surgery team in the emergency department or elsewhere in the hospital to surgical intervention): Group I, early (<6 h) and Group II, late (≥6 h). For these two groups, we compared baseline demographic characteristics, symptoms, and outcomes. Septic shock was defined as sepsis-induced hypotension in terms of systolic blood pressure <90 mmHg or a fall in systolic blood pressure of >40 mmHg that are persisting despite adequate fluid resuscitation.[9,10]

Statistical analysis

Data were presented as proportion, mean (±standard deviation), median (range), and interquartile range (IQR), whenever applicable. Student *t*-test was performed to compare continuous variables and the Pearson Chi-square (χ^2) test for categorical variables. Pearson correlation coefficient was used to assess for any correlation between the time to intervention and the ICU LOS. We considered any differences to be statistically significant when the two-tailed $P < 0.05$. Further, to assess for any correlation between the total hospital LOS and the time to intervention (<6 vs. ≥6 h), we used a side-to-side boxplot. To evaluate the clinical predictors of early diagnosis of NSTIs, we performed multivariate logistic regression analysis and determined the adjusted odds ratio and 95% confidence interval. For all of our data analysis, we used the Statistical Package for Social Sciences version 18 (SPSS Inc., Chicago, USA).

RESULTS

Our study population comprised a total of 87 patients (62% male, 38% female) with NSTIs. The mean age was 46 ± 17 years. In almost 50% of the patients, the anatomic location of the NSTIs was the lower

extremity, followed by the upper extremity, Fournier gangrene, buttocks, and trunk. Two patients had NSTIs on their face. The most common systemic presentation was tachycardia (70% in Group I vs. 57.4% in Group II), followed by hypotension (45% vs. 39%) and tachypnea (33.3% vs. 30%). The most common wound characteristic was erythema (92% vs. 87%), followed by tenderness (98% vs. 95%), necrosis (50% vs. 45%), bullae (24% vs. 17.5%), and foul smelling (15% vs. 21.7%). The mean number of surgical intervention in each group was 3 [Table 1].

Median time to intervention in the two groups was 3 h (range 2–4, IQR 2) and 24 (range 6–60, IQR 18), respectively. We found no statistically significant difference in morbidity and mortality between the two groups [Figure 1]. However, Group I had a significantly shorter time to surgery (2.95 ± 1.1 vs. 22.3 ± 17.8 h), a significantly shorter median hospital LOS (13.5 [4–33] vs. 18 [1–82] days), and a significantly shorter median ICU LOS (4 vs. 10 days) than Group II [Table 1].

The correlation between time to surgery and the total hospital LOS is shown in a side-by-side boxplot in Figure 2. Group I (early operative group) had a significantly shorter mean hospital LOS and a significantly shorter median ICU LOS. Moreover, there was a correlation between the time to surgery and ICU LOS (r = 0.27, P = 0.01). There were no significant differences between the two groups with regard to laboratory findings [Table 2], comorbidities [Table 3], and initial diagnosis (such as cellulitis or abscess) or location of that initial diagnosis [Table 4]. In addition, in our multivariate logistic regression analysis, we found no single clinical sign, on admission, that independently predicted early diagnosis of NSTIs [Table 5].

DISCUSSION

The present report demonstrates that surgical intervention within the first 6 h after diagnosis of NSTIs would improve hospital outcomes in terms of shortening both the hospital LOS and ICU LOS. In our study, the overall mortality was 11/87 or 12.5%, which is less than that reported in many previous studies.[1,2,3,7] Although there was a clinically significant difference in the mortality between the groups based on the timing of surgical intervention (17.5% in late vs. 7.5% in early intervention group), this did not reach statistical significance. NSTIs, in particular, necrotizing fasciitis, remain potentially the most deadly surgical infections and require aggressive resuscitation and surgical debridement. Early diagnosis, early antibiotic treatment, and early surgical debridement remain the cornerstone of care for these patients.[5,6,7,8] However, what “early” means has not been clearly defined. In the study by McHenry *et al*., the mean time from admission to operation was 45 h (1.7–312 h) while average time from admission to operation was 90 h for nonsurvivors versus 25 h in survivors group (P = 0.002).[5] In our study, we found that patients with NSTIs required an operation as soon as possible, but certainly no later than 6 h after their arrival or presentation to the emergency department. In fact, most of our Group I patients underwent an operation even earlier within a mean time of 2.95 ± 1.1 h. In patients with NSTIs, the most common reason for a delay in surgery is difficulty in making the correct diagnosis. Erythema, tenderness, and swelling are common. The clinical presentation can be deceiving, particularly in immunocompromised patients, ranging from indolent wound infections to severe gangrene with septic shock. Often, patients seem too sick to be immediately operated on, so clinicians will attempt to resuscitate them first, resulting in significantly delayed surgery or clinical presentation is deceiving in particular in immunocompromised patients.[11] However, one has to keep in mind that source control of the infection is priority in the management of any critically ill patients. These patients should be treated just like a gunshot wound or any other major insult to the body.

Historically, a number of comorbidities have been associated with NSTIs; however, our patients' comorbidities showed no effect on the in-hospital outcomes. The incidence of tachycardia, hypotension, and tachypnea was significantly higher in patients with NSTIs, but we found that none of them is specific enough or sensitive enough to predict NSTIs.

Despite numerous scoring systems and models introduced to discriminate between NSTIs and nonNSTIs, the diagnosis predicting mortality and limb loss in NSTIs is still difficult,[12,13] and the most important element remains early clinical recognition. So far, there is a considerable diagnostic challenge, when a surgeon is faced with "bad-looking" cellulitis and distinguishing it from NSTs. While we do not have a set protocol, most patients would get a computed tomography scan or magnetic resonance imaging (if available); if no clear clinical indication for surgery exists. On occasion, patient may get a plain film to rule out gas in the tissue; however, this is rare. As a rule, we may use frequent imaging techniques to confidently rule out the need for immediate surgery.

Laboratory test results in patients with NSTIs have been well studied by a number of authors. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) scoring system has been advocated to be helpful in distinguishing between NSTIs and nonNSTIs,[14] as well as in differentiating between severe and not severe NSTIs. However, in our study, we found that no single laboratory value independently predicted early diagnosis of NSTIs. Furthermore, most recent study of small group of patients strongly suggested that the LRINEC system is too insensitive for diagnosis of NSTIs.[15] Although hypoalbuminemia (<2 g/dl) is a known factor for postoperative complications, in our study, the albumin level did not significantly differ between our two groups (2.1 ± 0.7 vs. 1.9 ± 0.5; $P = 0.579$). Our microbiologic findings were similar to those of other reported series and reflected a wide spectrum of bacteria (data not shown).

We believe that our rapid surgical treatment of our patients, once the diagnosis was established – especially our relatively short time to surgery – was the main reason for our low mortality rate. The overall reported mortality rate has been reported to be very high (up to 72%) if the patient does not undergo surgical debridement as soon as possible. A median time to surgery of 8.4 h had a relatively low mortality rate of 16.4%,[2] while an interval >14 h from diagnosis to surgery in patients with septic shock was independently associated with in-hospital death.[7] At our institution, the in-house presence of a trauma surgeon (acute care surgeon) ensures that these patients are seen almost immediately. After the surgery resident is consulted by emergency medicine or internal medicine colleagues. This in turn ensures early intervention for patients with NSTIs, although for this study, we did not specifically assess the impact of our practice style. Hyperbaric oxygen therapy for NSTI, despite all commercial activities, continues to be controversial.[16] Our center does not have hyperbaric oxygen chamber, so none of our patients underwent such treatment. Although we have no experience with such treatment, we believe that hyperbaric therapy may actually delay treatment of patients with NTSI. Although there are a number of lower extremities NSTIs, those cases are managed by trauma or acute care surgeons in our institution.

In summary, evidence suggests that early surgical intervention is crucial in reducing morbidity and mortality in NSTI patients. However, there is still a lack of clear definition on "early." This is the main focus of the present study. Therefore, together with future studies, the present study may contribute to the definition of early intervention. McHenry *et al*. reported that early surgical intervention is associated with survival.[5] The mean time of surgical intervention (interval between diagnosis and surgical treatment) was 25 h in survivors. In their study, other risk factors previously associated with the development of NSTI did not affect mortality. Recently, Kobayashi *et al*. showed significantly lower mortality in the early intervention group.[17] Early surgical intervention in their study was performed within 12 h after diagnosis. The authors also showed that a delay of surgical treatment of >12 h is associated with an increased number of surgical debridement, septic shock, and acute renal failure.[17]

The present study reported outcomes of further earlier surgical treatment (within the first 6 h). Although there was no statistically significant difference in mortality between the study groups, higher mortality among late intervention group was clinically significant. Moreover, the outcomes in terms of duration of hospital and ICU stay were in favor of early intervention. Notably, the mean time for surgical treatment in

early intervention group was around 3 h. The comparable frequency of surgical debridement along with other comparable prognostic factors for morbidity and mortality such as age, gender, site of infection, comorbidities, and relevant physical and laboratory findings shows the significance of time of intervention.

Our study has several strengths. To the best of our knowledge, we believe that it is the first study to clearly show that operating early, within the first 4–6 h in patients with NSTIs, would shorten both ICU LOS and hospital LOS. Other studies including that of McHenry *et al*. and Bilton *et al*.[5,6] have shown that early and aggressive debridement is crucial. However, in the later study,[6] patients undergoing "early and aggressive" treatment had significantly lower mortality ($P = 0.0007$); however, timing from definite diagnosis to operation was not reported. This finding has significant implication, and it may set a new standard and goal to achieve. Clinicians must consider patients with NSTIs to be similar to those with severe trauma in their need for early surgical intervention. The concept of the golden hour resuscitation with simultaneous source control should be applied in patients with NSTIs as well. Although we could not prove a statistically significant difference in mortality between the two groups, our overall low mortality rate (12.5%), especially in earlier operative group with a mortality rate of 7.5%; is one of the lowest reported. We believe that our low mortality rate was the result of early surgery and in-house acute care surgery model.

Limitations

Our study also has a number of shortcomings. As with any retrospective study, we could not account for a number of variables beyond our control, such as the number of surgeons involved in each patient's care and the variability between surgeons. Different surgeons have different approaches; different degrees of surgical aggressiveness could account for differences in patient outcomes. Furthermore, we defined time to surgery as the interval from being diagnosed by the surgery team in the emergency department to undergoing the operation; we did not look at how long patients might have waited after first coming to the emergency department or after first being admitted to the hospital, nor did we take into account whether or not patients were transferred from other institutions. Moreover, the description of physical exam depends on the examiner, and more often than not, these are usually junior residents who perform the initial examination. The small sample size could affect the power of the study to adopt solid conclusions. Finally, we did not study other endpoint resuscitation parameters and their potential significance.

CONCLUSIONS

Early recognition of NSTIs is difficult, but their clinical presentation is of key importance. Patients who are thought to possibly have NSTIs must be seen, as soon as feasible, by the most experienced surgeons. Once NSTIs are diagnosed, the proper interventions must be conducted immediately. Emergent, timely surgical debridement remains crucial. Early surgery (within the first 6 h after diagnosis) improves hospital outcomes in patients with severe NSTIs. Further prospective studies are warranted to support these findings.

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Conflicts of interest

There are no conflicts of interest.

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Figures and Tables

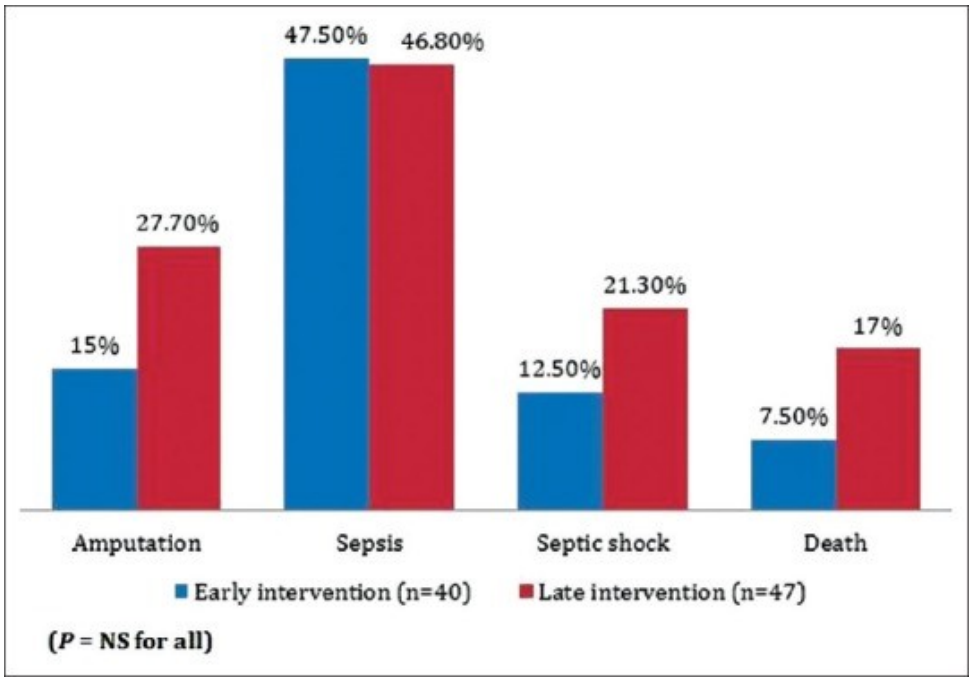
Table 1

Variable	Early intervention (*n*=40)	Late intervention (*n*=47)	*P*
Male, %	60	63.8	0.442
Age (mean±SD)	46.2±15.6	48.5±17	0.506
Wound locations, %			0.062
Fournier gangrene	15	8.5	
Lower extremity	50	44.7	
Upper extremity	22.5	14.9	
Buttocks	10	2.1	
Trunk	2.5	17	
Hip	0	6.4	
Face	0	4.3	
Multiple areas	0	2.1	
Clinical manifestations, %			
Erythema	92.5	87	0.402
Induration	25	30.4	0.575
Tenderness	95	97.8	0.476
Swelling	90	80.4	0.217
Necrosis	45	50	0.643
Bullae	17.5	23.9	0.466
Subjective bullae at home	2.5	0	0.281
Crepitus	20	4.3	0.024
Foul smell	15	21.7	0.423
Fever	55	46.8	0.446
Subjective fever at home	10	14.9	0.494
Tachycardia	70	57.4	0.226
Hypotension	45	39.1	0.582
Tachypnea	33.3	29.8	0.724
Gas forming organism, %	20	29.8	0.295
Time to surgery, mean±SD	2.95±1.1	22.3±17.8	0.001
Number of operations, mean±SD	3±1.6	2.9±2.2	0.846
ICU LOS, median (range)	4 (1-22)	10 (1-59)	0.034
Hospital LOS, median (range)	13.5 (4-33)	18 (1-82)	0.035

ICU: Intensive care unit, LOS: Length of stay, SD: Standard deviation

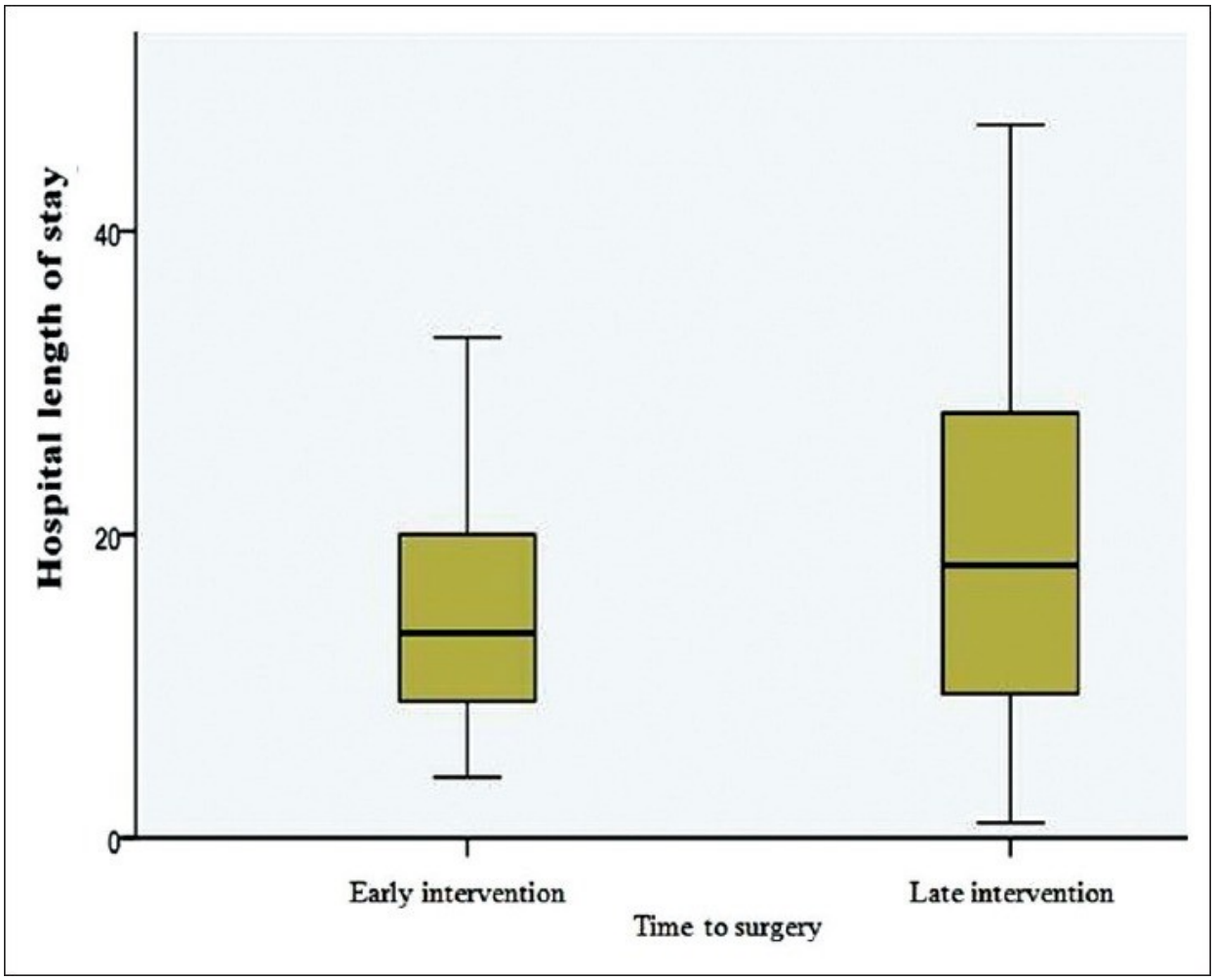
Patient characteristics and outcomes

Figure 1



Morbidity and mortality

Figure 2



Time to surgery and hospital length of stay

Table 2

Variable	Early intervention (*n*=40)	Late intervention (*n*=47)	*P*
WBCs count, mean±SD	16.1±9.7	15.9±13.1	0.936
Platelet count, mean±SD	271.5±126.9	317.2±162.9	0.153
Sodium (mmol/L), mean±SD	131.7±5.3	132.3±5.2	0.555
Creatinine (mg/dL), median (range)	1 (1-10)	1.2 (1-8)	0.455
BUN (mg/dL), mean±SD	19.9±16.4	29.7±25.1	0.031
Glucose (mg/dL), mean±SD	188.2±140.9	175.2±128.3	0.654
Lactate (mmol/L), mean±SD	3.2±2.6	3.5±2.6	0.718
pH, mean±SD	7.33±0.10	7.34±0.11	0.762
Albumin (g/dL), mean±SD	2.1±0.7	1.9±0.5	0.579

WBCs: White blood cells, BUN: Blood urea nitrogen, SD: Standard deviation

Laboratory findings

Table 3

Condition, %	Early intervention	Late intervention	*P*
Diabetes	35	48.9	0.190
Injection drug use	10	23.4	0.099
Alcohol abuse	20	21.3	0.884
Tobacco use	17.5	14.9	0.742
Hypertension	50	42.6	0.487
Renal disease	2.5	10.6	0.135
Liver disease	7.5	6.4	0.838
Cancer	2.5	4.3	0.655
Varicella infection	2.5	0	0.276
Prior infection	7.5	10.6	0.614
Chronic urinary tract infection	2.5	2.1	0.908
Obesity	7.5	14.9	0.281
Hyperlipidemia	10	12.8	0.687
Hypothyrodism	10	6.4	0.536
Anemia	5	8.5	0.520
Peripheral vascular disease	2.5	8.5	0.230

Associated comorbidities

Table 4

Variable	Early intervention (*n*=40)	Late intervention (*n*=47)	*P*
Initial diagnosis, %			
Necrotizing soft tissue infection	52.5	34.8	0.164 for all
Abscess	12.5	15.2	
Cellulitis	22.5	21.7	
Secondary infection	2.5	0	
Wound infection	5	6.5	
Sepsis	0	8.7	
Trauma	2.5	13	
Other	2.5	0	
Location of initial diagnosis, %			
Emergency department	65	63.8	0.88 for all
Imaging evaluation	10	6.4	
Operating room	15	17	

Initial diagnosis on admission and location

Table 5

	P	OR	95% CI
Induration	0.051	0.342	0.116-1.007
Erythema	0.326	0.435	0.083-2.287
Bullae	0.843	1.120	0.364-3.446
Crepitus	0.320	2.097	0.487-9.026
Fever	0.566	0.759	0.296-1.946
Tenderness	0.604	2.061	0.134-31.585

NSTIs: Necrotizing soft tissue infections, OR: Odds ratio, CI: Confidence interval

Clinical predictors, on admission, of early diagnosis of NSTIs