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HIGHER LRINEC SCORES AND ESCALATION OF ANESTHESIA CARE IN NECROTIZING SOFT TISSUE INFECTION

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Abstract

Background: The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score may distinguish necrotizing from non-necrotizing soft tissue infection. The association of higher preoperative LRINEC scores with escalations of intraoperative anesthesia care in necrotizing soft tissue infection is unknown and may be useful in communicating illness severity during patient handoffs.

Materials and Methods: We conducted a retrospective cohort study of first operative debridement for suspected NSTI in a single referral center from 2013 to 2016. We assessed the association between LRINEC score and vasopressors, blood products, crystalloid, invasive monitoring, and minutes of operative and anesthesia care.

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DISCLOSURE

The authors have no conflicts of interest, financial or otherwise related to this work.

Results: We captured 332 patients undergoing their first operative debridement for suspected NSTI. For every 1-point higher LRINEC score, there was a higher risk of norepinephrine and vasopressin use (RR =18% 95%CI 10%, 26%, and 10%, 27%, respectively), packed red blood cell use (RR= 28% (95%CI 13%, 45%)), and additional crystalloid (17.57 mL/hour (95%CI 0.37, 34.76)). Each additional LRINEC point was associated with longer anesthesia (3.42 min 95% 0.94, 5.91) and operative times (2.35 min 95%CI 0.29, 4.40) and a higher risk of receiving invasive arterial monitoring (RR 1.11 95%CI 1.05, 1.18). The negative predictive value for a LRINEC score<6 was >90% for use of vasopressors and packed red blood cells.

Conclusions: Preoperative LRINEC scores were associated with escalations in intraoperative care in patients with NSTI. A low score may predict patients unlikely to require vasopressors or blood and may be useful in standardized handoff tools for patients with NSTI.

Keywords

Necrotizing Soft Tissue Infection; LRINEC Score; NSTI; escalations of care

INTRODUCTION

Necrotizing Soft Tissue Infections (NSTIs) are a challenging clinical entity and a dangerous problem for patients with an estimated annual number of cases between 3,800 and 5,800 in the United States.¹ Commonly associated with toxin-producing bacteria, these rapidly progressive infections of the muscle, fascia, dermis, epidermis or adipose tissue can cause extensive local tissue damage and a profound systemic inflammatory response leading to cardiovascular collapse.² Mortality for NSTI is high and has been reported as 10–34%.³ Patients at increased risk for NSTI include those with diabetes, obesity, substance use, and compromised immune systems.^{4,5} This is a vulnerable population of patients often requiring emergency surgical care. Distinction of NSTI from non-necrotizing cellulitis or abscess remains a clinical challenge with the gold standard for diagnosis relying on surgical exploration. In light of these clinical difficulties, several investigators have attempted to use scoring systems, individual laboratory values, and history, to predict diagnosis, need for surgical intervention, and mortality.^{3,6–14}

Wong and colleagues developed and tested the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) in two separate patient cohorts. The LRINEC components include white blood cell count, hemoglobin, sodium, glucose, serum creatinine, and C-reactive protein. Using a cut point of six or higher, the LRINEC score has a positive predictive value of roughly 92% and a negative predictive value of 96% for distinguishing necrotizing soft tissue infection from non-necrotizing soft tissue infection.⁹ Although the LRINEC score provides clinicians with useful diagnostic clues, few data exist that specifically address the utility of this score in assessing hemodynamic instability during the clinical period of surgical debridement. Current anesthesiology practice does not include any standard scoring system to anticipate clinical deterioration or anticipation of escalation of care during operation for necrotizing soft tissue infection patients. Exposure to anesthetic medications, induction of general anesthesia, and surgical manipulation of infected and necrotic tissue may incite a physiologic cascade during surgery that requires intensive hemodynamic support. Our aim was to determine if preoperative LRINEC scores are associated with

intraoperative vasopressor use, fluid administration, duration of operative times, placement of invasive vascular access, and blood product transfusion in patients with NSTI.

METHODS

Design, setting, and patients

We performed a retrospective cohort study among adult patients 18 years or older treated at a regional referral center for NSTI. Harborview Medical Center in Seattle is the only high volume center for NSTI in Washington State.¹⁵ On-call acute care surgeons in conjunction with the on-call anesthesiologists care for patients with suspected NSTI 24 hours a day and 7 days a week. In our setting, few patients have arterial lines or central venous catheters placed in the emergency department and typical anesthetic care during surgery includes a volatile anesthetic, muscle relaxant, and opiates. Patients were identified by International Classification of Diseases codes for necrotizing fasciitis (728.86, M72.6), gas gangrene (040.0, A48.0), and Fournier's gangrene (608.83, N49.3) treated between January 2013 and December 2016. For patients with multiple operative dates, only the first date and first operation were considered for analysis. Only patients with a complete LRINEC score obtained from laboratory tests taken on the same date and time were included for analysis.

Perioperative Data source.

We obtained data from the Perioperative Quality and Research Database (PQRD) maintained by the Center for Perioperative and Pain Initiatives in Quality Safety Outcomes (PPiQSO) at the University of Washington in Seattle.¹⁶ PPiQSO extracts, curates, and links perioperative data for analysis with the aims of improving patient safety, clinical outcomes, and designing technologic solutions to clinical problems.¹⁶ Among other perioperative data, PQRD integrates information from the Anesthesia Information Management System (AIMS) that includes minute-by-minute vital sign readings, and detailed information on medication administration. The PPiQSO system also captures laboratory data for the entire hospitalization and patient demographic information. The Microsoft Amalga Unified Intelligence System (UIS) (Microsoft Corporation, Redmond, WA) which extracts data from the electronic health record was used to capture medications administered before patient arrival in the operating room.

Variables

Laboratory data for each patient consisted of preoperative blood serum laboratory tests. We collected the first and the last set prior to surgical debridement. We calculated the LRINEC score according to standard definitions (Table 1).⁹ LRINEC scores were calculated using only tests from the same date and time. The LRINEC score ranges from 0 to 13 and we calculated first pre-operative LRINEC, last pre-operative LRINEC, and change in LRINEC scores (2nd score – 1st score). Our outcome measures included numbers of patients receiving intraoperative vasopressor medications not used in routine general anesthesia cases (norepinephrine, epinephrine, vasopressin, dopamine, and dobutamine), amount of vasopressor medication administered, volume of total intravenous crystalloid administration (Plasmalyte, Lactated Ringer's Solution, and normal saline), number of patients receiving blood products (packed red blood cells (pRBCs) and fresh frozen plasma (FFP)) and overall

volumes for pRBCs and FFP. We coded the presence of central venous catheters and arterial lines during surgery as indication of placement in the operating room given these procedures are rarely performed pre-operatively at our institution. Duration of anesthesia and surgery times were calculated in minutes. Demographic data collected from PPiQSO included age, sex, American Society of Anesthesiologists (ASA) score, race, body-mass-index (BMI) and year of debridement.

Statistical Analysis

We calculated descriptive statistics of categorical and continuous variables using standard approaches. We dichotomized patients by whether or not they received vasopressor medications (unique outcomes for each medication including pre-operative administration), blood products (unique outcomes for pRBCs and FFP), and whether or not they had a central venous catheter or arterial line during surgery. We performed Poisson regression with robust standard errors to estimate incidence rate ratios (IRRs) for the risk of receiving vasopressor medications, blood products, or having invasive vascular access for each additional point in the first LRINEC score. We also performed linear regression to estimate the difference in quantities for medications, crystalloid, blood products, and durations of care with each additional LRINEC point.

We generated receiver operating curves for a continuous LRINEC score to determine sensitivity and specificity to predict the receipt of norepinephrine/epinephrine/vasopressin, pRBCs, or having invasive vascular access present during surgery. Because test performance is a manifestation of both the test characteristics (sensitivity/specificity) and the patient population under care (prevalence of the outcome), we also calculated positive and negative predictive values (PPV and NPV) for a range of different patient populations. We used a LRINEC cutoff of 6 or higher in calculating PPV and NPV for vasopressor use and pRBCs, using ranges of outcome prevalence from 5% to 25% in 5% intervals.⁹ This approach aims to provide PPV/NPV estimates using the sensitivity/specificity of the LRINEC score calculated in the current investigation but applied to other scenarios, knowing Harborview Medical Center is a high volume referral center and cares for sicker patients. For instance, in settings that care for fewer critically ill NSTI patients the overall prevalence of care escalation with vasopressors during operative debridement may be low, where at a high-volume center this number is likely higher. This proportion is important when considering positive and negative predictive values. We also identified a low LRINEC score group (less than or equal to 5) who received either vasoactive medications or blood products and compared demographic and LRINEC score components among low score patients who did not receive these escalating therapies. Statistical significance for hypothesis testing was set at $\alpha=0.05$. All statistical analyses were performed in Stata version 14.2/SE (StataCorp, College Station, TX).

This study was approved by the University of Washington Institutional Review Board (STUDY00002983).

RESULTS

Our search from the PPiQSO system captured 587 patients that underwent surgical debridement for NSTI according to ICD9 diagnosis from January 2013 to December 2016 and 332 patients had at least one complete LRINEC score. Patient characteristics were no different among patients with a complete LRINEC score and the available laboratory data on patients without a complete LRINEC score do not suggest a clinically sicker group. Restricting only to patients with a complete LRINEC score, the mean age was 50.6 years (SD 13.8) and 68.4% were male (Table 2). Most patients were ASA Class III, over 80% were white, and the median BMI was 28.7 (IQR=24.4, 35.6; range 17–89.1). Each year, the number of patients surgically treated for NSTI was larger than the prior year (Table 2).

The median first LRINEC score in this cohort was 8 (IQR=6, 10) and overall the score did not change for 278 (83.7%) patients prior to debridement (Table 3). The distribution of 1st LRINEC score and 2nd LRINEC score are shown in Supplemental Figure 1. In the first LRINEC score, the median CRP and white blood cell count were 241.15 mg/L (IQR = 161.20, 319.25) and 18.26 (IQR=13.7, 25.87), respectively (Table 3). Of the 332 patients, 121(36.5%) received norepinephrine, epinephrine, or vasopressin during anesthesia care during surgical debridement. Among patients who received intra-operative norepinephrine, epinephrine, or vasopressin, 45 of 121 (37.2%) received a vasoactive medication during the phase of care prior to operative debridement and in 28 of these 45, this was in the immediately preceding four hours. In terms of resuscitation with crystalloid, on average patients received 590 (SD=423) mL per hour of anesthesia and 26 (7.8%) received pRBCs in a nearly 1:1 ratio with FFP (Table 3). Only 12 patients (3.6%) had a central venous catheter, and 127 (38.4%) had invasive arterial monitoring. The mean anesthetic and operative times were approximately 136 and 61 minutes, respectively (SD= 61 and 50, respectively) (Table 3).

For every additional point on the first LRINEC score, there was an 18% (95%CI 10%–26%) higher chance of receiving norepinephrine (Table 4). There was a similar association between LRINEC score and vasopressin (Table 4). Each additional LRINEC point was also associated with 28% (95%CI 13%–45%) higher risk of receiving pRBCs and a 16% (95% CI 1%–32%) higher risk of receiving FFP. There was also an association between LRINEC score and total dosage for norepinephrine and vasopressin (Table 4 and Figure 1). Each additional LRINEC point was associated with an 11% higher risk of invasive arterial monitoring (95%CI 5%–18%). The point estimate for risk of central venous catheter placement suggests higher risk for higher LRINEC scores, but the confidence interval crosses one (Table 4). Higher scores were associated with higher total volumes of pRBCs but not FFP (Table 4). There was an association with higher LRINEC score and higher volumes of crystalloid fluid and duration of operating room care (Table 4).

The receiver operating curve for the LRINEC score and receiving vasopressors is shown in Supplemental Figure 2. The area under the curve (AUC) is 0.64. For pRBCs administration, central venous catheter placement, and arterial catheter placement, the AUCs were similar at 0.66, 0.61, and 0.62 respectively. As Harborview Medical Center is a referral center for patients with higher acuity of illness with NSTI, we considered contexts where the

prevalence of escalation of care (vasopressors, pRBC, etc.) occurs in a smaller proportion of patients. The negative predictive value of a LRINEC cutoff of six was >90% for use of vasopressors and pRBC administration in all tested circumstances (Table 5). In the case where escalation of care occurs in 15% or fewer patients, the LRINEC score cutoff of six yielded a negative predictive value (NPV) of nearly 95% for vasopressor use (Table 5). There were 65 patients with a LRINEC score of five or lower. Among these patients only 8 (12.3%) received vasoactive medications and none received blood products. Compared to the low-score group without escalation of care, there were no differences in demographics, ASA scores, or year of presentation. For the LRINEC score components, the white blood cell count was higher (20.3 vs 13.6, $p=0.01$) among those who received vasoactive medications.

DISCUSSION

To our knowledge, this is the first evaluation of LRINEC scores and escalations of anesthesia care in NSTI. Our analysis demonstrates an association between higher LRINEC scores and receiving intraoperative norepinephrine, vasopressin, and pRBCs, as well as with the total fluid volumes administered. Higher scores were also associated with higher risk of arterial line placement, possibly reflecting labile blood pressures intraoperatively, and longer anesthetic and operative times. As a continuous score, the areas under the ROC curves for the different measures of intraoperative escalation of care were low. Among low score patients, higher white blood cell count was associated with receiving vasoactive medications. However, using the standard LRINEC cutoff of six or higher, the negative predictive values were 90% or higher for vasopressor use and pRBC administration.

Assessing patient severity of illness is a cornerstone of clinical medicine and communicating this assessment within and between inpatient services during transitions of care is known to be vulnerable times for patient safety.^{17,18} For surgical patients, most of the transitions-of-care data focuses on post-operative transfer from the operating room to the intensive care unit and between emergency medical service personnel and the trauma service in the case of injured patients.^{19–23} These practice patterns have not permeated the culture of standardized preoperative hand-offs between surgeons and anesthesiologists in emergency general surgery cases. Few studies have investigated communicating patient illness severity preoperatively between surgeons and anesthesiologists for the purpose of anticipating escalations of anesthesia care. Ensuring that all providers are familiar with the necessary risk stratification scores is imperative to maintaining quality care and patient safety and requires additional study.

While 37% of patients who received intraoperative vasoactive medications also received them prior to operation, this may reflect a proportion of patients transferred in for care from an outside hospital. In NSTI patient deterioration (such as the requirement of vasoactive agents prior to operation) may suggest a scenario where in the ideal situation this individual would have already undergone operative debridement. These efforts signify escalations of care and while those maneuvers did not begin during operative debridement they highlight the importance of additional tools to anticipate clinical deterioration especially in the context of inter-hospital patient transfer.

Hemodynamic lability in NSTI may be related to a combination of anesthetic agents, blood loss, and circulating cytokines associated with severe sepsis.^{24,25} Our findings suggest that beyond lending a data point for the diagnosis of NSTI, two enhancements to clinical care of these patients may be warranted: 1) calculation of LRINEC score manually (or within the electronic health record) among all providers caring for NSTI patients and second, confirming and communicating between surgeons and anesthesiologists the assessment of critical illness using the LRINEC score and other clinical data as routine part of the preoperative handoff. This approach may be important to expedient and proactive (not reactive) hemodynamic resuscitation.

Harborview Medical Center is a tertiary care facility which treats a large number of patients with NSTI annually, many of whom are more critically ill than those treated in the community. Since predictive values vary with prevalence of the outcome (here, escalation of care), and to increase the generalizability of study findings, we explored these test statistics for lower prevalence of care escalations than those at our institution. Wong and colleagues developed the LRINEC score to distinguish necrotizing from non-necrotizing soft tissue infection using a total score of 6 or higher to predict necrotizing infection.⁹ While the score was not developed to evaluate illness severity, investigators have found associations between LRINEC scores and mortality, amputations, and intensive care utilization, however, some results have been mixed.^{7,11,13,26} We chose the standard LRINEC cutoff for the diagnosis of NSTI (6 points) to maintain consistency with use of the score. The fact that the NPV exceeded 90% regardless of the prevalence of escalation is useful to treating clinicians when anticipating resources that may be necessary during resuscitation.

The areas under the curve for our three indicators of care escalation were low. The area under the curve is the probability that an individual with the outcome is randomly chosen from the population and has a higher test result than a randomly chosen individual without the outcome.²⁷ In our results, the continuous LRINEC score may be limited when predicting escalations of care.

While our focus is on the LRINEC score and intraoperative escalation of care in NSTI patients, no prior data is available for comparison and recent data on diagnosis using the LRINEC score are mixed.²⁸ There are, however, other scores used in the care of NSTI patients. These include measures by Wall and colleagues, Anaya and colleagues, and the modified Sequential Organ Failure Assessment (mSOFA).^{6,14,29} Given the most recent definitions of sepsis, greater emphasis on the SOFA score in routine data collection will enable easier and more accurate investigation into its utility in clinical decision-making.³⁰ Studies comparing the utility of these scores in making useful clinical predictions are warranted.

This study has limitations. We investigated the utility of a score for purposes distinct from the original intent. In addition, this is a single center study from a high volume NSTI center and so results may not be generalizable to all settings. Analyses using large databases are subject to errors around accuracy of diagnosis and procedure coding. Our outcomes of interest may be modified by each other (fluids, vasopressors, vascular access, blood product resuscitation, operative times, etc.) and our data capture events prior to operative

debridement was limited to vasopressor use only. Our data did not include surface area of NSTI debridement. While this is a critical piece of clinical information, preoperative estimates of this value may be less accurate than operative measurements and the focus of the current investigation is to anticipate the risk of intraoperative deterioration.

CONCLUSIONS

Despite limitations, these data suggest an association between preoperative LRINEC scores and escalations of anesthesia care during operative debridement for NSTI. The findings highlight the potential utility of the preoperative LRINEC score in communication between surgeons and anesthesiologists to anticipate intraoperative escalations of care for hemodynamic resuscitation in NSTI patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Linear Fit of Total Norepinephrine (left) and Total Vasopressin (right) Dosages
Administered During Operative Debridement for Presumed NSTI by Pre-Operative LRINEC
Score

Table 1.

LRINEC Score Calculation *

Test	Point Value
C-Reactive Protein (mg/L)	
<150	0
150	4
Total White Blood Cell (per mm ³)	
<15	0
15–25	1
>25	2
Hemoglobin (g/dL)	
> 13.5	0
11–13.5	1
<11	2
Sodium (mEq/L)	
135	0
<135	2
Creatinine (mg/dL)	
1.6	0
>1.6	2
Glucose (mg/dL)	
180	0
>180	1

*
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Table 2.

Patient Characteristics

Variable	Value (N=332)
AGE, mean (SD)	50.6 (13.8)
<i>Sex</i>	
Male	227 (68.4%)
Female	105 (31.6%)
<i>ASA</i>	
1	13 (3.9%)
2	58 (17.5%)
3	161 (48.5%)
4	90 (27.1%)
5	10 (3.0%)
<i>Race</i>	
White	267 (80.4%)
Black or African American	21 (6.3%)
Other	44 (13.3%)
BMI, median (IQR)	28.7 (24.4, 35.6)
<i>Year</i>	
2013	69 (20.8%)
2014	74 (22.3%)
2015	90 (27.1%)
2016	99 (29.8%)

Table 3.

Clinical Characteristics

Variable	Value
<i>1st LRINEC Score, median (IQR)</i>	
Total	8 (6, 10)
CRP	241.15 (161.2, 319.25)
Sodium	132 (129, 134)
Hemoglobin	11.1 (9.4, 12.8)
Creatinine	1.085 (.8, 1.665)
White Blood Cells	18.255 (13.67, 25.865)
Glucose	131.5 (105, 189.5)
<i>2nd LRINEC Score, median (IQR)</i>	
Total	8 (6,9)
Change between first and last LRINEC Score [*] , median (IQR)	0 (0,0)
Central Venous Catheter	12 (3.6%)
Arterial Line Placement	127 (38.4%)
Anesthesia Start Time between 6PM and 6AM	176 (53.0%)
<i>Durations (min), mean (SD)</i>	
Anesthesia	136 (61)
Surgery	61 (50)
<i>Vasopressors, N%</i>	
Norepinephrine	90 (27.1%)
Epinephrine	7 (2.1%)
Dobutamine	0 (0.0%)
Dopamine	0 (0.0%)
Vasopressin	86 (25.9%)
<i>IV Fluids, mean (SD)</i>	
Total IVF (ml/anesthesia hour)	590 (423)
<i>Blood Products</i>	
PRBC, N (%)	26 (7.8%)
FFP, N (%)	25 (7.5%)

^{*}
2nd Score - 1st Score

Table 4.

LRINEC score and Intra-Operative Care

Outcome	Risk of Outcome (Y/N)		Coefficient** (unit) per 1 point higher LRINEC Score	
	RR*	95%CI	Coefficient (units)	95%CI
<i>Vasopressor use</i>				
Norepinephrine	1.18	(1.10–1.26)	0.15 (mcg)	(0.04–0.27)
Epinephrine	1.16	(0.86–1.59)	0.00 (mcg)	(–0.00–0.00)
Vasopressin	1.18	(1.10 –1.27)	2.10 (units)	(0.24 – 3.97)
<i>Blood Products</i>				
pRBCs	1.28	(1.13–1.45)	11.65 (ml)	(2.86–20.44)
FFP	1.16	(1.01 –1.32)	6.93 (ml)	(–0.15 –14.01)
<i>IV Fluids</i>				
Total IVF (ml/anesthesia hour)	NA	NA	17.57	(0.37–34.76)
<i>Duration(min)</i>				
Anesthesia	NA	NA	3.42	(0.94 – 5.91)
Surgery	NA	NA	2.35	(0.29 – 4.40)
Central Venous Catheter Placement	1.19	(0.97 –1.47)	NA	NA
Arterial Line	1.11	(1.05–1.18)	NA	NA

* Poisson regression with robust standard errors, incidence rate ratio for dichotomous outcome for every additional LRINEC point

** Linear regression, coefficient is the additional quantity associated with a one point higher LRINEC score

Table 5.

Positive and Negative Predictive Values for Vasopressor Use and pRBCs based on Prevalence of Population Outcomes

Prevalence of Outcome in Population (%)	Outcome			
	Vasopressor Use*		Receiving pRBCs	
	PPV	NPV	PPV	NPV
	%, (95%CI)	%, (95%CI)	%, (95%CI)	%, (95%CI)
5	6.7 (6.0, 7.5)	98.4 (97.3, 99.1)	6.5 (5.9, 7.2)	99.3 (95.2, 99.9)
10	13.2 (11.9, 14.6)	96.7 (94.4, 98.0)	12.9 (11.8, 14.1)	98.5 (90.4, 99.8)
15	19.4 (17.7, 21.3)	94.8 (81.4, 96.9)	19.0 (17.5, 20.7)	97.6 (85.6, 99.6)
20	25.4 (23.3, 27.7)	92.8 (88.2, 95.7)	25.0 (23.1, 27.0)	96.7 (80.7, 99.5)
25	31.3 (28.8, 33.8)	90.6 (84.8, 94.3)	30.7 (28.6, 33.0)	95.6 (75.9, 99.3)

* Includes norepinephrine, epinephrine, or vasopressin

** MAP<65 mmHg for 5 minutes or longer

PPV = Positive Predictive Value

NPV= Negative Predictive Value

Exact binomial confidence intervals for all PPV and NPV values