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A comparison of outcomes between transferred patients versus patients who presented directly to the emergency department with necrotizing fasciitis

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Abstract

Introduction Necrotizing Fasciitis (NF) is a rare life-threatening bacterial infection that necessitates emergent resuscitation and operative intervention. Most of the literature has emphasized the need for early surgical intervention. This is problematic for patients being treated at a facility lacking surgical support, with concerns for increasing mortality and morbidity rates.

Methods This is a 10-year retrospective study of emergency department (ED) documentation and surgical operative reports of patients seen at Arrowhead Regional Medical Center from January 1, 2011, to December 31, 2020. The patients were divided into two groups: the Transfer Group (TG), consisting of those transferred from another facility, and the Direct Admit Group (DAG), comprising those who presented directly to the ED. A comparison was conducted to identify statistically significant differences between the 2 groups of patients with a final diagnosis of NF, with specific emphasis on mortality rate, hospital length of stay (LOS), and intensive care unit (ICU) LOS.

Results A total of 134 patients with a confirmed diagnosis of NF were included in the final analysis. More than half (50.8%, $n=68$) of the patients presented as transfers from area hospitals. Compared to the DAG, the TG had a significantly higher percentage of patients undergoing surgical intervention within six hours of ED presentation (95.6% vs. 10.6%, respectively; $p<0.0001$). The TG had a lower mortality rate compared to the DAG (11.8% vs. 22.7%), though the difference did not reach statistical significance. There was no statistically significant difference in hospital LOS (13 days vs. 13.5 days, $p=0.9046$) or ICU LOS (3 days for both groups, $p=0.4845$) between these two groups.

Conclusion Aggressive management with broad-spectrum antibiotics and intravenous fluid resuscitation may mitigate the effect on mortality in patients with necrotizing fasciitis when prompt surgical intervention is not available.

Keywords Necrotizing fasciitis, Operative report, Soft tissue infection, Cellulitis, Skin abscess

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Introduction

Necrotizing fasciitis (NF) is a rapidly progressive, life-threatening soft tissue infection characterized by necrosis of subcutaneous tissues and fascia. While exact figures can be difficult to pinpoint due to underreporting, estimates suggest that the incidence ranges from 0.3 to 15 cases per 100,000 people [1]. Risk factors associated with a higher incidence of NF include immunocompromised states, diabetes mellitus, drug use disorder, alcoholism, peripheral vascular disease, renal failure, cirrhosis, and obesity [2, 3]. Any history of recent trauma, including surgery or minor injuries, may lead to NF. The mortality rate varies widely, ranging from 20–80%.[1] Prognosis depends on several factors, including time to diagnosis, anatomical region affected, causative agent, and underlying comorbidities [4].

Accurate early diagnosis can be challenging. The classic triad of pain, swelling, and erythema are nonspecific findings that can be confused with other soft tissue infections such as cellulitis or deep skin abscesses [5, 6]. Patients with compromised immune systems such as Human Immunodeficiency Virus infection are less likely to present with skin erythema [7]. Decision making tools such as the LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score have been shown to lack appropriate sensitivity and specificity in diagnosing NF [8]. Imaging studies may be helpful in identifying NF when gas-forming bacteria are present. Computed tomography (CT) and magnetic resonance imaging (MRI) may show gas tracking along the fascial planes, which is pathognomonic for NF in the proper clinical settings, as this is not typically seen in other soft-tissue infections [9]. However, this phenomenon may not be present in the early course of NF, or if the causative agent is a non-gas forming organism [9]. Therefore, the lack of soft-tissue emphysema does not exclude the diagnosis, and relying on imaging studies to confirm the diagnosis may delay appropriate care.

Early diagnosis and appropriate treatment are important as NF may progress to septic shock and multi-organ failure. Prior studies reported that only 15–34% of patients are accurately diagnosed with NF on initial presentation [10, 11]. Delays in diagnosis and surgical interventions were also noted in NF patients admitted under a non-surgical service. Kongkaewpaisan et al. reports the median time to surgical intervention was significantly longer when patients were admitted to non-surgical services (24.8 h versus 3.9 h; $p < 0.001$) [7].

Initial resuscitation involves the use of broad-spectrum antibiotics, including coverage for Pseudomonas and methicillin-resistant Staphylococcus aureus species [2, 6]. Clindamycin should also be considered when Clostridium is suspected [6]. Additionally, timely surgical intervention, such as debridement and fasciotomy, has been identified as the mainstay treatment for NF [12]. Pakula and colleagues noted lower morbidity and mortality associated with timely surgical intervention [13]. In addition, Hadeed and colleagues noted significantly shorter lengths of hospital and ICU stays when surgery was performed within 6 h of initial presentation to the ED [14].

However, the time to definitive operative management can be hindered for patients who initially presented to a hospital that does not have the appropriate surgical service. These patients would often need to be transferred to another facility for a higher level of care. The delay in access to surgical management can be severe based on the availability of an accepting hospital, the time of transportation for the transfer, and the existing patient load at the accepting facility. Traditionally, the physician caring for these patients from the transferring facility is limited to the use of broad-spectrum antibiotics and aggressive intravenous fluid resuscitation. This study analyzes two patient cohorts: those transferred to Arrowhead Regional Medical Center (ARMC) and those who presented directly. This study aims to identify differences in patients' outcomes that may be impacted by the potential delay of care. We hypothesized that the transferred patients are associated with higher mortality.

Method

This is a 10-year retrospective study at ARMC from January 1, 2011 to December 31, 2020. ARMC is a 456-bed acute care teaching facility and an American College of Surgeons certified Level I trauma center in San Bernardino County, California. The ED at ARMC is one of the busiest emergency departments in California with more than 100,000 annual visits. Patients 18 years and older were included in this study. Patients diagnosed with NF as the primary diagnosis at admission and discharge were identified using the International Classification of Disease, Ninth and Tenth Revision (ICD-9, ICD-10) Code. Patient demographics in this study were abstracted from their electronic medical records and included race, marital status, and insurance status. This study was approved by the institutional review board at ARMC with approval number 19–22.

The patients were divided into two cohorts for comparison. The Transfer Group (TG) includes patients who were transferred from surrounding hospitals for a higher level of care. The Direct Admit Group (DAG) includes patients who presented directly to the emergency department (ED) at ARMC. Demographic and clinical variables were compared between the two groups.

All statistical analyses were conducted using the SAS software for Windows version 9.4 (Cary, North Carolina, USA). Descriptive statistics were presented as mean and standard deviations or median with the first and

third interquartile for continuous variables, along with frequency and proportions for categorical variables. Chi-square tests were conducted to assess the association between various categorical variables with the NF status (NF vs. non-NF) for the combined group, TG and DAG separately. Fisher's exact tests were utilized if the expected cell count is less than five. The analysis of variance tests was conducted to assess whether there was a statistically significant difference in the continuous variables between the NF vs. non-NF group. Wilcoxon rank-sum tests were conducted to assess statistically significant differences in the no-normal variables between the NF vs. non-NF group. All statistical analyses were two-sided. P-value < 0.05 was considered to be statistically significant.

Results

A total of 134 patients with a confirmed diagnosis of NF on tissue biopsy was included in the final analysis. Table 1 presents the comparison of demographic and clinical variables between TG and DAG. More than half (50.8%, $n = 68$) of the patients were identified as TG. Patients in TG were statistically younger (46.96 vs. 52.17 years, $p = 0.0186$), and had a higher c-reactive protein (28.26 vs. 18.66, $p = 0.0298$) than those in DAG. Patients in TG also had a shorter time from ED presentation at ARMC to surgery (3.25 vs. 8.75 h, $p < 0.0001$). Nearly all patients in TG (65 out of 68, 95.6%) were taken to surgery within six hours of presentation, whereas only 10.6% (7 out of 66) of patients in DAG underwent surgery within this timeframe (Table 2). There was no statistically significant difference in the hospital length of stay (LOS) or ICU LOS between TG and DAG (all p-values > 0.05, Table 1).

There were 8 (11.8%) deaths in TG and 15 (22.7%) in DAG. Table 3 presents a detailed summary of clinical variables of the expired patients for both groups. Among these patients in DAG, less than half (6/15, 40%) received surgical intervention within 6 h of arrival. Expired patients in DAG had a higher incidence of end-stage renal disease and hypertension as compared to the TG.

Discussions

Necrotizing fasciitis is a devastating infectious disease with high mortality and morbidity. Multiple studies have noted that time to surgical intervention continues to be the most important factor in survival [6, 10, 15]. However, for patients who were initially seen at a facility without a proper surgical specialist, the need for transfer will delay the time to operative care. This delay in surgical intervention would have expected to result in a cohort with a higher incidence of mortality and/or morbidity. However, this was not demonstrated in our study. It is

Table 1 Comparison of demographic and clinical variables between the transfer group (TG) and direct admit group (DAG)

	TG *N* = 68	DAG *N* = 66	*P*-value
Age	46.96 ± 12.42	52.17 ± 12.82	0.0183
Gender, male (%)	43 (63.2%)	48(72.7%)	0.2393
Body mass index	32.56 ± 7.58	31.23 ± 8.03	0.3251
Initial vital signs			
Heart Rate	100.75 ± 19.1	101.14 ± 22.1	0.9139
Respiratory Rate	19.65 ± 3.14	20.38 ± 4.06	0.2466
Temperature	98.46 ± 1.55	98.42 ± 2.11	0.9141
Systolic Blood Pressure	119.71 ± 28.17	117.68 ± 26.53	0.6694
Diastolic Blood Pressure	70.94 ± 16.21	72.73 ± 18.09	0.5494
Shock index	0.9 ± 0.3	0.9 ± 0.29	0.8740
Pulse pressure	49.09 ± 17.52	44.95 ± 16.13	0.1592
Initial lab values			
White Blood Cell count	21.91 ± 11.85	25.3 ± 12.85	0.1151
Hemoglobin	12.5 ± 2.93	12.88 ± 3.49	0.4918
Glucose	216.88 ± 157.31	212.47 ± 155.83	0.8707
pH	7.11 ± 0.59	7.15 ± 0.49	0.6293
Creatinine	1.89 ± 1.65	2.06 ± 1.76	0.5776
C-Reactive Protein	28.26 ± 16.97	18.66 ± 11.39	0.0298
Sodium	136.07 ± 28.54	136.3 ± 28.4	0.9629
LRINEC score	6.94 ± 3.04	7.19 ± 3.41	0.8055
Time to OR	3.25 (2.1, 4.3)	8.75 (7, 14)	< 0.0001
ICU LOS	3 (2, 4)	3 (2, 3)	0.4845
Hospital LOS	12 (8.5, 23.5)	13.5 (8, 23)	0.9046

TG = Transfer Group; DAG = Direct Admit Group; LRINEC = Laboratory Risk Indicator for Necrotizing Fasciitis; OR = Operation Room; LOS = length of stay. All values were presented as mean ± standard deviations or median with first and third quartiles inside the parenthesis

Table 2 Comparison of clinical outcomes between the transfer group (TG) and direct admit group (DAG)

	TG *N* = 68	DAG *N* = 66	*P*-value
Hours from ED presentation to surgery			< 0.0001
0 to 6	65 (95.6%)	7 (10.6%)	
6.1 to 12	1 (1.5%)	34 (51.5%)	
12.1–18	1 (1.5%)	11 (16.7%)	
> 18	1 (1.5%)	14 (21.2%)	
Site of infection			0.0499*
Abdominal wall and chest	3 (4.4%)	5 (7.6%)	
Perineum and buttock	15 (22.1%)	9 (13.6%)	
Upper extremity	17 (25%)	30 (45.5%)	
Lower extremity	33 (48.5%)	22 (33.3%)	
Intravenous/subcutaneous drug injection	21 (30.9%)	20 (30.3%)	0.9420
Diabetes mellitus	42 (61.8%)	37 (56.1%)	0.5022
End stage renal disease (dialysis)	3 (4.4%)	10 (15.2%)	0.0357
Hypertension	27 (39.7%)	32 (48.5%)	0.3061
Dead at hospital discharge	8 (11.8%)	15 (22.7%)	0.0925
Extremity amputation	13 (19.1%)	11 (16.7%)	0.7114
Skin graft	22 (32.4%)	16 (24.2%)	0.2977

TG = Transfer Group; DAG = Direct Admit Group; ED = emergency department; * p-values were calculated based on Fisher's exact test

difficult for a direct comparison with regards to time to operative management, as we did not collect time data for patients in TG before they arrived at ARMC ED over the 10-year span of this study.

The mortality rate among patients with NF was lower in TG when compared to DAG (11.8% vs. 22.7%). Nearly all patients (95.6%) in TG received operative management within 6 h of arrival to ARMC ED. Patients who are transferred for suspected NF would routinely have a surgical consult requested soon after arrival and initial assessment by the ED. In contrast, only 10.6% of all patients in DAG underwent surgical intervention within 6 h. Anchoring bias may have benefitted these transferred patients. The surgical team at ARMC may be more in agreement with the presumed diagnosis of NF if the patients already received a surgical consultation at the transferring facility. Additionally, the surgeons may be more aggressive with transferred patients as their care has already been delayed.

Patients who present to an ED with symptoms concerning for NF or other serious soft tissue infections likely would meet criteria for a sepsis evaluation, including the implementation of the sepsis bundle [16]. The sepsis bundle is a standardized approach to the management of sepsis, consisting of a series of interventions designed to improve early recognition, diagnosis, and treatment of sepsis. Key components include early broad-spectrum antibiotics, aggressive intravenous fluid resuscitation, and continual reassessment. Published studies demonstrated that the implementation of the sepsis bundle has a positive effect on patient's mortality. Nguyen and colleagues noted that in-hospital mortality was less in patients with the sepsis bundle completed (20.8 vs. 39.5%) compared to patients who did not get a completed bundle [17]. When mandated in the state of New York, the protocolized sepsis care resulted in a decrease of in-hospital mortality [18].

This approach aligns with recommendations for treating suspected NF. While the specific focus on NF in the sepsis bundle may be limited, the principles underlying the bundle are directly applicable to this condition. NF is characterized by tissue necrosis and systemic inflammation, which can rapidly progress to sepsis. The inflammatory response can lead to tissue damage, organ dysfunction, and ultimately, death. Therefore, early recognition and aggressive treatment are critical in improving outcomes for patients with NF. While timely operative management is still recommended, for patients transferred from facilities lacking surgical specialists, aggressive management with broad-spectrum antibiotics and intravenous fluids can be effective in stabilizing the patient.

The findings of the current study may be limited by several factors. As a retrospective review of a single institution, it is possible that our findings represent a cohort of subjects unique to a particular region. Additionally, it is difficult to collect data on the time spent from presentation at the transferring facility to arrival at ARMC ED, nor could we control for the amount of time patients spent at the transferring facility. Furthermore, practice patterns amongst providers may also affect outcomes observed. We feel that these limitations have merit for investigation. However, for the scope of our study we feel these limitations are relatively minor and likely do not change the overall trajectory of care in patients with suspected NF.

Table 3 Detailed summary of expired patients for the TG and DAG respectively. P-value could not be calculated due to low N values

	TG Expired Patients ***N*** **= 8**	**DAG Expired Patients** ***N*** **= 15**
Age	46.96 ± 12.42	52.17 ± 12.82
Gender, male (%)	7 (87.5%)	10 (66.7%)
Body mass index	32.56 ± 7.58	31.23 ± 8.03
Initial vital signs		
Heart Rate	100.75 ± 19.1	101.14 ± 22.1
Respiratory Rate	19.65 ± 3.14	20.38 ± 4.06
Temperature	98.46 ± 1.55	98.42 ± 2.11
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Sodium	136.07 ± 28.54	136.3 ± 28.4
LRINEC score	6.94 ± 3.04	7.19 ± 3.41
Time to OR	3.25 (2.1, 4.3)	8.75 (7, 14)
ICU LOS	3 (2, 4)	3 (2, 3)
Hospital LOS	12 (8.5, 23.5)	13.5 (8, 23)
Hours from ED presentation to surgery		
0 to 6	5 (62.5%)	6 (40%)
6.1 to 12	1 (12.5%)	1 (6.7%)
12.1–18	1 (12.5%)	1 (6.7%)
> 18	1 (12.5%)	7 (46.7%)
Site of infection		
Abdominal wall and chest	1 (12.5%)	0 (0%)
Perineum and buttock	2 (25%)	2 (13.3%)
Upper extremity	4 (50%)	9 (60%)
Lower extremity	1 (12.5%)	4 (26.7%)
Intravenous/subcutaneous drug injection	4 (50%)	8 (53.3%)
Diabetes mellitus	5 (62.5%)	7 (46.7%)
End stage renal disease (dialysis)	0 (0%)	4 (26.7%)
Hypertension	2 (25%)	6 (40%)
Extremity amputation	2 (25%)	3 (20%)
Skin graft	1 (12.5%)	1 (6.7%)

TG = Transfer Group; DAG = Direct Admit Group; ED = emergency department

Conclusions

Suspected NF presents a difficult challenge to emergency physicians, especially for those working at institutions lacking appropriate surgical services. While prompt surgical interventions continue to be a crucial aspect of patient care, aggressive management with broad-spectrum antibiotics and intravenous fluid resuscitation may have a positive impact on a patient's outcome. It is highly probable that this aggressive management can temporize the need of surgical intervention for patients requiring transfer to a facility with an available surgical specialist for higher level of care.

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Author contributions
AM JK SCN SP NLS MM CW: literature review, IRB application, chart review, data extraction, manuscript revision.MMN FD LT RB DW: literature review, design of the study, data extraction, data analysis, and manuscript revision.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Ethical approval to report this case was obtained from Arrowhead Regional Medical Center Institutional Review Board with the IRB approval number 19–22. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Written informed consent was obtained from all participants and from a parent and/or legal guardian.

Consent for publication
Not applicable. This study is a retrospective chart review. Patients' identifiers were removed before the data analysis. Patients' data were reported in aggregated format. No individual patient will be identified in this manuscript. This study was approved by the Institutional Review Board at Arrowhead Regional Medical Center with the approval number 19–22.

Competing interests
The authors declare no competing interests.

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