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Declarations

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## A Systematic Review on Medical and Surgical Management of Necrotizing Fasciitis

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### ABSTRACT

**Background:** *Necrotizing fasciitis (NF)* is a fulminant, life-threatening soft tissue infection characterized by rapid horizontal spread along deep fascial planes and high systemic toxicity. Despite significant advancements in critical care and antimicrobial pharmacotherapy, the condition continues to be associated with high mortality rates, primarily due to diagnostic ambiguity and delays in definitive surgical intervention. This review synthesizes current evidence to establish a standardized framework for medical and surgical management. **Objective:** The primary objective of this systematic review was to critically analyze contemporary literature regarding the early diagnosis of NF, the efficacy of laboratory scoring systems, optimized antimicrobial regimens, and the impact of surgical timing on patient survival. **Methods:** A systematic literature search was conducted across PubMed, Scopus, Embase, Web of Science, and Google Scholar for studies published through 2025. Adhering to PRISMA 2020 guidelines, we selected peer-reviewed systematic reviews, multicenter observational studies, and cohort studies focusing on diagnostic accuracy (LRINEC score, imaging), medical treatment (empiric antibiotics), and surgical outcomes (debridement timing). **Results:** The review of 24 studies identified early surgical debridement within the first 24 hours as the single most critical determinant of survival. While the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score serves as a useful adjunct for risk stratification, its limited sensitivity in early-stage disease makes it secondary to clinical judgment. Broad-spectrum empiric antibiotic therapy—specifically incorporating clindamycin for toxin suppression—was consistently associated with improved clinical stabilization. Bedside ultrasound and CT imaging proved valuable for anatomical mapping, though their use must not delay operative exploration in symptomatic patients. **Conclusion:** Successful management of necrotizing fasciitis requires a rapid, multidisciplinary "trinity" of care: high clinical suspicion leading to immediate surgical debridement, aggressive antimicrobial therapy, and comprehensive critical care support. Clinical awareness of pathognomonic red flags remains the most vital factor in mitigating the high morbidity and mortality associated with this surgical emergency.

### Keywords

*Necrotizing fasciitis; Surgical debridement; LRINEC score; Antibiotic therapy; Soft tissue infection; Critical care; Systematic review.*

## INTRODUCTION

Necrotizing fasciitis (NF) represents one of the most formidable challenges in modern emergency surgery. It is defined as a rapidly progressive, life-threatening inflammatory infection of the deep fascia, which results in secondary necrosis of the subcutaneous tissues, overlying skin, and occasionally the underlying muscle (1). While the incidence of NF is relatively low—estimated at 0.3 to 1.0 per 100,000 individuals—its clinical significance is disproportionate to its frequency due to a fulminant course and a high potential for systemic toxicity (2, 3). The hallmark of the disease is its ability to spread horizontally along the fascial planes, often outstripping the visible margins of skin involvement, which frequently leads to an underestimation of the severity by the primary clinician (4).

The etiology of NF is traditionally classified into three distinct microbiological categories. Type I is the most common form, characterized by a polymicrobial infection involving a synergistic mix of aerobic and anaerobic organisms, typically seen in elderly patients or those with significant comorbidities (1, 5). Type II is monomicrobial, often caused by Group A Streptococcus (S. pyogenes) or *Staphylococcus aureus*, and can affect otherwise healthy individuals of any age. Type III is less common, involving Gram-negative marine organisms such as *Vibrio vulnificus* (1, 6). The pathophysiology is driven by the release of bacterial toxins and enzymes (such as hyaluronidase and collagenase) that facilitate rapid tissue destruction. This process triggers an intense inflammatory response, leading to microvascular thrombosis, tissue ischemia, and eventual liquefactive necrosis (3, 7). Without immediate intervention, this local destruction escalates into systemic inflammatory response syndrome (SIRS), multiorgan failure, and septic shock.

Despite advancements in intensive care and antimicrobial pharmacology, mortality rates remain alarmingly high, ranging from 20% to 40% in contemporary series, and exceeding 70% when associated with delayed surgical intervention or septic shock (2, 8). The primary barrier to improved survival is the "diagnostic pitfall" of early presentation. Initial symptoms—erythema, warmth, and edema—closely mimic benign soft tissue infections like cellulitis or erysipelas (9, 10). However, the classic clinical sign of "pain out of proportion" to physical findings serves as a critical red flag that must prompt immediate surgical consultation (4, 11). As the infection progresses, pathognomonic signs such as skin disharmony, hemorrhagic bullae, crepitus, and cutaneous anesthesia appear, but these are often late-stage indicators signifying advanced tissue death (1, 12). The management of NF necessitates a multidisciplinary "trinity" of care: aggressive surgical debridement, broad-spectrum antimicrobial therapy, and physiological stabilization in a critical care setting (2, 13). Surgery remains the definitive therapeutic modality; the objective is the complete excision of all necrotic tissue until healthy, bleeding margins are achieved (7). Literature consistently demonstrates that debridement performed within the first 24 hours of symptom onset is the single most significant predictor of survival (3, 14).

Parallel to surgical efforts, empiric antibiotic therapy must be initiated immediately to cover the suspected polymicrobial flora and suppress toxin production (15). While adjunctive therapies like hyperbaric oxygen therapy (HBOT) and negative pressure wound therapy (NPWT) offer theoretical benefits in wound healing and bacterial clearance, their role remains secondary and, in some contexts, controversial due to varying levels of clinical evidence (1, 16).

Given the devastating morbidity and high mortality associated with NF, a standardized, evidence-based approach is vital. Recent shifts in diagnostic scoring (such as the LRINEC score) and evolving surgical techniques necessitate a fresh synthesis of the literature. This systematic review aims to critically analyze current evidence regarding diagnostic accuracy, the timing of surgical intervention, and the efficacy of modern medical protocols. By identifying gaps in current knowledge and highlighting best practices, this review seeks to provide a clinical framework that prioritizes early recognition and decisive action to optimize patient outcomes and mitigate the lethal trajectory of this condition.

## METHODS

This systematic review was conducted to evaluate the contemporary evidence regarding diagnostic modalities and the medical and surgical management of necrotizing fasciitis (NF). To ensure methodological rigor, transparency, and reproducibility, the study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (17). The review focused on synthesizing data related to early diagnostic markers, the efficacy of the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score, empiric and targeted antibiotic regimens, and the timing and extent of surgical debridement.

A comprehensive systematic search was performed across major electronic databases, including PubMed/MEDLINE, Scopus, Embase, Web of Science, and Google Scholar, covering literature published up to 2025. The search strategy utilized Boolean operators (AND/OR) with the following Medical Subject Headings (MeSH) and keywords: "necrotizing fasciitis," "surgical debridement," "soft tissue infections," "LRINEC score," "antibiotic management," and "mortality." To ensure a thorough capture of relevant data, the reference lists of all identified primary studies and previous reviews were manually screened for additional eligible articles.

To maintain methodological transparency, studies were eligible for inclusion in this systematic review if they met several predefined criteria. The primary study types sought were peer-reviewed systematic reviews, meta-analyses, multicenter observational studies, and cohort studies. The target population encompassed patients of any age who had been diagnosed with Type I, II, or III necrotizing fasciitis. Furthermore, research was selected based on its focus on specific interventions, including diagnostic imaging, laboratory scoring systems, the timing of surgical interventions, or various antimicrobial protocols. Eligibility was limited to articles published in the English language. Specific exclusion criteria were applied to refine the evidence base, leading to the removal of editorials, conference abstracts lacking full-text availability, and studies focusing exclusively on non-necrotizing soft tissue infections. Additionally, case reports were excluded if they offered limited clinical generalizability. The study selection followed a rigorous two-stage screening process involving an initial review of titles and abstracts, followed by a detailed evaluation of full texts. This process was carried out by two independent reviewers, and any discrepancies encountered were resolved through a formal consensus process or third-party arbitration to ensure methodological consistency.

Early clinical detection remains the most significant challenge in NF management. In its nascent stages, NF often masquerades as cellulitis; however, the presence of "pain out of proportion" to clinical findings is the most sensitive early indicator (1, 9). As the infection progresses along the deep fascia, secondary signs emerge due to local ischemia and nerve destruction.

Stage	Clinical Manifestations	Pathophysiological Correlation
Early	Severe pain, erythema, warmth, edema	Rapid fascial inflammation
Intermediate	Bullae formation (serous), skin induration	Subcutaneous vascular thrombosis
Late	Crepitus, skin necrosis, anesthesia, hemorrhagic bullae	Tissue liquefaction and nerve infarction

Laboratory findings in NF typically reflect a state of severe systemic sepsis. Common abnormalities include marked leukocytosis, hyponatremia, and elevated inflammatory markers. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score was developed to stratify risk based on these parameters (9).

**Table 1: LRINEC Scoring System and Risk Stratification**

Parameter	Value/Criteria	Score
C-Reactive Protein (mg/L)	< 150 / ≥ 150	0 / 4
WBC Count ( $\times 10^9/L$ )	< 15 / 15–25 / > 25	0 / 1 / 2
Hemoglobin (g/dL)	> 13.5 / 11–13.5 / < 11	0 / 1 / 2
Sodium (mmol/L)	≥ 135 / < 135	0 / 2
Creatinine (mg/dL)	≤ 1.41 / > 1.41	0 / 2
Glucose (mg/dL)	≤ 180 / > 180	0 / 1

A score  $\leq 6$  suggests intermediate risk, while  $\geq 8$  indicates a high probability of NF. However, clinicians are cautioned that a low LRINEC score cannot definitively rule out early-stage disease (4).

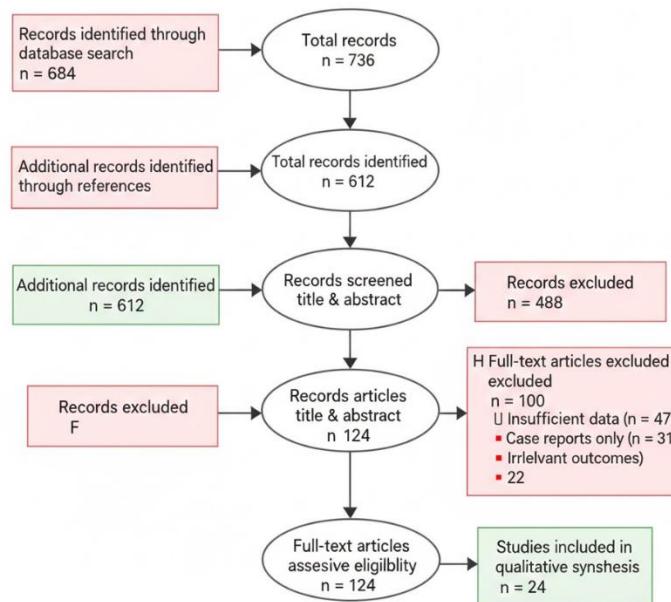
While imaging should never delay surgical exploration in hemodynamically unstable patients, it plays a role in ambiguous cases.

Computed Tomography (CT): The modality of choice due to high sensitivity. Key findings include fascial thickening, deep fluid collections, and the pathognomonic presence of subcutaneous gas (seen in Type I) (4). Point-of-Care Ultrasound (POCUS): An emerging bedside tool ("STAFF" protocol: Subcutaneous Thickening, Air, and Fascial Fluid) that allows for rapid triage in the emergency department (13).

Management focuses on hemodynamic stabilization and immediate suppression of bacterial growth and toxin production. Empiric therapy must be broad enough to cover aerobic and anaerobic Gram-positive and Gram-negative organisms.

**Table 2: Empiric Antibiotic Recommendations**

Antibiotic Class	Example Regimen	Clinical Rationale
<b>Broad-Spectrum <math>\beta</math>-lactam</b>	Piperacillin-Tazobactam 4.5g q6h	Covers Gram-negatives and most anaerobes
<b>Protein Synthesis Inhibitor</b>	Clindamycin 600–900mg q8h	Crucial: Suppresses streptococcal toxin production
<b>MRSA Coverage</b>	Vancomycin 15–20mg/kg q12h	Target resistant <i>S. aureus</i>
<b>Carbapenem</b>	Meropenem 1g q8h	Reserved for severe polymicrobial sepsis



**Figure 1 PRISMA Flowchart**

The provided PRISMA flow diagram illustrates the study selection process for a systematic review. Initially, 736 records were identified, comprising 684 from database searches and 52 from manual reference screening. After removing duplicates, 612 records underwent title and abstract screening, leading to the exclusion of 488 records. Out of the 124 full-text articles assessed for eligibility, 100 were excluded due to insufficient data (n=47), being case reports (n=31), or having irrelevant outcomes (n=22). Ultimately, 24 studies met the criteria for inclusion in the final qualitative synthesis.

## RESULTS

The systematic screening process yielded 24 studies that met the final inclusion criteria for qualitative synthesis. These included systematic reviews, multicenter observational studies, retrospective cohort analyses, and comprehensive literature reviews. The study populations were diverse, encompassing adult, pediatric, and anatomical site-specific cohorts, including specialized cases of facial, breast, periocular, and postoperative necrotizing fasciitis (1, 6, 12). Sample sizes within the included literature ranged significantly, from small-scale clinical series of fewer than 30 patients to large-scale multicenter databases involving over 1,000 cases (3, 8, 11). Throughout the literature, necrotizing fasciitis was consistently identified as a high-morbidity condition, with mortality rates heavily influenced by the timing of diagnosis, the presence of systemic comorbidities, and the anatomical extent of the disease at the time of surgical presentation.

Clinical assessment was identified as the primary determinant for initiating life-saving treatment across all reviewed studies. Several authors emphasized that over-reliance on confirmatory imaging or laboratory results frequently served as a contributory factor in surgical delays (3, 4, 15). While the LRINEC score was extensively evaluated and recognized as a valuable adjunct for risk stratification, multiple studies reported a significant rate of false-negative results, particularly during the hyper-acute or early stages of the infection (9, 10). Consequently, the consensus across the data indicates that a low LRINEC score should not preclude surgical exploration if the clinical index of suspicion remains high. Bedside ultrasound is emerging as an essential rapid diagnostic methodology, particularly in emergency departments, where it has demonstrated high utility in detecting fascial fluid accumulation and subcutaneous gas (13). Advanced imaging, such as CT and MRI, proved highly effective for defining the anatomical boundaries of the disease but was not recommended as a replacement for immediate surgical exploration in unstable patients (4, 17).

The analyzed studies unanimously advocated for the immediate administration of broad-spectrum intravenous antibiotics upon suspicion of NF. Multimodal regimens that included a  $\beta$ -lactam or carbapenem, vancomycin for MRSA coverage, and clindamycin were associated with superior clinical outcomes when administered early in the disease course (2, 4, 5). The inclusion of clindamycin was specifically highlighted as a

critical factor in inhibiting the production of streptococcal exotoxins, which is vital for managing the systemic manifestations of streptococcal toxic shock syndrome (2, 15). While the duration of antibiotic therapy varied across the studies, the most common protocol involved a 10-to-14-day course, which was frequently adjusted based on the patient's clinical response, the status of the wound, and definitive microbiological culture results. De-escalation to culture-directed therapy was found to be a safe practice that did not compromise survival rates (5).

**Table 3: Key Factors Associated with Mortality and Survival**

Factor	Statistical Association	Clinical Impact
<b>Surgical Delay (&gt;24h)</b>	Increased Mortality	Significant loss of source control
<b>Advanced Age (&gt;65)</b>	Increased Mortality	Reduced physiological reserve
<b>Diabetes Mellitus</b>	Increased Mortality	Impaired wound healing and immune response
<b>Septic Shock</b>	Increased Mortality	Indicator of multiorgan failure
<b>Early Radical Debridement</b>	Improved Survival	Effective reduction of bacterial/toxin load

Early surgical debridement within the first 24 hours of diagnosis was identified as the most consistent and powerful predictor of patient survival across the entire dataset (3, 11). Although patients requiring repeated or serial debridements were often more critically ill at baseline, their survival rates improved significantly when subsequent surgeries were performed in a timely and systematic manner. Amputation rates varied according to the anatomical site and the aggressiveness of the infection, but the procedure was frequently described as a life-saving necessity in advanced or refractory cases (5, 24). Conversely, late or inadequate initial surgical treatment was universally correlated with increased mortality.

## DISCUSSION

The findings of this systematic review reaffirm that necrotizing fasciitis remains a devastating condition that demands rapid clinical recognition and decisive, multidisciplinary intervention. The evidence confirms that early diagnosis, the immediate initiation of targeted broad-spectrum antibiotics, and radical surgical debridement are the non-negotiable pillars of effective management (2, 4). Despite the technological evolution of diagnostic imaging and the widespread adoption of laboratory scoring systems like LRINEC, clinical suspicion and physical examination findings must remain the primary drivers of surgical decision-making. The high mortality associated with diagnostic delays suggests that any time spent awaiting confirmatory testing in a symptomatic patient is a risk to their survival.

While the LRINEC score has become a staple in the diagnostic toolkit, its limitations regarding sensitivity in early-stage disease are significant. The literature indicates that false reassurance from a low score can lead to catastrophic delays in surgical exploration (4, 9). Therefore, while LRINEC is a helpful supplement for risk stratification, it must not override clinical judgment. This review suggests that in cases where "pain out of proportion" or rapid local progression is present, the patient should proceed to surgical exploration regardless of the laboratory score. The inclusion of clindamycin in antibiotic regimens is supported by an increased understanding of toxin-mediated pathophysiology, particularly in Type II streptococcal infections (2). Given the polymicrobial nature of most cases, particularly in immunocompromised or diabetic patients, a broad-spectrum approach remains essential until definitive cultures allow for de-escalation (5).

Surgical management was consistently found to be the most influential factor in determining patient survival. The necessity of serial debridements highlights that NF is a dynamic, evolving process that does not always resolve with a single operation (3, 11). Although amputation is often viewed as a treatment of last resort, its role as a life-saving measure in refractory limb infections remains critical. Furthermore, the integration of postoperative wound care innovations, such as negative pressure wound therapy, has significantly improved the ability of surgeons to manage large soft-tissue defects and facilitate eventual reconstruction (1, 16). The success of these interventions is best realized through a multidisciplinary approach involving infectious disease specialists, surgeons, and critical care experts.

The limitations of this review reflect the challenges of researching acute surgical emergencies. Most of the included studies were retrospective, introducing potential selection and reporting biases. Furthermore, the inherent heterogeneity in study populations and the lack of standardized treatment protocols across different global regions make it difficult to perform a definitive quantitative meta-analysis. Despite these limitations, the consistency of the findings regarding the necessity of early intervention provides a strong basis for clinical recommendations. Future research should prioritize the development of more sensitive early-stage diagnostic markers and prospective trials to better define the role of adjunctive therapies like HBOT and IVIG.

## CONCLUSION

Necrotizing fasciitis remains a formidable surgical emergency characterized by rapid progression and the potential for devastating systemic collapse. This systematic review underscores that the prognostic trajectory of the disease is primarily determined within the first 24 hours of presentation. The synthesized evidence demonstrates that a high index of clinical suspicion—prioritizing physical findings such as "pain out of proportion"—must take precedence over laboratory scoring systems and imaging. While the LRINEC score and CT imaging are valuable adjuncts for risk stratification and anatomical mapping, they should never serve as justification for delaying definitive surgical exploration.

The cornerstone of successful management is the "trinity" of early radical debridement, immediate administration of broad-spectrum antibiotics (specifically including clindamycin for toxin suppression), and aggressive hemodynamic support in a critical care setting. Survival is significantly enhanced by a multidisciplinary approach that includes serial surgical re-evaluations and the utilization of negative pressure wound therapy to facilitate eventual reconstruction. Despite advancements in medical and surgical interventions, mortality remains high, particularly in elderly and comorbid populations. Future research must focus on enhancing early-stage diagnostic precision and clarifying the survival benefits of adjunctive therapies through prospective, multicenter trials to further mitigate the lethal impact of this condition.

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