## **REVIEW ARTICLE**

# Use of an Objective Tool in Management of Necrotizing Fasciitis

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## ABSTRACT

Necrotizing fasciitis is on the right end of the spectrum with associated high morbidity and mortality. Although the descriptions of this can be dated to the times of Hippocrates, the mortality associated with the disease remained high. Early surgical debridement without any controversy is accepted as the single best prognostic indicator, but due to the masked and overlapped clinical findings relying on the clinical provess of the treating surgeon is questionable. Due to which we need to have an objective method of assessment, many researchers have assessed the use of various biochemical, imaging, and histopathological investigation, which has been reviewed in the same.

Keywords: LRINEC, MRI, Necrotizing fasciitis.

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#### INTRODUCTION

There is no definition, but multiple descriptions such as "Necrotizing fasciitis represents a group of highly lethal infections characterized by rapidly progressing inflammation and necrosis. The spectrum of the disease ranges from necrosis of the skin to life-threatening infections involving the subcutaneous tissue, fascia, and muscle."<sup>1–3</sup> The incidence of this condition is noted as ranges from 0.3 to 15 cases per 100,000 population.<sup>20,21</sup> Necrotizing fasciitis can occur in any region of the body but is often encountered in the extremities, as a result of a disruption to the skin due to trivial trauma such as insect bite, burn, surgical incision, laceration,<sup>4,5</sup> in developing countries, herbal mixtures of unknown contents are used to treat wounds by local application. It is toxic and highly contaminated and can initiate and exacerbate the progression of soft tissue infection. Its use can lead to progressive necrosis in the patient.<sup>6</sup>

The mortality rate of necrotizing fasciitis ranges from 24 to 80%.<sup>7</sup> Wong et al. in their study have published the correlation between delay in diagnosis with increased risk of mortality (relative risk of 9.4, p < 0.05).<sup>8</sup> The same has been noted in various other case reports and studies.<sup>9</sup> The reason for this is the rarity of the disease with minimal specific signs, which often overlap with the clinical findings of non-necrotizing soft tissue infections like cellulitis.<sup>10,11</sup> Most of the patients developing NF have some of the other preexisting condition that makes them vulnerable to the disease<sup>25,26</sup> such as elderly age, diabetic, IV drug users, immunocompromised state, peripheral vascular disease, renal failure, obesity, malnutrition, congestive heart failure, and chronic liver disease.<sup>12–16</sup> Chronic use of NSAID before hospital admission is at present being studied as a risk factor, with no established evidence,<sup>15,17-20</sup> although multiple studies are emphasizing the correlation between diabetes mellitus and necrotizing fasciitis.<sup>21–23</sup> But some authors have published results contradicting it.24

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# DEMOGRAPHY, ETIOPATHOLOGY, AND CLINICAL FEATURES

#### Demographics

NF is precipitated in most of the conditions by trivial trauma such as insect bites, abrasions, and lacerations, blunt trauma even tattooing as noted in multiple independent studies.<sup>11,13,25</sup>

#### Etiopathogenesis

"Synergistic gangrene" is another nomenclature used to describe NF as the presence of polymicrobial growth is seen in the necrotic tissue. After gaining entry into the host, the bacteria as well and the host factors influence it to spread in the deep tissue planes leading to the formation the gangrene.<sup>26-28</sup>

#### **Clinical Features**

Whereas Fernando et al. studied the sensitivity and specificity of three clinical parameters that they in their meta-analysis study found to be common in most of the patients in the seven studies they

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reviewed, the three parameters being fever, hemorrhagic bullae, and hypotension (Table 1).<sup>29</sup>

After assessing the parameters, it is seen that none of the above parameters are sensitive to NF but the specificity of the signs is significant to differentiate necrotizing from non-necrotizing soft tissue infections.<sup>29,30</sup> With the above two studies, we can infer that clinical suspicion should be high in differentiating the two entities of soft tissue infections.<sup>10,29</sup> Moreover, there is poor sensitivity and specificity in diagnosing with clinical examination alone.<sup>29</sup>

## INVESTIGATIONS

## Laboratory Parameters

Early surgical intervention is one of the cornerstones in the favorable outcome of  $\rm NE^{10,31}$ 

Wall et al. in their retrospective study trying to establish a model differentiating NSTI from non-necrotizing soft tissue infections studied the use of two laboratory parameters, i.e., WBC counts (>15.5 × 10<sup>9</sup>/L) and serum sodium value (<135 mmol/L). Ninety percent of the necrotizing and 24% of the non-necrotizing infection cases met the criteria for the model and showed a negative predictive value of 99% and a poor positive predictive value of 26%.<sup>32</sup>

Wong et al. came up with another model based on the laboratory values (LRINEC) used to distinguish necrotizing from non-necrotizing soft tissue infection in equivocal cases. Their model is comprised of six parameters as follows (Table 2).

They defined the grading as a max score of 13 a score of 6 or more should raise the suspicion of necrotizing fasciitis and a score of 8 or more is strongly predictive of this disease. They did a retrospective observational study with a positive predictive value of 92% and a negative predictive value of 96%.<sup>30</sup>

Multiple studies validated the LRINEC scoring and found a significant statistical correlation between LRINEC and true diagnosis of NF.<sup>33–35</sup> A few reported not only the reliability of LRINEC scoring in diagnosing NF but also the higher score correlating with higher SOFA score, prolonged hospital stay, prolonged ICU stay, and mortality. They also added that LRINEC had a decreased sensitivity in immunocompromised patients.<sup>34,36</sup>

El-Menyar et al. concluded in their retrospective study the significance of LRINEC in diagnosing NF. They classified the patients into two groups: (1) less than 6 and (2) more than or equal to 6, thus also proving that the scoring used in these two grading classifications is sufficient to diagnose NF.<sup>34</sup>

Imaging has always been the cornerstone of the diagnosis of NF. With most of the studies validating LRINEC to be a robust tool in the early diagnosis of necrotizing fasciitis, there are a few studies that have shown conflict in results (Table 3).<sup>34</sup>

Radiograph that is a commonly used diagnostic modality shows soft tissue opacities in NF same as that seen in non-necrotizing soft tissue infections such as cellulitis.<sup>39–41</sup> Gas along the fascial plane is a classical sign, which is present in 24.8–55% of the cases,<sup>31,39–41</sup>

Table 1: The sensitivity and specificity of clinical signs in diagnosing NSTI according to Fernando et al.  $^{\rm 29}$ 

Clinical features	Sensitivity (%)	Specificity (%)
Fever	46	77
Hemorrhagic bullae	25.2	95.8
Hypotension	21.0	97.7

although we cannot rule out NF in the absence of this classical sign.<sup>42</sup> This can also be used to identify the etiology such as a foreign body or a fracture.<sup>40,43</sup>

### Sonology

Clark and Fisher<sup>44</sup> studied the role of sonography in the workup of NF and concluded that its role is limited due to the lack of better resolution in the deeper structures. And it is better for identifying gas in the soft tissue planes, whereas non-specific changes such as hypotonicity of the overlying fat, cobblestone appearance due to subcutaneous edema but if used it is better to use to differentiate NF from abscess, deep vein thrombosis,<sup>45</sup> and in children<sup>44</sup> where exposure to radiation in CT or MRI requiring the patient to be still might have technical difficulties.

Sensitivity is 88.2% and specificity is 93.3% as stated by Yen et al.<sup>46</sup> However, a few studies stated the addition of Doppler duplex scan and laboratory investigation to correlate with B mode ultrasound findings.<sup>46,47</sup> As this investigation has an operator-based study, there can be subjective variation.

### **Computer Tomography**

Computed tomography is generally the investigation go to due to its wide availability and high spatial resolution it is better than both radiograph and ultrasound.<sup>43</sup> Wysoki et al. studied a total of 20 cases of NF in which 80% of the cases had thickening and fat stranding, 55% had soft tissue gas, but all these are not specific to NF.<sup>48</sup> However, CT can help assess the bone and soft tissue involvement and also identify the source of infection.<sup>40,42,48,49</sup> Gas within the fluid collection is pathognomonic to NF.<sup>49,50</sup> CT has a sensitivity of 80% and has low specificity, especially when done in the early stages and aerobic infections.<sup>49</sup>

#### **Magnetic Resonance Imaging**

Two independent studies have stated that the MRI due to its excellent soft tissue delineation and contrast resolution is the gold standard modality of investigation for NF with a sensitivity of 93%.<sup>42,51</sup>

Ali et al. have described the findings of NF in MRI as the presence of a thick hyperintense signal in deep fascia of the muscle in T2 weighted or short tau inversion-recovery images, thickness >3 mm is described to be significant.<sup>52</sup>

#### Table 2: LRINEC scoring system of Wong et al.

Criteria	Value	Points
CRP (mg/L)	<150	0
	≥150	+4
WBC per mm <sup>3</sup>	<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



Table 3: Various studies showing statistical outcomes for LRINE
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Studies	Positive predictive value (%)	Negative predictive value (%)	Sensitivity (%)	Specificity (%)
Wong et al. study <sup>30</sup>	92	96	NA	NA
Hsiao et al. study <sup>37</sup>	25	92	43	83
Liao et al. study <sup>38</sup>	37.9	92.5	59.2	83.8

Study	Sensitivity (%)	Specificity (%)
Masood et al. <sup>54</sup>	100	86
Schmid et al. <sup>55</sup>	100	86
Malghem et al. <sup>56</sup>	100	86

Kim et al. studied MRI in a total of seven cases with NF and 23 cases with non-necrotizing soft tissue infection and reported the following findings: (1) Thick hypointense signal density on fat suppression and T2 sequence. (2) Low signal intensity with the thickness of >3 mm in the deep fascia. (3) Focal or diffuse non-enhancing area in the portion of abnormal signal intensity in deep fascia. (4) Extensive and involvement of three or more compartments in one extremity.<sup>53</sup> Both Chaudhry et al. and Gok et al. have concluded that if subcutaneous edema is not the predominant feature, then necrotizing fasciitis should be considered as the diagnosis rather than cellulitis (Table 4).<sup>40,42</sup>

#### **Tissue Specimen**

As of tissue biopsy, Hietbrink et al. studied a total of 21 patients of suspected NF with their study design of "Triple assessment" where surgical macroscopic findings, frozen section biopsy, grams staining was used and compared the results and found a positive correlation between the two.<sup>57</sup> They have also defined the macroscopic features such as lack of bleeding, lack of tissue resistance, gray necrotic tissue, non-contracting muscles, fascial edema, and purple blisters on the skin.<sup>57</sup> Another advantage is the ability to isolate the causative organism.<sup>39</sup> But sectional biopsy techniques tend to implant an otherwise superficial infection in the deeper fascial plane it is controversial.<sup>58</sup>

There is strong evidence of MRI being a better diagnostic tool as compared to LRINEC in the early diagnosis of necrotizing fasciitis and in turn in better clinical outcomes. Further research is required in creating a better tool for the same.

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