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MUSCULOSKELETAL

Distinguishing necrotizing from non-necrotizing fasciitis: a new predictive scoring integrating MRI in the LRINEC score

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Abstract

Objectives To develop and validate a scoring system integrating MRI and laboratory findings to differentiate necrotizing fasciitis (NF) from non-necrotizing fasciitis (non-NF).

Methods This retrospective study included 144 subjects who underwent surgery in one of three tertiary referral centers for NF or cellulitis with non-NF. The development cohort consisted of 96 subjects (NF = 47; non-NF = 49) from one center, and the validation cohort consisted of 48 subjects (NF = 23; cellulitis with non-NF = 25) from two different centers. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) scoring system and five MRI findings (thickening of the intermuscular deep fascia ≥ 3 mm, extensive involvement of the deep fascia, multi-compartmental involvement in one extremity, presence of gas, and contrast-enhancement pattern) were included in univariate and multivariate logistic regression analysis to identify independent predictors of NF. An additive scoring system was developed using the coefficients of the final regression model. Model performance was assessed for discrimination and calibration. The scoring system was externally validated.

Result The final scoring system consisted of three variables: thickening of the deep fascia ≥ 3 mm, multi-compartmental involvement, and LRINEC score. The new predictive model showed improved performance (area under the receiver operating characteristic curve [AUC], 0.862; positive and negative predictive values, 82% and 79%, respectively), compared with the LRINEC score alone (0.814, 77% and 67%, respectively). The model also showed good discrimination with the external validation dataset (AUC, 0.933).

Conclusions Differentiation of NF from severe cellulitis with non-NF can be achieved with the new predictive scoring system.

Key Points

- *The new predictive scoring system integrating two MRI findings with the LRINEC score can help in the differentiation of necrotizing fasciitis from severe cellulitis with non-necrotizing fasciitis.*
- *Thickening of the deep fascia ≥ 3 mm and multi-compartmental involvement were the most important MRI findings for the differentiation.*

Keywords Fasciitis, necrotizing · Cellulitis · Fasciitis · Magnetic resonance imaging

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Abbreviations

AUC	Area under the receiver operating characteristic curve
CRP	C-reactive protein
LRINEC	Laboratory Risk Indicator for Necrotizing Fasciitis
MRI	Magnetic resonance imaging
NF	Necrotizing fasciitis
NPV	Negative predictive value
PPV	Positive predictive value
ROC	Receiver operating characteristic
WBC	White cell count

Introduction

Necrotizing fasciitis (NF) is a rapidly progressing fulminant soft tissue infection that mainly involves the fascia and subcutaneous tissue [1]. The mortality rate of this necrotizing soft tissue infection is proportional to the time to intervention, and therefore, an accurate and prompt diagnosis allowing early aggressive treatment is essential. However, a non-specific clinical presentation in the early course of the disease, variable rates of progression, and the rarity of the disease may hinder accurate diagnosis [1, 2]. In particular, the differentiation of NF from cellulitis is often difficult both clinically and radiologically, and one previous study reported that the majority (76%) of 89 cases of necrotizing fasciitis were misdiagnosed as cellulitis or abscess on admission [1].

In 2004, Wong et al proposed a scoring system (Laboratory Risk Indicator for Necrotizing Fasciitis, LRINEC) to distinguish necrotizing fasciitis from other soft tissue infections including severe cellulitis or abscess [3]. This system is based on six readily available laboratory variables obtained on admission: C-reactive protein (CRP), total white cell count (WBC), hemoglobin, sodium, creatinine, and glucose. A LRINEC score of ≥ 6 indicates a high risk of necrotizing fasciitis [3]. Several studies have attested to the robustness of the LRINEC score [4–6]; however, there is some disagreement between the studies on the performance of LRINEC alone in differentiating necrotizing fasciitis from cellulitis [4–11].

Diagnostic imaging studies such as MRI can be performed in doubtful cases, but should not delay treatment [12]. The utility of MRI for differentiating NF from cellulitis with non-NF has been described in previous studies [12–17], with the reported MRI findings including (a) thickening of the deep fascia ≥ 3 mm, (b) extensive involvement of deep fascia, (c) multi-compartmental (three or more) involvement in one extremity, (d) presence of low signal intensity representing gas in the fascia, and (e) focal or diffuse non-enhancement in thickened deep fascia [13–17]. However, these studies were limited to a small number of subjects, and no study has attempted to integrate laboratory findings and MRI findings.

Therefore, the purpose of this study was to develop and validate a predictive scoring system for the differentiation of NF from cellulitis with non-NF by integrating MRI and laboratory findings.

Materials and methods

Study population

This retrospective study was approved by the institutional review boards of all three involved institutions, and the requirement to obtain informed consent was waived. The hospital database was searched for patients who underwent MR examination and required surgical intervention (fasciotomy, incision and drainage, and/or amputation) between January 2005 and April 2018 for NF or cellulitis and/or abscess (Fig. 1).

The definition of reference diagnosis for NF was (a) postoperative diagnosis of NF on surgical record or (b) principal diagnosis of NF with description of NF on surgical record, including presence of necrotic fascia or loss of resistance to blunt dissection [12, 13]. The definition of reference diagnosis for cellulitis with non-NF was (a) postoperative diagnosis of cellulitis and/or abscess on surgical record or (b) principal diagnosis of cellulitis and/or abscess with description of cellulitis and without description pertaining to NF on surgical record. The exclusion criteria were as follows: (a) absence of fat-suppressed T2-weighted images from the MRI protocol; (b) presence of pyomyositis, osteomyelitis, or infectious arthritis written on medical records; (c) history of surgery or major trauma

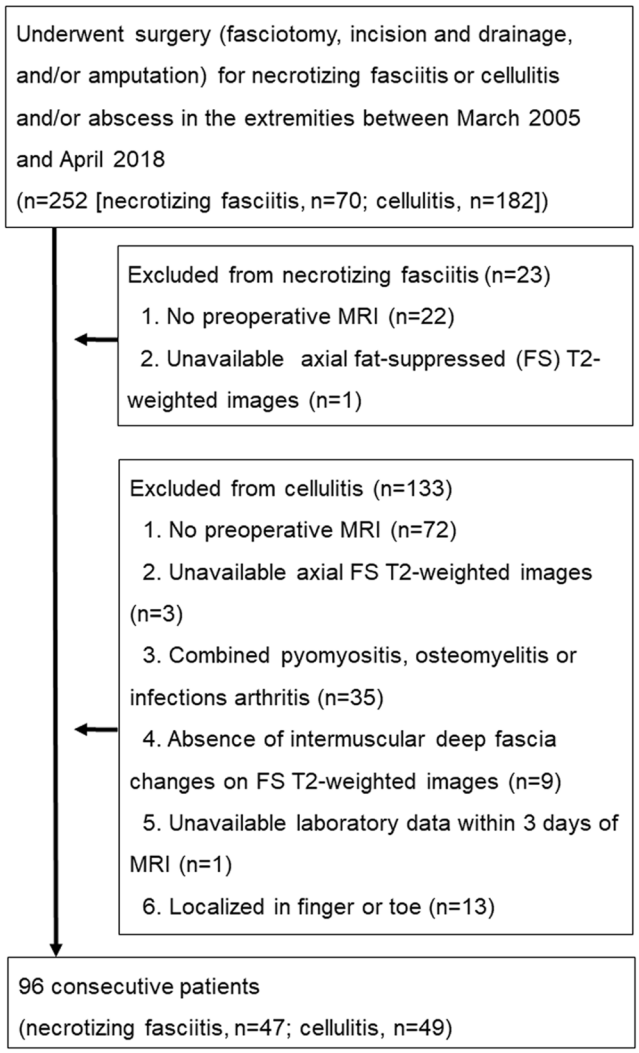

Fig. 1 Flowchart of patient selection for the model developmental cohort

at the site of infection; (d) absence of laboratory data including any of CRP, WBC, hemoglobin, sodium, creatinine, and glucose obtained within the 3 days prior to the MR examination; (e) absence of intermuscular deep fascial change on fat-suppressed T2-weighted images in subjects with cellulitis with non-NF; or (f) infection localized to fingers or toes.

The final cohort used to develop the model consisted of 96 consecutive adult subjects (63 males and 33 females; mean age ± standard deviation, 57.92 ± 14.85 years; range, 19–90 years) from one tertiary referral center (Asan Medical Center) (NF [$n = 47$] and cellulitis with non-NF [$n = 49$]). The model validation cohort consisted of 48 subjects (34 males and 14 females; mean age ± standard deviation, 56.58 ± 16.32 years; range, 20–84 years) from two other tertiary referral centers (Seoul National University Hospital and Seoul National University Bundang Hospital). These patients also underwent both MR examinations and surgical intervention during the same period for NF ($n = 23$) or cellulitis with non-NF ($n = 25$).

Demographic and clinical data including age, gender, presence of diabetes or non-atherosclerotic peripheral vascular disease such as Buerger's disease, presence of body temperature > 38 °C, and hypotension (blood pressure lower than 90 mmHg systolic or 60 mmHg diastolic) on admission were collected. Results of laboratory tests, including CRP, WBC, hemoglobin, sodium, creatinine, and glucose, were also collected, with the data obtained within the 3 days prior to and closest to the date of MRI examination being used for analyses. The LRINEC score was calculated using the method of Wong et al [3] (Table 1).

Table 1 The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score

Variables (unit)		Score
C-reactive protein (mg/L)	< 150	0
	≥ 150	4
Total white cell count (10^9/L)	< 0.02	0
	0.02–0.03	1
	> 0.03	2
Hemoglobin (mmol/L)	> 8.38	0
	6.83–8.38	1
	< 6.83	2
Sodium (mmol/L)	≥ 135	0
	< 135	2
Creatinine (μmol/L)	≤ 141	0
	> 141	2
Glucose (mmol/L)	≤ 10	0
	> 10	1

MRI and image analyses

Ninety-two of the 96 subjects in the developmental cohort underwent MR examinations in our institution on a 3-T (Ingenia or Achieva, Philips Healthcare; or Magnetom Skyra; Siemens Healthineers) or 1.5-T unit (Magnetom Avanto, Siemens Healthineers) with phased-array or extremity coils. The MR sequence parameters varied depending on the anatomical region; however, all the routine MRI protocols included axial and either coronal or sagittal T1- and T2-weighted fast spin-echo (FSE) sequences, fat-suppressed T2-weighted FSE, and contrast-enhanced fat-suppressed T1-weighted sequences in all three planes. Four of the NF patients in the developmental cohort underwent MRI examination at an outside institution before referral; however, all four subjects had fat-suppressed T2-weighted images in the axial plane. Six of the 96 subjects in the developmental cohort did not undergo contrast-enhanced studies (NF [$n = 5$], cellulitis with non-NF [$n = 1$]). The mean interval between MRI and surgical intervention was 3.3 days (range, 0–25 days) (NF [mean, 2.6 days; range, 0–17 days] and cellulitis with non-NF [mean, 3.9 days; range 0–25 days].

Reasons for MRI exam in NF patients in our institution were as follows: (a) difficulties in early definitive diagnosis of NF with the necessity for the differentiation of NF from other infectious diseases, (b) progression of presumed cellulitis despite antibiotic therapy, (c) atypical systemic presentation or cutaneous manifestation, (d) difficult to express pain with impaired verbal communication, and/or (e) preoperative evaluation of depth and extent of tissue infection in surgical planning.

From a comprehensive systematic review [13–18], five MRI parameters were selected as potential predictors: (a) thickening of the intermuscular deep fascia ≥ 3 mm, (b) extensive involvement of the deep fascia, (c) multicompartmental (three or more) involvement in one extremity, (d) presence of low signal intensity representing gas in the fascia, and (e) focal or diffuse non-enhancement in thickened deep fascia on contrast-enhanced images.

The presence or absence of thickening of the deep fascia ≥ 3 mm was evaluated on fat-suppressed T2-weighted images of the thickest portion of the intermuscular deep fascia with abnormal signal intensity.

Because "extensive" deep fascia involvement was poorly defined in a prior study [13], we graded the extent of deep fascia involvement as follows: (a) partial: abnormal signal intensity seen in less than one third of the depth of the intermuscular deep fascia from the superficial investing layer of the deep fascia; (b) moderately extensive: abnormal signal intensity seen in more than one third of the depth of the intermuscular layer of the deep fascia but not involving all deep fascia; (c) severely extensive: abnormal signal intensity seen in all deep fascia in at least one compartment. The extent

Table 2 Demographic and clinical characteristics of the model development and validation cohorts

	Model developmental cohort ($n = 96$)			Validation cohort ($n = 48$)			
	Cellulitis with non-necrotizing fasciitis ($n = 49$)	Necrotizing fasciitis ($n = 47$)	p value*	Cellulitis with non-necrotizing fasciitis ($n = 25$)	Necrotizing fasciitis ($n = 23$)	p value*	p value**
Age	58.8 ± 16.1	57.0 ± 13.6	0.547	57.7 ± 18.1	55.3 ± 14.4	0.620	0.624
Male gender	30 (61.2)	33 (70.2)	0.357	15 (60)	19 (82.6)	0.089	0.178
Presence of diabetes	20 (40.8)	12 (25.5)	0.114	8 (32)	12 (52.2)	0.161	0.243
Presence of non-atherosclerotic peripheral vascular disease	0	2 (4.3)	0.147	0	1 (4.3)	0.297	< 0.001
Body parts							
Upper extremity	9	7	0.650	2	1	0.605	0.083
Lower extremity	40	40		23	22		
Temperature > 38 °C on admission	6 (12.2)	10 (21.3)	0.256	3 (12)	7 (30.4)	0.120	0.962
Presence of hypotension (lower than 90 mmHg systolic or 60 mmHg diastolic) on admission	5 (10.2)	17 (36.2)	*0.003*	0	9 (39.1)	*0.001*	0.624

Categorical variables were tested with the chi-square test and continuous variables with t tests. Numbers in parentheses are percentages. Numbers in italics indicate a statistically significant difference

*p values between necrotizing fasciitis and cellulitis in each cohort

**p values between model development cohort and validation cohort

Table 3 Radiologic characteristics and LRINEC score of the model development cohort and results of the univariate analysis

	Cellulitis with non-necrotizing fasciitis		Necrotizing fasciitis		95% CI			
	$n = 49$	%	$n = 47$	%	OR*	Lower	Upper	p value
Thickening of intermuscular deep fascia (≥ 3 mm)								
Absent	36	73.47	11	23.4				
Present	13	26.53	36	76.6	8.581	3.42	21.533	< 0.0001
Extensive involvement of deep fascia								
Partial	14	28.57	2	4.26				
Moderate extensive	33	67.35	35	74.47	6.146	1.423	26.543	0.6971
Severe extensive	2	4.08	10	21.28	24.36	3.317	178.881	0.0054
Multi-compartmental (3 or more) involvement								
Absent	48	97.96	28	59.57				
Present	1	2.04	19	40.43	22.126	3.79	129.166	0.0006
Presence of low signal intensity (gas) in deep fascia								
Absent	48	97.96	41	87.23	1			
Present	1	2.04	6	12.77	5.061	0.725	35.32	0.1019
Enhancement pattern on contrast-enhanced images								
Diffuse enhancement	25	52.08	7	16.67				
Enhancement with non-enhancing area	13	27.08	29	69.05	7.429	2.593	21.288	0.0005
No enhancement	10	20.83	6	14.29	2.105	0.571	7.753	0.6559
LRINEC score								
Low risk (≤ 5)	41	83.67	20	42.55	1			
Moderate risk (6–7)	6	12.24	10	21.28	3.27	1.045	10.232	0.8247
High risk (≥ 8)	2	4.08	17	36.17	14.17	3.289	61.044	0.0062

OR odds ratio

*Using penalized maximum likelihood estimation

Table 4 Multivariate logistic regression model results for predictors of necrotizing fasciitis

	Beta	SE	OR*	95% CI Lower	95% CI Upper	*p* value	Score
Thickening of intermuscular deep fascia (≥ 3 mm)							
Absent	0		1				0
Present	1.6797	0.7504	5.364	1.232	23.346	0.0252	1.5
Multi-compartmental (3 or more) involvement							
Absent	0		1				0
Present	2.4668	1.2534	11.784	1.01	137.478	0.0491	2.5
LRINEC score							
Offset	1	0					

OR odds ratio

*Using penalized maximum likelihood estimation

of deep fascia involvement was also evaluated on fat-suppressed T2-weighted images.

The presence or absence of multi-compartmental (three or more) involvement was evaluated at the most severely affected location on axial fat-suppressed T2-weighted images.

The presence of gas in the fascia was evaluated using all available sequences.

Finally, the enhancement patterns of deep fascia with abnormal increased signal intensity on fat-suppressed T2-weighted images were evaluated on fat-suppressed contrast-enhanced T1-weighted images and were categorized into three categories: (a) diffuse enhancement, (b) enhancement with a non-enhancing area, and (c) no enhancement.

Two musculoskeletal radiologists (M.A.Y. and Y.Y.), with 7 years and 1 year of experience in musculoskeletal MRI interpretation after board certification, respectively, who were blinded to the final diagnoses and laboratory data, independently evaluated the five MRI parameters and then reached a consensus. All images were reviewed on our institution's picture archiving and communication system (Petavision, Asan Medical Center).

For external validation, a senior musculoskeletal radiologist with 21 years of experience in musculoskeletal MRI interpretation (H.W.C.) who was not involved in the image analysis of the model developmental cohort and who was blinded to the final diagnoses and laboratory data evaluated the MRI of the external validation cohort for the MRI variables included in the final predictive scoring system.

Statistical analyses

Differences between the groups were tested with chi-square test for categorical variables and *t* test for continuous variables.

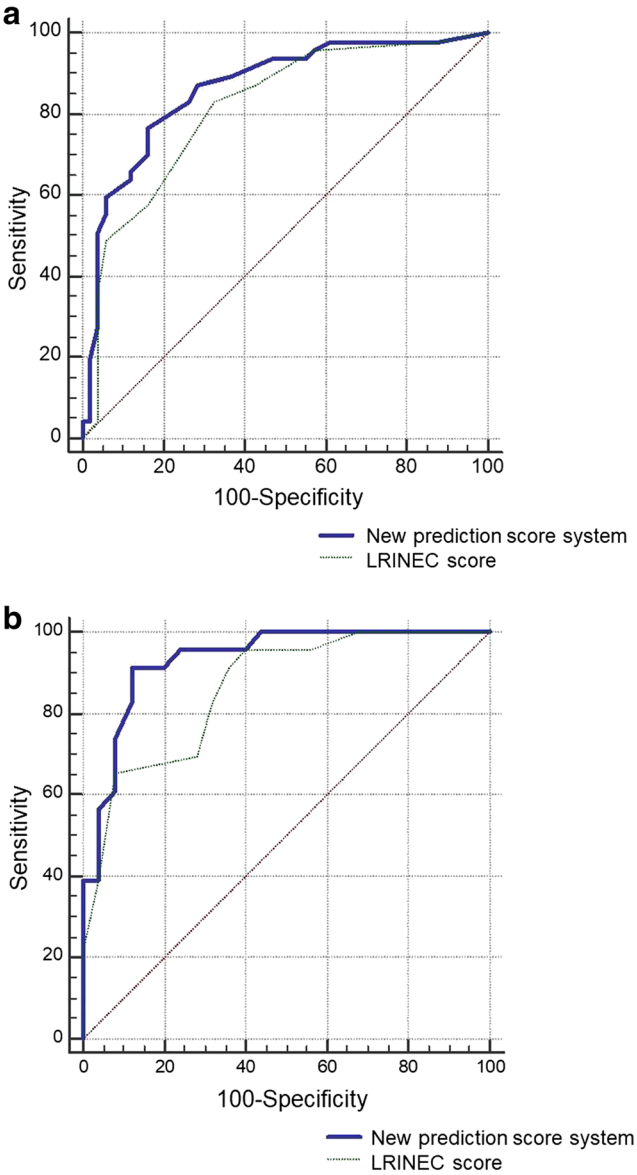

Fig. 2 Receiver operating characteristic curves of the new predictive scoring system and LRINEC score for (**a**) the model development cohort (area under the curve, 0.862 [95% confidence interval (CI), 0.787–0.938] and 0.814 [95% CI, 0.727–0.900] for the new predictive scoring system and LRINEC score, respectively) and (**b**) validation cohort (area under the curve, 0.933 [95% CI, 0.864–1.000] and 0.861 [95% CI, 0.759–0.962], respectively)

Univariate and multivariate logistic regression analyses with backward elimination using penalized maximum likelihood estimation were performed to identify independent predictors of NF among the six variables (the five MRI parameters and the LRINEC score). An additive scoring system was then developed using the coefficients of the final regression model [19].

Model performance was evaluated using the area under the receiver operating characteristic (ROC) curve for the discrimination [20]. A Hosmer-Lemeshow goodness-of-fit test [21] was performed for calibration. The presence of a significant

difference in discrimination between the LRINEC score and our new scoring system was tested using the method of Delong et al [22]. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the LRINEC score and our new scoring system at 50% probability of developing NF (a LRINEC score of ≥ 6) [3] were compared.

External validation was performed using the independent dataset obtained at the two other tertiary referral centers. Model performance was also assessed by ROC curve analysis.

Interobserver agreement between the two readers for the five MRI parameters in the developmental cohort was assessed with weighted kappa statistics interpreted as a κ value of less than 0.20 = poor agreement, 0.21–0.40 = fair agreement, 0.41–0.60 = moderate agreement, and 0.61–0.80 = good agreement and more than 0.81 = excellent agreement [23]. P values < 0.05 were considered significant. Statistical analyses were performed with SAS version 9.4 (SAS Inc.) and MedCalc version 18.5 (MedCalc Software).

Results

The baseline demographic and clinical characteristics of the model development and validation cohorts are summarized in Table 2. The radiological characteristics and LRINEC scores of the model development cohort and the results of the univariate analysis are summarized in Table 3. Among the six variables (five MRI parameters and LRINEC score), the multivariate logistic regression identified thickening of the deep fascia ≥ 3 mm, multi-compartmental involvement in one extremity, and the LRINEC score as predictors of NF (Table 4). The scores were approximated by rounding the adjusted coefficient for each predictor to the nearest half-integer. Our final scoring system is defined in Table 4. The total score for the system is calculated by adding the score for each variable, with a maximum total score of 17.

Total score (range, **0**–**17** points) = thickening of the deep fascia ≥ 3 mm (**0** or **1.5** points) + multi-compartmental (three or more) involvement (**0** or **2.5** points) + LRINEC score (range, **0**–**13** points)

In the model development cohort, the area under the ROC curve (AUC) for differentiating NF from non-NF was 0.814 (95% confidence interval (CI), 0.727–0.900; $p < 0.001$) for the LRINEC score alone, while for our new model integrating MRI and LRINEC, it was 0.862 (95% CI, 0.787–0.938; $p < 0.001$; Fig. 2). The improvement in discrimination with our new model (AUC, 0.049; 95% CI, 0.019–0.079) was statistically significant ($p = 0.001$). The Hosmer-Lemeshow test indicated a good fit ($\chi^2 = 4.43$; df = 7; $p = 0.729$). Compared with the LRINEC score (at a cutoff of ≥ 6), the new model with a cutoff of ≥ 5.5 (corresponding to 50% probability of NF) achieved higher sensitivity, PPV, and NPV (77%, 82%,

Table 5 Risk groups according to the total score for the development and validation cohorts

		Number of patients			
Total score	Predictive probability (%)	Developmental cohort		Validation cohort	
		Cellulitis with non-necrotizing fasciitis	Necrotizing fasciitis	Cellulitis with non-necrotizing fasciitis	Necrotizing fasciitis
Low					
1	1.28	35 (71.4)	6 (12.8)	12 (48)	0
2	3.41				
3	8.76				
4	20.71				
Intermediate					
4.5	30.10	8 (16.3)	10 (21.3)	7 (28)	1 (4.3)
5	41.51				
5.5	53.92				
6	65.86				
High					
6.5	76.08	6 (12.2)	31 (66.0)	6 (24)	22 (95.7)
7.5	89.63				
8.5	95.92				
9.5	98.46				

Numbers in parentheses are percentages

and 79%, respectively, for the new model and 57%, 77%, and 67%, respectively, for the LRINEC score alone) ($p < 0.001$, for all). There was no significant difference in specificity (84%, for both).

The risks for NF were categorized according to the total score into three categories (low risk ≤ 4, intermediate risk 4.5–6, and high risk ≥ 6.5; Table 5 and Fig. 3). Examples of the predictive ability of the scoring system are shown in Figs. 4, 5, and 6.

In the external validation set, the AUCs were 0.861 (95% CI, 0.759–0.962; $p < 0.001$) for the LRINEC score alone and 0.933 (95% CI, 0.864–1.000; $p < 0.001$) for the new scoring system (Fig. 2). The discrimination improved significantly with the new scoring system (AUC, 0.072; 95% CI, 0.012–0.133; $p = 0.020$). The new scoring system with a cutoff of ≥ 5.5 achieved sensitivity of 96%, specificity of 60%, PPV of 69%, and NPV of 94%, while the LRINEC score alone with a cutoff ≥ 6 had sensitivity of 70%, specificity of 72%, PPV of 70%, and NPV of 72% in the external validation.

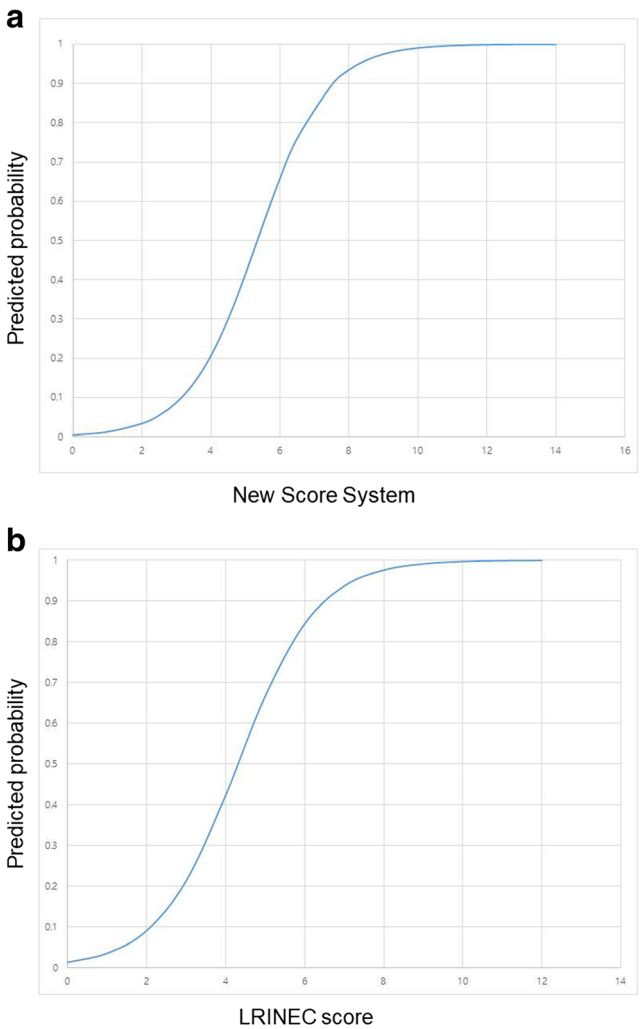

Fig. 3 Probability plot of necrotizing fasciitis against (**a**) the new scoring system and (**b**) LRINEC

Interobserver agreements for the five MRI parameters in the model development cohort were thickening of the intermuscular deep fascia, $k = 0.692$; extensive involvement of deep fascia, $k = 0.493$; multi-compartmental involvement, $k = 0.633$; presence of low signal intensity in deep fascia, $k = 0.679$; and enhancement pattern on contrast-enhanced images, $k = 0.464$.

Discussion

In this study, we developed a new predictive scoring system for the differentiation of NF from cellulitis with non-NF. This scoring system comprised two MRI parameters (thickening of the deep fascia ≥ 3 mm and multi-compartmental involvement) and the LRINEC score. This model was validated with

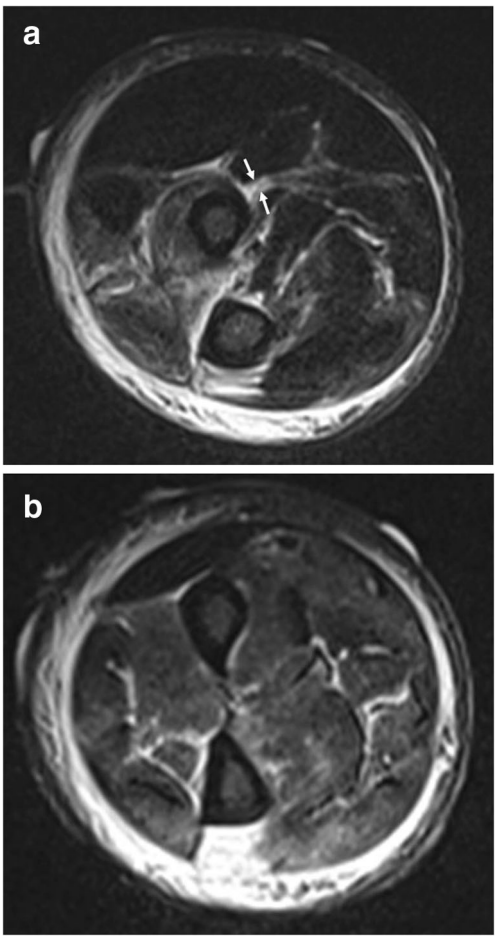

Fig. 4 A 51-year-old male with necrotizing fasciitis. **a** Axial fat-suppressed T2-weighted image of the right forearm demonstrates thickening of intermuscular deep fascia. **b** Another axial image distal to (**a**) demonstrates multi-compartmental involvement of the forearm. The LRINEC score was 5, which did not indicate a high risk of necrotizing fasciitis. However, the total score using the new scoring system was 9 (thickening of intermuscular deep fascia ≥ 3 mm [1.5 points] + multi-compartmental involvement [2.5 points] + LRINEC score [5 points]), with a predicted probability of 97.5% for necrotizing fasciitis

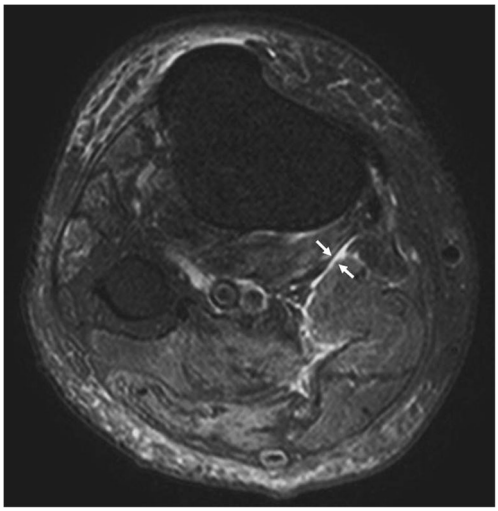

Fig. 5 A 65-year-old female with cellulitis with non-necrotizing fasciitis. Axial fat-suppressed T2-weighted image of the right lower leg demonstrates the absence of thickening of the intermuscular deep fascia or multi-compartmental involvement. The LRINEC score was 4. Total score using the new score system was 4 (thickening of intermuscular deep fascia ≥ 3 mm [0 point] + multi-compartmental involvement [0 point] + LRINEC score [4 points]) with a predicted probability of 20.7% for necrotizing fasciitis

a separate cohort of patients from two different tertiary hospitals. By integrating two MRI findings and the LRINEC score, the new predictive model showed improvement in AUC, sensitivity, PPV, and NPV (0.862, 77%, 82%, and 79%, respectively), compared with the LRINEC score alone (0.814, 57%, 77%, and 67%, respectively), while there was no significant difference in specificity (84%, for both). Moreover, the two

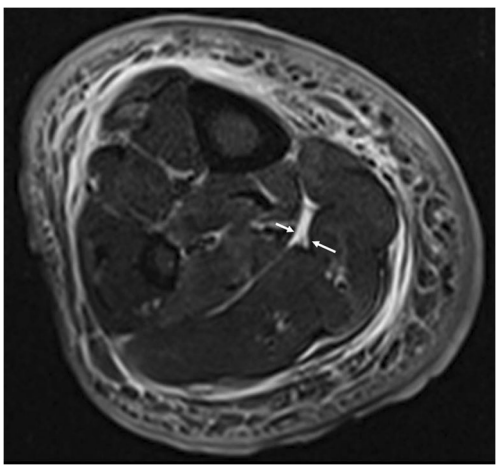

Fig. 6 A 52-year-old male with necrotizing fasciitis. Axial fat-suppressed T2-weighted image of the right lower leg demonstrates thickening of intermuscular deep fascia (arrows) without multi-compartmental involvement. The LRINEC score was 4, while the total score using the new scoring system was 5.5 (thickening of intermuscular deep fascia ≥ 3 mm [1.5 points] + multi-compartmental involvement [0 point] + LRINEC score [4 points]) with a predicted probability of 53.9% for necrotizing fasciitis. Note that although the LRINEC score was the same as that for the patient in Fig. 5, the total score using the new system was different

MRI parameters used in the new scoring system require only axial fat-suppressed T2-weighted images for assessment, which can be obtained without a substantial time delay when diagnosis is in doubt. Therefore, we believe that this scoring system will be generally applicable and helpful for differentiating NF from severe cellulitis with non-NF when there is uncertainty over the diagnosis.

Wong et al reported PPV and NPV of over 90% for distinguishing NF from other soft tissue infections (severe cellulitis or abscesses) at a cutoff of a LRINEC score ≥ 6 [3]. Later studies have attested to the robustness of the LRINEC using different cohorts and have reported high sensitivity (80–85%) and specificity (67–75%) [4, 5]. However, some studies reported cases where the LRINEC failed to diagnose NF and raised questions over its reliability due to high false negative rates [7–11, 24]. Our results were similar to those of the latter studies with lower sensitivity, PPV, and NPV of the LRINEC score alone.

While abnormal signal in the deep fasciae representing liquefactive tissue necrosis and inflammatory edema is the integral feature for diagnosis of NF on MRI, this finding alone has high sensitivity but lower specificity [12, 16, 17]. In particular, signal change in the intermuscular fascia may also be present in severe cellulitis with non-NF [13, 16, 25]. Therefore, distinguishing NF from cellulitis with non-NF according only to the presence of signal change extending to the deep fasciae can lead to diagnostic uncertainty. Kim et al sought to evaluate additional MRI findings of NF and compared the prevalence of individual MRI findings, but their study was limited by a small number of cases [13]. Therefore, it remained difficult to integrate multiple MRI findings into the diagnosis of NF in clinical practice because no prior study has evaluated which of the multiple findings has significant additive predictive value over other findings. Our study also identified that thickening of the intermuscular fascia and multi-compartmental involvement were independent predictors for differentiating NF from cellulitis with non-NF.

In our study, contrast enhancement pattern was not an independent predictor in the multivariate analysis, making our prediction model applicable even in case of shortened examination.

While gas in the fascia is one of the most specific signs of NF [2], presence of gas was not an independent predictor in the multivariate analysis in our study. One possible explanation would be that patients with gas seen on more readily accessible modalities such as plain radiographs did not undergo MRI exam and the prevalence of gas was low in our study population of NF.

The possibility of a selection bias and referral bias in our cohorts should be acknowledged. Our study included only those who underwent MRI including fat-suppressed T2-weighted images and surgical intervention. Patients with a high clinical suspicion of NF received immediate surgical

intervention, without MRI. Moreover, those who did not require surgical intervention and who were managed with antibiotic therapy alone (especially cellulitis) were not included in our study. In addition, all the study cohorts were from tertiary referral centers, and some of our study cohorts received antibiotic therapy before referral, which could possibly have affected the laboratory results and clinical course. Finally, although our study included a larger sample size than prior studies on MR imaging of NF, the sample size was still small, particularly in the validation cohort, mainly because of unavailability of fat-suppressed T2-weighted images.

In conclusion, our predictive scoring system integrating two MRI findings and the LRINEC score showed an improved performance over LRINEC alone and was validated with external data. This predictive scoring system improves the differentiation of NF from severe cellulitis with non-NF and enables prompt management.

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Compliance with ethical standards

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Methodology
- retrospective
- diagnostic or prognostic study
- multicenter study

References

1. Wong CH, Chang HC, Pasupathy S, Khin LW, Tan JL, Low CO (2003) Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. J Bone Joint Surg Am 85-A(8): 1454–1460
2. Sarani B, Strong M, Pascual J, Schwab CW (2009) Necrotizing fasciitis: current concepts and review of the literature. J Am Coll Surg 208(2):279–288
3. Wong CH, Khin LW, Heng KS, Tan KC, Low CO (2004) The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med 32(7):1535–1541
4. Holland MJ (2009) Application of the Laboratory Risk Indicator in Necrotising Fasciitis (LRINEC) score to patients in a tropical tertiary referral centre. Anaesth Intensive Care 37(4):588–592
5. Sirikurnpiboon S, Sawangsangwattana T (2017) Early diagnosis of necrotizing fasciitis using Laboratory Risk Indicator of Necrotizing Fasciitis (LRINEC) score. J Med Assoc Thail 100(Suppl 1):S192–S199
6. Bechar J, Sepehripour S, Hardwicke J, Filobbos G (2017) Laboratory risk indicator for necrotising fasciitis (LRINEC) score for the assessment of early necrotising fasciitis: a systematic review of the literature. Ann R Coll Surg Engl 99: 341–346
7. Swain RA, Hatcher JC, Azadian BS, Soni N, De Souza B (2013) A five-year review of necrotising fasciitis in a tertiary referral unit. Ann R Coll Surg Engl 95(1):57–60
8. Wilson MP, Schneir AB (2013) A case of necrotizing fasciitis with a LRINEC score of zero: clinical suspicion should trump scoring systems. J Emerg Med 44(5):928–931
9. Syed A, Alvin T, Fazrina A, Abdul R (2017) Determining if positive predictive value using Laboratory Risk Indicator for Necrotising Fasciitis is applicable in Malaysian patients with necrotising fasciitis. Malays Orthop J 11(2):36–39
10. Al-Hindawi A, McGhee J, Lockey J, Vizcaychipi M (2017) Validation of the laboratory risk indicator for necrotising fasciitis scoring system (LRINEC) in a Northern European population. J Plast Reconstr Aesthet Surg 70(1):141–143
11. Fernando SM, Tran A, Cheng W et al (2018) Necrotizing soft tissue infection: diagnostic accuracy of physical examination, imaging, and LRINEC score: a systematic review and meta-analysis. Ann Surg. https://doi.org/10.1097/SLA.0000000000002774
12. Malghem J, Lecouvet FE, Omoumi P, Maldague BE, Vande Berg BC (2013) Necrotizing fasciitis: contribution and limitations of diagnostic imaging. Joint Bone Spine 80(2):146–154
13. Kim KT, Kim YJ, Won Lee J et al (2011) Can necrotizing infectious fasciitis be differentiated from nonnecrotizing infectious fasciitis with MR imaging? Radiology 259(3):816–824
14. Brothers TE, Tagge DU, Stutley JE, Conway WF, Del Schutte H Jr, Byrne TK (1998) Magnetic resonance imaging differentiates between necrotizing and non-necrotizing fasciitis of the lower extremity. J Am Coll Surg 187(4):416–421
15. Fugitt JB, Puckett ML, Quigley MM, Kerr SM (2004) Necrotizing fasciitis. Radiographics 24(5):1472–1476
16. Rahmouni A, Chosidow O, Mathieu D et al (1994) MR imaging in acute infectious cellulitis. Radiology 192(2):493–496
17. Schmid MR, Kossmann T, Duewell S (1998) Differentiation of necrotizing fasciitis and cellulitis using MR imaging. AJR Am J Roentgenol 170(3):615–620
18. Ali SZ, Srinivasan S, Peh WC (2014) MRI in necrotizing fasciitis of the extremities. Br J Radiol 87(1033):20130560
19. Sullivan LM, Massaro JM, D'Agostino RB Sr (2004) Presentation of multivariate data for clinical use: the Framingham Study risk score functions. Stat Med 23(10):1631–1660
20. Egan JP (1975) Signal detection theory and ROC analysis. Academic Press, New York
21. Lemeshow S, Hosmer DW Jr (1982) A review of goodness of fit statistics for use in the development of logistic regression models. Am J Epidemiol 115(1):92–106
22. DeLong ER, DeLong DM, Clarke-Pearson DL (1988) Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 44(3):837–845

23. Cohen J (1968) Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. Psychol Bull 70(4):213–220
24. Neeki MM, Dong F, Au C et al (2017) Evaluating the laboratory risk indicator to differentiate cellulitis from necrotizing fasciitis in the emergency department. West J Emerg Med 18(4):684–689
25. Loh NN, Ch'en IY, Cheung LP, Li KC (1997) Deep fascial hyperintensity in soft-tissue abnormalities as revealed by T2-weighted MR imaging. AJR Am J Roentgenol 168(5):1301–1304