

## นิพนธ์ต้นฉบับ

### คะแนนความเสี่ยงและปัจจัยทำนายการเสียชีวิตในโรงพยาบาลของผู้ป่วยติดเชื้อผิวนัง และเนื้อเยื่ออ่อนที่คุกคามชีวิตอย่างรวดเร็วในโรงพยาบาลนครพิงค์

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#### บทคัดย่อ

**ความเป็นมา:** Necrotizing fasciitis (NF) เป็นการติดเชื้อผิวนังและเนื้อเยื่ออ่อนที่คุกคามชีวิต อย่างรวดเร็วขณะนี้ยังไม่มีเครื่องมือประเมินคะแนนความเสี่ยงในการทำนายการเสียชีวิตในโรงพยาบาลในผู้ป่วย NF

**วัตถุประสงค์:** เพื่อพัฒนาและตรวจสอบความถูกต้องภายในของเครื่องมือในการทำนายการเสียชีวิตในโรงพยาบาลของผู้ป่วย NF ในโรงพยาบาลนครพิงค์

**วิธีการศึกษา:** การศึกษาย้อนหลังรวมข้อมูลจากเวชระเบียนของผู้ป่วย NF ตั้งแต่เดือน มกราคม 2562 ถึง ธันวาคม 2563 ได้แก่ อายุ เพศ ตำแหน่งรอยโรค ผลการตรวจทางห้องปฏิบัติการ ความเจ็บป่วย สิ่งมีชีวิตก่อโรค และอัตราการเสียชีวิตในโรงพยาบาล วิเคราะห์ข้อมูลโดยใช้สถิติ การทดสอบภายในรีทลารีตัวแปร และใช้วิธี Backward stepwise elimination คัดเลือกเพื่อระบุชุดของปัจจัยพยากรณ์ที่ได้รับการชี้นำนักจากค่าสัมประสิทธิ์ ทำการแปลงคะแนน และสรุปคะแนนความเสี่ยงทั้งหมดแบ่งได้เป็น 3 กลุ่ม ได้แก่ ความเสี่ยงต่ำ ปานกลาง และสูงสำหรับการทำนายการเสียชีวิตในโรงพยาบาล

**ผลลัพธ์:** ผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็น NF ทั้งหมด 293 ราย, 25 ราย (ร้อยละ 8.4) เสียชีวิตในโรงพยาบาล พบรับปัจจัยพยากรณ์ 4 ปัจจัยทำนายการเสียชีวิตในโรงพยาบาลอย่างมีนัยสำคัญ ได้แก่ การเป็นเบาหวาน (Adj. RR 3.18, 95% CI 1.05-9.68) ตับแข็ง (Adj. RR 7.40, 95% CI 4.18-13.09) จำนวนเม็ดเลือดขาวมากกว่า 20,000/uL (Adj. RR 2.61 95% CI 2.13-3.20) และระดับค่าแอลกอเทตในเลือด (Adj. RR 1.12 95% CI 1.09-1.15) สามารถใช้ในการทำนายการเสียชีวิตในโรงพยาบาลได้ถึง ร้อยละ 91.3 (AuROC 91.3%, 95% CI 82.5-100). ค่า Likelihood ratio of positive ของกลุ่มความเสี่ยงต่ำ (<5 คะแนน) ความเสี่ยงปานกลาง (5-8 คะแนน) และความเสี่ยงสูง (>8 คะแนน) คือ 0.18 (95%CI 0.05-0.67, p <0.001), 0.86 (95%CI 0.34-2.17, p=0.744), และ 9.06 (95%CI 3.88-21.14, p <0.001) ตามลำดับ

**สรุป:** กลุ่มคะแนนความเสี่ยงที่พัฒนาขึ้นประกอบด้วยปัจจัยพยากรณ์สี่ปัจจัยมีความง่ายต่อการประเมินความสามารถในการแยกแยะและทำนายการเสียชีวิตในผู้ป่วย NF ได้ดีมาก แต่ควรนำเครื่องมือนี้ไปทดสอบความถูกต้อง (validation) เพิ่มเติมในโรงพยาบาลระดับทุติยภูมิถึงตertiary ไป

**คำสำคัญ:** Necrotizing fasciitis, คะแนนความเสี่ยง, การเสียชีวิตในโรงพยาบาล, ปัจจัยเสี่ยง

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#### ติดต่อข้อมูล

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Original Article

**Prediction score for in-hospital mortality among patients with necrotizing fasciitis: derivation and internal validation**

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**ABSTRACT**

**Background:** Necrotizing fasciitis (NF) is a rapidly progressive, life-threatening skin and soft tissue infection. Currently, a risk score tool to predict in-hospital mortality in NF patients is not warranted.

**Objective:** This study aimed to develop a tool to predict in-hospital mortality in NF patients.

**Material and Methods:** A retrospective study was conducted during January 2019 to December 2020. The hospital records of 293 NF patients were reviewed. Data including age, sex, location of lesion, laboratory results, comorbidity, pathogen organism, and in-hospital mortality were collected. Multivariable binary regression with backward stepwise elimination was used to identify a set of prognostic factors, whose regression coefficients were weighed, assigned, and summed to a total risk score. Finally, three risk groups low, moderate, and high for in-hospital mortality in NF patients were classified.

**Results:** A cohort of 293 patients diagnosed with NF was investigated, among whom 25 cases, accounting for 8.4% of in-hospital mortality. Four prognostic factors significantly associated with predicting in-hospital mortality were identified: diabetes mellitus (Adj. RR 3.18, 95% CI 1.05-9.68), cirrhosis (Adj. RR 7.40, 95% CI 4.18-13.09), leukocytosis exceeding 20,000/uL (Adj. RR 2.61, 95% CI 2.13-3.20), and blood lactate levels (Adj. RR 1.12, 95% CI 1.09-1.15). These factors exhibited the prediction for in-hospital mortality up to 91.3% (AuROC 91.3%, 95% CI 82.5-100.0). The Likelihood Ratio of a positive result for the low-risk (<5 points), moderate-risk (5-8 points), and high-risk (>8 points) groups were 0.18 (95% CI 0.05-0.67,  $p < 0.001$ ), 0.86 (95% CI 0.34-2.17,  $p = 0.744$ ), and 9.06 (95% CI 3.88-21.14,  $p < 0.001$ ), respectively.

**Conclusion:** The developed risk scoring system in this study, consisting of four prognostic factors, demonstrates a high feasibility in assessing the ability to discriminate and predict mortality in NF patients. However, further validation of this tool should be conducted in tertiary and subsequent healthcare settings to ensure its accuracy and applicability

**Keywords:** Necrotizing fasciitis, risk score, in-hospital mortality, risk factor

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## Background

Necrotizing fasciitis (NF) was a threatening infectious disease. Its progression was extremely fast, with extensive necrosis in the skin, subcutaneous tissue, superficial fascia, or may be muscle. The treatments of choice for NF were rapid surgical debridement and broad-spectrum antibiotic therapy<sup>[1]</sup>. Sepsis and toxemia leaded to multiorgan failure and ended up with abrupt and high mortality<sup>[2]</sup>. Delayed treatment might result in extensive loss of soft tissue associated with limb loss and increase the risk of mortality.

NF was defined by the presence of extensive necrosis involving at least the fascia and subcutaneous tissue, including myonecrosis.<sup>[3]</sup> The gray necrotic fascia and myonecrosis were detected intraoperatively by surgeons and used to identically follow Practice Guidelines for the Diagnosis of Skin and Soft Tissue Infections by the Infectious Diseases Society of America.<sup>[4]</sup>

Previous studies had reported independent risk factors for mortality among NF

patients, including female<sup>[4]</sup>, advanced age, diabetes mellitus<sup>[5]</sup>, heart disease<sup>[2, 6]</sup>, liver cirrhosis<sup>[1, 6-7]</sup>, serum creatinine level 2 mg/dL<sup>(1-247)</sup>, white blood cell count >30,000/mm<sup>[2,6,8]</sup>, hypoalbuminemia<sup>[9]</sup>, presence of hemorrhagic bleb<sup>[10-11]</sup>, and skin necrosis<sup>[10]</sup>. And we also had a study report of a novel scoring model for predicting mortality in patients with NF.<sup>[1]</sup>

The following 6 clinical predictors were included: female gender; age > 60 years; white blood cell (WBC) <5000/mm<sup>3</sup>; WBC ≥ 35,000/mm<sup>3</sup>; creatinine ≥ 1.6 mg/dL; and pulse rate > 130/min. The positive likelihood

ratios of mortality in patients with low-risk scores (≤2.5) and high-risk scores (≥7) were 11.30 (95% confidence interval [CI]: 6.16-20.71) and 14.71 (95%CI: 7.39-29.28).

The result from the previous studies provided clinical information on the predicted mortality rate of NF, but we need to make some earlier tools to predict mortality risk scores. In this study, we generate a prediction mortality risk score that would help clinicians identify mortality-risk patients so they can make earlier decisions on investigations and interventions to reduce the mortality rate among patients with NF.

## Objective

This study aimed to identify prognostic factors and develop a simple scoring tool to predict in-hospital mortality in NF patients.

## Patients and methods

*Theoretical design and data collection:* This study was prognostic prediction research with retrospective cohort data collection. A medical records review was performed on surgically confirmed NF patients who were registered between January 2019 and December 2020 at Nakomping Hospital

*Inclusion criteria:* the patient who was diagnosed with NF by ICD 10 M72.6 and ICD 9 CM 728.86

*Exclusion criteria:* the patient who was diagnosed with NF but whose clinical and surgical findings were not available to confirm the diagnosis of NF

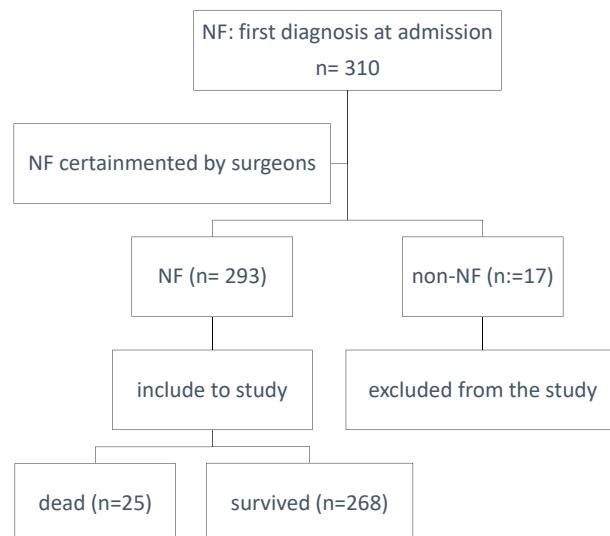
Clinical data and demographic characteristics, including sex, age (<60, >60 years), underlying disease, and vital signs, were

collected within the first day of admission. Important data associated with the investigation and treatment of NF; wound appearance, site of infection, organisms, laboratory data within the first day of admission, length of stay (LOS), and outcome were extracted from the medical records.

#### **Data analytical design and prediction score development:**

Patients were divided into two groups: those who died and those who survived. Continuous variables were analyzed by the Student's *t*-test or rank-sum test as appropriate. Differences in proportion were analyzed by Fisher's exact test. Crude risk ratios (RR) were estimated from univariable binary risk regression to identify potential prognostic predictors. A *P*-value less than 0.05 was considered statistically significant.

## **Results**



**Picture 1** Study Flow

In this study, the classified risk score was divided into 3 groups (mild, moderate, and severe) in relation to the risk of mortality. All potential predictors were included in the multivariable binary risk regression. The predictors in the final model were selected with a backward elimination strategy. The regression coefficients of the final model were transformed into prediction scores. The predictive performance of the score was evaluated with c-statistics after logistic regression.

#### **Ethical consideration:**

This study was approved by the Ethics Committee of the Nakornping Hospital, Chiangmai, Thailand. The date of approval was September 28, 2020, EC number 211/63.

## Prediction score for in-hospital mortality among patients with necrotizing fasciitis: derivation and internal validation

Of the total 310 cases with an NF diagnosis, 17 cases were excluded due to the lack of clinical and surgical findings. The study enrolled 293 patients who were diagnosed as compatible with NF. The total mortality rate was 8.4% (n=25). The differences in patients' characteristics categorized by mortality were analyzed.

Comparing baseline characteristics, comorbidities, and laboratory results between the death and survived groups

was not statistically significant ( $p > 0.05$ , Fisher's exact test, T-test, or rank sum test) except for the cirrhotic patient ( $p = 0.030$ ).

High white blood cell (WBC), blood lactate, diabetic mellitus, and cirrhosis patients were observed more in the mortality group. Table 1, shown a high survival rate in the patients who had  $Hb > 13\text{ g/dL}$  and  $Cr < 2\text{ mg/dL}$ .

**Table 1** Baseline characteristics of 293 necrotizing fasciitis patients

	Total (n=293)	Death (n=25)	Survived (n=268)	Crude RR (95%CI)	p -value
	n	n (%)	n (%)		
<b>Age</b>					
≥60 years	166	15 (60.0)	151 (56.34)	1.15 (0.53-2.47)	0.725
<60 years	127	10 (40.0)	117 (44.15)	1	
<b>Sex</b>					
Male	193	17 (8.81)	176 (91.19)	0.91 (0.40-2.04)	0.824
Female	100	8 (8.00)	92 (92.00)	1	
<b>LOS, days</b> Median (iqr) (min, max)	6 (9) (1, 71)	5 (8) (1, 40)	6 (9) (1, 71)	0.97 (0.93-1.02)	0.289
<b>Comorbidity</b>					
DM	43	4 (9.30)	39 (90.70)	1.11 (0.40-3.07)	0.844
HT	38	3 (7.89)	35 (92.11)	0.91 (0.29-2.91)	0.881
DLP	2	0	2 (100)	N/A	0.007
CKD	11	1 (9.09)	10 (90.91)	1.07 (0.16-7.20)	0.946
Cirrhosis	15	4 (26.67)	11 (73.33)	3.53 (1.39-8.99)	0.008
<b>Laboratory result</b>					
Blood lactate > 2 mmol/L	68	14 (20.59)	54 (79.41)	2.26 (0.70-7.33)	0.173
WBC > 20,000/uL	67	9 (13.43)	58 (86.57)	1.85 (0.86-4.00)	0.115
Hb>13 g/dL	221	18 (8.14)	203 (91.86)	1.00 (0.06-0.12)	<0.001
Creatinine <2 mg/dL	275	24 (8.72)	251 (91.27)	1.21 (1.11-1.33)	<0.001
Na ≥ 135 mmol/L	117	9 (7.69)	108 (92.31)	0.83 (0.38-1.84)	0.657
Glucose > 180 mg/dL	42	2 (4.76)	40 (95.24)	1.80 (0.26-12.38)	0.546
Blood culture sent	135	19 (76.0)	116 (43.3)	N/A	N/A

**Table 1** Baseline characteristics of 293 necrotizing fasciitis patients (Cont.)

	Total (n=293)	Death (n=25)	Survived (n=268)	Crude RR (95%CI)	p -value
	n	n (%)	n (%)		
Blood culture positive for bacteria	33	6 (31.6)	17 (14.7)	N/A	N/A
Pus culture sent	190	13 (52.0)	177 (66.0)	N/A	N/A
Pus culture positive for bacteria	119	9 (69.2)	110 (62.1)	N/A	N/A

Lower extremity was the most common site of infection, with 250 cases (85.3%), and legs were most common, with 148 cases (50.5%), followed by foot 102 cases (34.8%). Other sites of infection were the upper extremity in 29 cases (9.8%) and the buttock, coccyx, and groin in 5 cases (1.7%).

Total 135 (46.1%) blood cultures were sent from 293 cases, 19 (76.0%) samples in death group, and 116 (43.3%) cases in survived group. In death group, positive blood cultures for bacteria were 6/19 (31.6%) while in survived group were 17/116 (14.7%).

Total 190 (64.9%) cases had sent for pus cultures, 13 (52.0%) in death group, and 177 (66.0%) in survived group which were positive for bacteria 69.2%, and 62.1%

respectively, detail of positive cultures was presented in table 2, one case had blood culture positive for 2 organisms.

Both blood and wound cultures were performed in 101 patients (34.5%). The number of patients who had mixed infected organisms (gram-positive organisms and gram-negative organisms) in the wound or the blood culture were 3 patients and 3 patients, respectively. The number of patients who had multiple infected organisms (more than one gram-positive or gram-negative organism) in wound culture and blood culture was 12 patients and 18 patients, respectively. The pathogenic organism of NF patients in Nakomping Hospital, the most common, was Streptococcus spp., as shown in Table 2.

**Table 2** Microorganisms in blood and wound cultures of patients with necrotizing Fasciitis

Organism	Pus culture (n=119)		Hemoculture (n=23)	
	n	n	n	n
<b>Gram-positive:</b>				
Staphylococcus spp.	76		16	
Streptococcus spp.	24		9	
Other gram-positive	51		5	
	1		2	

**Table 2** Microorganisms in blood and wound cultures of patients with necrotizing Fasciitis (Cont.)

Organism	Pus culture (n=119)		Hemoculture (n=23)	
	n		n	
<b>Gram-negative:</b>	43		8	
Acinetobacter spp.	9		4	
Escherichia spp.	22		1	
Klebsiella spp.	2		0	
Pseudomonas aeruginosa	5		0	
Proteus spp.	5		0	
Other gram-negative	0		3	
<b>Culture negative for bacteria</b>	71/190 (59.7%)		112/135 (83.0%)	
<b>Culture positive for bacteria</b>	119/190 (40.3%)		23/135 (17.0%)	

Multivariable risk regression analysis found that predictors of mortality among patients with NF were diabetic mellitus (risk ratio (RR)=3.18, 95% confidence interval (CI)=1.05-9.68, p=0.041), cirrhosis

(RR=7.40, 95% CI=4.18-13.09, p<0.001), WBC > 20,000/uL (RR=2.61, 95%CI = 2.13-3.20, p<0.001), blood lactate (RR=1.12, 95%CI=1.09-1.15, p<0.001) in Table 3.

**Table 3** Final model with prediction score derivation

Death	Adjusted RR	p-value	95% CI	Coefficient	Transform score	Assigned score
DM	3.18	0.041	1.05-9.68	2.54	3.79	4
Cirrhosis	7.40	<0.001	4.18-13.09	2.93	4.37	4.5
WBC >20,000/uL	2.61	<0.001	2.13-3.20	1.84	2.75	3
Blood Lactate level in mmol/L	1.12	<0.001	1.09-1.15	0.67	1	1

Risk factors associated with an increased risk of death in NF patients were shown in Table 4. Risk scores had been developed to detect individuals at high risk of mortality, thereby enabling targeted screening. Risk score and classify grading that could predict the risk of in-

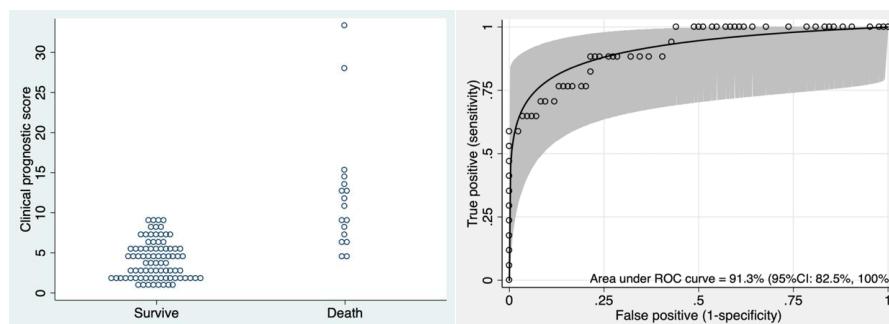
hospital mortality in NF patients by the risk factor as shown. The predictive score was developed to 3 grading that classify as low risk <5 (%death=3.5), moderate risk 5-8 (%death ≥14.8) and high risk >8 (%death ≥64.7).

Table 4 Risk classification for in-hospital mortality of patients with Necrotizing fasciitis

Risk Scoring	Classification	Patients		Likelihood ratio of positive (95% CI)	p-value
		Survived (%)	Death (%)		
<5	Low risk	55 (96.5)	2 (3.5)	0.18 (0.05-0.67)	<0.001
5-8	Moderate risk	23 (85.2)	4 (14.8)	0.86 (0.34-2.17)	0.744
>8	High risk	6 (35.3)	11 (64.7)	9.06 (3.88-21.14)	<0.001
	Total	84 (83.2)	17 (16.8)		

Variables that predicted the presence of  $\geq 14.8\%$  and  $\geq 64.7\%$  of deaths independently were determined using multivariable logistic regression. Internal validation was performed using bootstrapping techniques. Discrimination was assessed using area under the receiver operating characteristic curves

(AuROCs) and agreement between predicted and observed cases using calibration plots. Predictors of  $\geq 14.8\%$  and  $\geq 64.7\%$  of death were DM, liver cirrhosis, WBC  $> 20,000/\mu\text{L}$ , and blood lactate  $> 2 \text{ mmol/L}$  with an AuROC of 91.3% (95% CI 82.5%-100%). Picture 2



Picture 2 calibration plots and Area under ROC curve

## Discussion

The total in-hospital mortality rate in this cohort between 2019 and 2020 in Nakorpling Hospital was 8.4%. Age, sex, LOS, comorbidities, and laboratory results were comparable except for high cirrhotic cases in the death group. Blood culture was positive 24.4%, and pus culture was positive 62.3%. The most common site of infection was the lower extremity, and the most common organism was gram-positive

bacteria. Multivariable risk regression analysis among patients with NF found that diabetic mellitus, cirrhosis, WBC  $> 20,000/\mu\text{L}$ , and blood lactate level were associated with mortality, which were included in the model for prediction score derivation. This study showed the final risk classification and defined 3 risks: low risk <5 score (risk of death = 3.5%), moderate risk 5-8 score (risk of death  $\geq 14.8\%$ ), and high risk >8 score (risk of death  $\geq 64.7\%$ ), with a high

confidence of prediction at AuROC of 91.3% (95% CI 82.5%-100%).

As NF is an important surgical infection and has a high mortality rate, even with sufficient treatment, this study had lower mortality than other studies<sup>[1,9,12]</sup>, that may be due to many factors, such as the fact that this study cohort time was a recent cohort year that may be associated with new technologies and treatments. The overall mortality rate in this study was 8.4%. These patients died rapidly from multiorgan failure with systemic inflammatory response syndrome (SIRS). However, most NF patients were investigated and treated with broad-spectrum antibiotics by emergency physicians. So, identification of independent risk factors for death could help the physician's awareness and more proper management that is possible to achieve a successful outcome of treatment in all patients.

At admission time, this study identified the following risk factors for mortality: white blood cell more than 20,000/ $\mu$ L, blood lactate more than 2 mmol/L, and in the patient with underlying disease, such as diabetic mellitus and cirrhosis, having worse prognosis factors, similar to previous studies reporting that advanced age<sup>[13]</sup> (more than 60 years old) and females with chronic heart disease and liver cirrhosis were significantly associated with an increased risk of mortality. However, this study and some others found that advanced age had no effect on mortality. Previous studies

reported that poorly controlled DM in NF patients could cause adverse outcomes<sup>[13]</sup>; in this study, a similar outcome was that DM was associated with a high mortality rate. In this study, we classified DM as blood glucose at more than 180 mg%. But in the liver cirrhosis patient, we did not explore in detail the severity of cirrhosis, such as the Child Pugh Score, in terms of survival, as this data could not be extracted from the medical records. The patients with liver cirrhosis had a higher susceptibility to infection. The mechanism of infection was abnormalities in immune function, including humoral immunity, T lymphocyte and B lymphocyte dysfunctions. Abnormality of the defensive mechanism decreased phagocytic activity of the reticuloendothelial system, impaired monocyte function, and incomplete chemotaxis.<sup>[14]</sup> The previous study found that skin necrosis was associated with higher mortality as infection and toxin-producing bacteria could cause skin necrosis and multiple organ failure. All necrotic tissue, including fascia, must be removed by surgical debridement to reduce the bacteria, and broad-spectrum antibiotics should be administered promptly whenever NF is diagnosed.<sup>[10]</sup>

Clinical suspicion of septic shock was needed to provide adequate fluid resuscitation with intravenous broad-spectrum antibiotics and aggressive debridement. In the previous study, a pulse rate greater than 130 beats per minute and a systolic blood pressure less than 90

mmHg were associated with increased mortality; septic shock, hypotension (a systolic blood pressure below 90 mmHg), and multiorgan failure were the most common complications of NF that could cause of death.<sup>[11,15]</sup>

In this study, we found an association between serum blood lactate and WBC had an increased risk of death. The other studies showed the other laboratory finding: increased serum creatinine had been an associated risk factor for death<sup>[4]</sup>, which was used to predict impaired renal function. Because of this factor, acute renal failure was a life-threatening condition in sepsis patients, especially in NF patients.

In the literature review had a several prognostic tools to evaluate the severity of NF patients on admission for classified who need to admit to the ICU and need more aggressive treatment include the LRINEC (laboratory risk indicator for NF) score<sup>[7]</sup>, composed of six marker variables, including C-reactive protein, total white blood cell count, hemoglobin, serum sodium, serum creatinine, and serum glucose ; and APACHE II<sup>[16]</sup> (acute physiology and chronic health evaluation II) scores including vital signs (temperature, mean arterial pressure, heart rate, and respiratory rate), oxygenation (A-PaO<sub>2</sub>[FiO<sub>2</sub>>50%] or PaO<sub>2</sub>[FiO<sub>2</sub><50%], metabolic parameters (sodium, potassium, creatinine, bicarbonate concentrations [Arterial pH or HCO<sub>3</sub>], hematocrit, white blood cell count).

In this study, we found that diabetic mellitus, cirrhosis, WBC > 20,000/uL, and blood lactate level were suitable to include in the model for prediction score derivation. The limitations of this study were that we could not apply either of these scoring systems, LRINEC and APACHE II, because in this retrospective study we had insufficient medical data and limitations of laboratory testing in provincial hospitals, such as unexamined serum C-reactive protein, and some laboratory tests were not tested in all patients which were depended on physicians, such as arterial blood gas. The aim of this study was to examine this limitation.

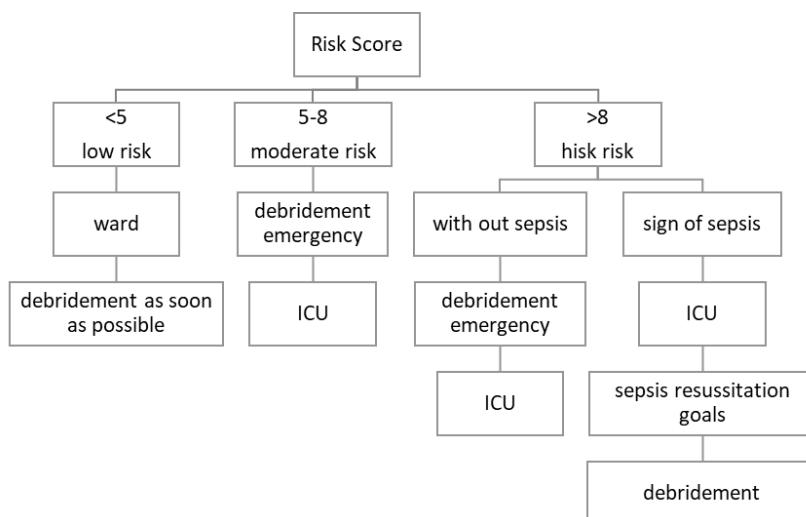
This study had shown the risk score that could be used for proper management. The score less than 5 in this group had a lower risk of death. We might have more time for management before the clinical progression of the sepsis condition, and then we could admit the patient to the correct laboratory before the operation as soon as possible. The score of moderate risk<sup>[1,7-9]</sup>, in this group, might be the most benefit of the score because it provided a rapid awareness for physicians to early treatment to these patients as early as possible due to the delay in controlling the source of infection resulting in more unfavorable outcomes. The patient might have sepsis so quickly that we have to set an emergency debridement and transfer to the ICU or surgical ward. The score of more than 8 was very significant to in-hospital death, and

most of the patients in this group were prone to have sepsis and multiorgan failure, so the patients in this group with sepsis had to follow the sepsis protocol and achieve the resuscitation goal before emergency operative management. If not sepsis, we could manage as moderately as possible, but ICU was needed in this group. On the other hand, the patients without signs of sepsis in this group had to get an emergency debridement as soon as possible, as this group was prone to sepsis. With the limitations of in-patient department (IPD) management and the tightness of the ICU, we could classify the patient as intermediate risk for management in the surgical ward with close monitoring.

Sepsis/septic shock<sup>[16]</sup> was a life-threatening and time-dependent condition that required timely management to reduce mortality. A diagnosis of sepsis was

confirmed in the case of a Sequential Organ Failure Assessment (SOFA) score  $\geq 2$  or use of the National Early Warning Score (NEWS) or systemic inflammatory response syndrome (SIRS). Septic shock was defined by the need for a vasopressor to maintain a patient's mean arterial pressure (MAP)  $\geq 65$  mmHg and a serum lactate level  $\geq 2$  mmol/L. And in the sepsis campaign 2023, had a recommendation on a direct sepsis goal that aimed toward  $\text{SpO}_2$  94–98% or  $\text{SpO}_2$  88–92% if the patient was at risk of hypercapnic respiratory failure (e.g., they have a history of chronic obstructive pulmonary disease, severe obesity, etc.), and  $\text{MAP} \geq 65$  mmHg. From NF scoring, we would like to propose the algorithm to manage the case as shown in picture 2.

To evaluate the efficacy of this algorithm, it may need further study.



Picture 3 Algorithm to management of NF patient by Risk Score

### Conclusion

Risk factors for mortality in patients with NF included diabetic mellitus, liver cirrhosis, WBC  $> 20,000/\mu\text{L}$ , and blood lactate  $> 2 \text{ mmol/L}$ . Thus, patient presentation of clinical predictors; risk grade classified to low risk, moderate risk, and high risk should direct concern toward progression of disease and might be considered for early investigation, close monitoring, or aggressive treatment with antibiotics and debridement or amputation to prevent morbidity and mortality. The risk

model predicted the prevalence of death in NF patients reliably and performed very easily to predict in emergency care at secondary and tertiary hospitals. Initiation or intensification of risk management in detected cases might help to reduce both morbidity and mortality in NF patients.

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### Disclosure

The author reports no conflict of interest in this work.

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