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Predicting septic shock in obstructive pyelonephritis associated with ureteral stones

A retrospective study

Kyungchan Min, MD[a], Bum Soo Kim, MD, PhD[b], Yun-Sok Ha, MD, PhD[c], Jae-Wook Chung, MD, PhD[c], Gyuho Jang, MD[a], Myung-giun Noh, MD, PhD[d], Hyeok Ahn, BS[e], Jun Nyung Lee, MD, PhD[b], Hyun Tae Kim, MD, PhD[b], Eun Sang Yoo, MD, PhD[b], Tae Gyun Kwon, MD, PhD[c], So Young Chun, PhD[f], Hansoo Park, MD, PhD[a,g,*]

Abstract

To identify the best combination of potential predictors of septic shock in patients with obstructive acute pyelonephritis associated with ureteral stones (OAPN-US) according to Sepsis-3 criteria. Patients who underwent percutaneous nephrostomy (PCN) with OAPN-US were retrospectively evaluated. Recursive feature elimination (RFE) was applied to patients with and without septic shock to identify factors associated with the prediction of progression to septic shock. We compared combinations of the selected features based on area under the receiver operating curve (AUROC) to determine which combination was most effective. This study included 81 patients who were treated with PCN due to OAPN-US. A comparison was made between 37 patients with septic shock (SS) and 44 patients without septic shock (NSS). SS group had a higher age, poorer Eastern Cooperative Oncology Group status, and significantly higher levels of positivity in urine cultures and blood cultures. There were also differences in laboratory tests between the 2 groups. Procalcitonin (PCT), international normalized ratio (INR), and absolute lymphocyte count (ALC) were selected based on RFE. We compared the predictive power for SS when each marker was used alone, when 2 markers were combined, and when all 3 markers were combined. Among these combinations, using all 3 variables together yielded the highest AUROC of 0.942. Of the 3 variables, PCT had the highest Gini importance score, indicating that it was the most influential factor. Clinical characteristics were different between the SS and the NSS groups. In patients with OAPN-US, the combination of PCT, ALC, and INR was an excellent predictor of septic shock.

Abbreviations: ABGA = arterial blood gas analysis, ALC = absolute lymphocyte count, ALT = alanine aminotransferase, AST = aspartate transaminase, AUROC = area under the receiver operating curve, Cr = creatinine, CRP = C-reactive protein, DM = diabetes mellitus, DRR = De Ritis Ratio, ECOG = Eastern Cooperative Oncology Group, eGFR = estimated glomerular filtration rate, HTN = hypertension, INR = international normalized ratio, OAPN = obstructive acute pyelonephritis, OAPN-US = obstructive acute pyelonephritis associated with ureteral stones, PCN = percutaneous nephrostomy, PCT = procalcitonin, PT = prothrombin time, RFE = recursive feature elimination, SS = septic shock, US = ureteral stones, WBC = white blood cell.

Keywords: international normalized ratio, lymphocyte count, procalcitonin, septic, shock

KM and BSK contributed equally to this work.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

All data analysis was carried out in accordance with applicable laws and regulations described in the Declaration of Helsinki and approved by Kyungpook National University Hospital institutional review board approval, reference number KNUH-2020-07-013. The need for written informed consent was waived by the Kyungpook National University Hospital institutional review board ethics committee due to retrospective nature of the study.

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[a] Department of Biomedical Science and Engineering, Gwangju Institute of Science and Technology, Gwangju, Korea, [b] Department of Urology, School of Medicine, Kyungpook National University, Kyungpook National University Hospital, Daegu, Korea, [c] Department of Urology, School of Medicine, Kyungpook National University, Kyungpook National University Chilgok Hospital, Daegu, Korea, [d] Department of Pathology, School of Medicine, Ajou University, Suwon, Korea, [e] Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [f] BioMedical Research Institute, Kyungpook National University Hospital, Daegu, Korea,[g] Genome and Company, 7F GWANGGYO FLAX DESIAN, Yeongtong-gu, Suwon-si, Gyeonggi-do, Korea.

** Correspondence: Hansoo Park, Department of Biomedical Science and Engineering, Gwangju Institute of Science and Technology, Gwangju 61045, Korea (e-mail: hspark27@gist.ac.kr).*

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1. Introduction

Patients with obstructive acute pyelonephritis (OAPN) commonly experience flank pain and fever, typically resulting from ureteral stones (US), tumors, or strictures. Prompt decompression of the collecting system is considered essential during the treatment of such patients. Without proper diagnosis and treatment, OAPN can progress to sepsis, septic shock (SS), or even death.[1] OAPN associated with ureteral stones (OAPN-US) should be managed differently from OAPN without US.

Additionally, several studies have identified potential biomarkers for SS associated with OAPN-US. Based on previous criteria for systemic inflammatory response syndrome, various variables, including thrombocytopenia, positive blood cultures, reduced serum albumin, increased procalcitonin (PCT), leukocytosis, diabetes mellitus (DM), elevated C-reactive protein (CRP), absence of hypertension (HTN), and decreased erythrocyte sedimentation rate, have been identified as predictors of SS in OAPN-US.[2–8] However, only 3 studies have employed the Sepsis-3 criteria[9–11] and concluded that PCT, CRP, DM, presepsin, age, history of chronic kidney injury, and serum creatinine (Cr) are predictive factors for SS in cases of OAPN-US. As we can see from these studies, no confirmatory predictor has yet been identified based on the Sepsis-3 criteria. Moreover, to our knowledge, no study has yet developed a combination of predictors that enhances the accuracy of such predictions. Our aim in this study is to develop a better model for predicting SS based on the Sepsis-3 criteria.

2. Materials and methods

2.1. Study population and variables

This retrospective study was approved by the Institutional Review Board of Kyungpook National University Hospital (approval number: KNUH-2020-07-013) and was conducted by reviewing the medical records of patients admitted to a tertiary general hospital in South Korea from March 2014 to February 2020. Initially, we screened patients with obstructive uropathy who underwent percutaneous nephrostomy (PCN) in the emergency department. Specifically, only patients with OAPN-US were included in this study. The study excluded patients with bilateral obstructions, urological malignancies, and ureteral strictures; those requiring long-term PCN; those with congenital anomalies, a single kidney, or a nonfunctional contralateral kidney; patients who did not follow up after nephrostomy; and patients with concomitant infections (such as pneumonia) or those with no infections. Figure 1 summarizes the selection process for patients.

The follow-up period was defined as the duration from hospital admission to discharge. Parameters assessed in the present study included: age, sex, performance status, hydronephrosis, renal parenchymal thinning, underlying diseases such as HTN, DM, and chronic kidney disease (CKD); culture positivity; a complete blood count including white blood cell (WBC) count, platelet count, absolute lymphocyte count (ALC), and absolute neutrophil count; liver function tests including bilirubin, albumin, globulin, aspartate transaminase (AST), and alanine aminotransferase (ALT); renal function tests including blood urea nitrogen, Cr, and estimated glomerular filtration rate (eGFR); electrolytes including sodium and potassium; inflammatory markers including CRP and PCT; blood coagulation tests including prothrombin time (PT), activated partial thromboplastin time, and international normalized ratio (INR); and indices such as neutrophil to lymphocyte ratio (NLR), albumin to globulin ratio, and De Ritis Ratio (DRR). Acute pyelonephritis (APN) was defined as having > 5 WBCs per high power field in centrifuged urine specimens, $>10^4$ colony forming units per mL in urine specimens obtained via Foley catheters, and fever with characteristic symptoms. SS was defined by the Sepsis-3 criteria as a suspected infection necessitating vasopressor therapy to maintain a mean arterial pressure of 65 mm Hg and serum lactate value >2.0 mmol/L, despite adequate fluid resuscitation.[12] Eastern Cooperative Oncology Group (ECOG) performance status scale was used to categorize the performance status of participants. Accordingly, ECOG grades 0 and 1 were considered good, while ECOG grades 2 and 3 were considered poor. In addition, hydronephrosis was classified as either low or high grade based on the degree of renal calyceal dilatation.

2.2. Treatment protocol

In the emergency room of our facility, patients presenting with signs of infection were administered ciprofloxacin or third-generation cephalosporins, along with fluids for hydration. Routine laboratory examinations, urine and blood cultures, and imaging studies, including X-rays and computed tomography, were conducted. PCT, lactic acid, and arterial blood gas analysis (ABGA) were evaluated only in patients at high risk of SS. If a computed tomography scan revealed an obstruction in the urinary tract, a percutaneous nephrostomy was performed. In cases where patients did not respond to the initial antibiotic treatment, we switched to piperacillin/tazobactam or carbapenem and provided intensive care even before culture results were available. When cultured bacteria demonstrated resistance to antibiotics, other appropriate antibiotics were administered.

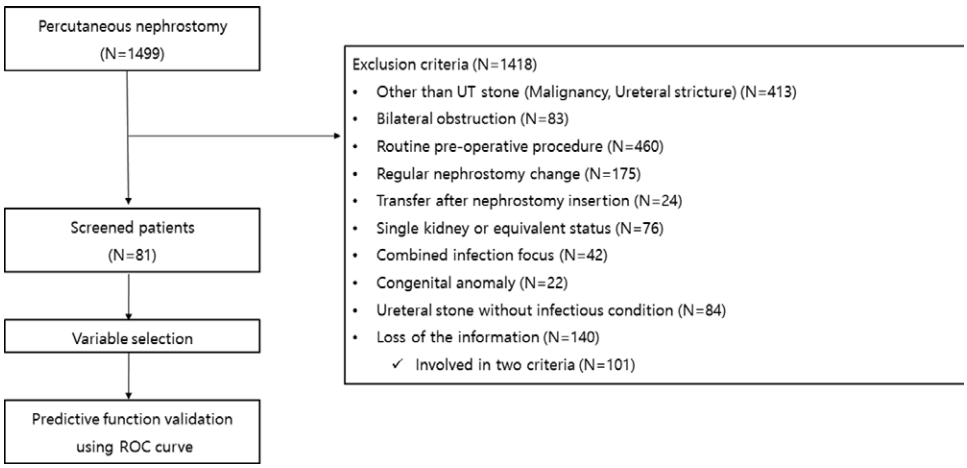

Figure 1. Overview of the development of a prediction model for septic shock.

2.3. Variable selection, predictive performance validation, and importance of variables

We utilized recursive feature elimination (RFE) to select variables, employing the "rfe" function from the "caret" package[13] in R Studio version 4.1.2 (Vienna, Austria). For the outer resampling, a cross-validation of 1000 folds was conducted. Variables were selected based on accuracy. The performance of each combination of parameters was compared. Based on the area under the receiver operating curve (AUROC) values, the best combination of parameters was selected. To determine the optimal cutoff value and merge multiple kinds of receiver operating characteristic (ROC) curves, we used the "multipleROC" package in R.[14] Additionally, the Gini importance scores of the variables were calculated using the "varImp" function of the "caret" package in R.

2.4. Statistical analyses

To determine whether the results were distributed normally or not, we employed the Shapiro–Wilk test. For normally distributed continuous variables, *t* tests were utilized. For nonnormally distributed variables, we conducted the Kruskal–Wallis rank sum test. Additionally, Fisher exact test and Pearson chi-squared tests were used with Yates' continuity correction for categorical variables. All statistical analyses were performed using R Studio software version 4.1.2. Moreover, for all analyses, a 2-sided *P* value of <.05 was considered to indicate statistical significance.

3. Results

3.1. Patient characteristics

A total of 1499 patients underwent PCN. Of these, 413 were treated for conditions other than US, predominantly malignancies and ureteral strictures. Furthermore, 83 patients had bilateral obstructions of the urinary tract, 460 underwent routine preoperative procedures without infectious conditions, 175 experienced nephrostomy-related changes, 24 were lost to follow-up after PCN, 76 had a single kidney, 42 had combined foci of infection, 22 presented with congenital anomalies, and 84 received treatment for US without infectious conditions. Additionally, data for 140 patients were lost, and 101 patients met 2 exclusion criteria. After excluding those who did not meet the eligibility criteria, 81 patients were included in the study. Figure 1 illustrates the process of selecting patients and the overall study design.

The SS group had significantly longer follow-up periods compared to the NSS group (14 vs 10 days; $P = .016$). The median age was also significantly higher in the SS group than in the NSS group (77.0 vs 70.5 years; $P = .010$). However, there were no significant differences in gender ($P = .283$), presence of combined renal stone ($P = .324$), high-grade hydronephrosis ($P = .578$), or renal parenchymal thinning ($P = .121$). Similarly, no significant differences were found in underlying conditions such as HTN ($P = .545$), diabetes mellitus ($P = .107$), and CKD ($P = 1.000$). Of the 37 patients in the SS group, four died during treatment, compared to 1 in the NSS group.

Significant differences were also observed in several laboratory biomarkers between the SS and NSS groups. In the SS group, platelet counts (thrombocytopenia), ALC, albumin, albumin to globulin ratio, eGFR, and potassium levels were significantly lower. Additionally, a significantly higher percentage of patients in the SS group showed poor performance (81.1% vs 50.0%; $P = .007$). The mean lactic acid level in the SS group was 4.5 mmol/L (range, 2.1–14.7 mmol/L), meeting the Sepsis-3 diagnostic criteria. ABGA revealed abnormal values for all factors except pH in the SS group. Moreover, partial pressure of carbon dioxide (pCO_2), bicarbonate (HCO_3), and base excess values decreased in the SS group, while oxygen partial pressure (pO_2) levels significantly increased compared to the NSS group.

Bacterial culture data indicate that *Escherichia coli, Proteus mirabilis*, and *Pseudomonas aeruginosa* were the most frequently cultured bacteria in both the SS and NSS groups. In the urine samples of the SS group, 56.7% contained *E coli* (including ESBL-positive strains), 16.2% contained *P mirabilis*, and 8.1% contained *P aeruginosa*. For blood samples in the SS group, *E coli* (including ESBL-positive strains) was present in 45.9%, *P mirabilis* in 16.2%, and *P aeruginosa* was not detected. In contrast, in the NSS group, a lower proportion of *E coli* (including ESBL-positive strains) was found in both urine (27.3%) and blood (11.3%) compared to the SS group. Additionally, *P mirabilis* was detected in 4.5% of urine samples, and *P aeruginosa* was more frequently detected at 13.6%, compared to 8.1% in the SS group. In the blood samples from the NSS group, the detection rates were 11.3% for *E coli* (including ESBL-positive strains), 2.3% for *P mirabilis*, and *P aeruginosa* was not detected. Overall, the rates of urine culture positivity significantly differed between the SS and NSS groups (83.8% vs 52.3%; $P = .006$). Similarly, significant differences were observed in blood culture positivity between the groups (70.3% vs 20.5%; $P < .001$).

3.2. Performance of the prediction models

Variables presented in Table 1, excluding ABGA and lactic acid levels, were used for variable selection via RFE. The primary endpoint of the variable selection was the incidence of SS. Based on the number of variables used, Figure 2 illustrates the corresponding accuracy. The combination of 3 variables, including PCT, ALC, and INR, achieved the highest accuracy of 0.8889 (Table S1, Supplemental Digital Content, http://links.lww.com/MD/N222).

To compare the predictive function between models with different combinations of parameters, the AUROC was utilized. We compared 3 types of models with a single parameter, 3 types of models with 2 parameters, and a model with all 3 parameters. According to the AUROC curve, models using a single parameter had a lower predictive function than those combining 2 or 3 parameters. According to Figure 3, PCT had the highest AUROC among the single parameters (PCT 0.929, INR 0.827, ALC 0.805). For PCT, the optimal cutoff value was determined to be 30.07 ng/mL, for ALC, it was 380/μL, and for INR, it was 1.19.

As shown in Figure 4, the combination of 2 parameters demonstrated better predictive performance with an AUROC of 0.909 (ALC + INR), 0.917 (PCT + INR), and 0.933 (PCT + ALC). Figure 4 also presents the optimal cutoff values for each model. The combination of all 3 parameters showed the best predictive performance with an AUROC of 0.942 (Fig. 5). The optimal cutoff values for this comprehensive model were PCT at 3.9 ng/mL, ALC at 220/μL, and INR at 1.02. Additionally, we calculated Gini importance scores for each variable, with PCT identified as the most influential factor, as depicted in Figure 6. The Gini importance score is also reflected in Figure 3, which shows PCT as the most useful predictive parameter among the 3 variables.

4. Discussion

We found that the combination of 3 variables (PCT, ALC, and INR) demonstrated the best predictive performance for the progression to SS according to Sepsis-3 criteria. Although previous studies have reported PCT, ALC, and INR levels as biomarkers, these variables have not been combined to estimate their predictive performance. Our study highlights that these 3 types of parameters are effective markers for predicting the progression to SS. While they can be used independently as biomarkers, their combination, either in pairs or as a trio, shows improved predictive power. This advancement over previous studies is significant

Table 1

Description of the characteristics of patients with and without septic shock.

	Septic shock (+) (N = 37)	Septic shock (–) (N = 44)	*P* value
Follow-up period (d), Median (IQR)	14.0 (10.0, 17.5)	10.0 (6.3, 15.0)	**.016**
Age (yr), Median (IQR)	77.0 (61.0, 82.0)	70.5 (57.3, 78.8)	**.010**
Sex, n (%)			.283
Female	27 (73.0%)	26 (59.1%)	
Male	10 (27.0%)	18 (40.9%)	
Number of patients who died, n (%)	4 (10.8%)	1 (2.3%)	.173
Renal stone, n (%)	13 (35.1%)	10 (22.7%)	.324
ECOG status, n (%)			**.007**
Good	7 (18.9%)	22 (50.0%)	
Poor	30 (81.1%)	22 (50.0%)	
High-grade hydronephrosis, n (%)	8 (21.6%)	13 (29.5%)	.578
Renal parenchymal thinning, n (%)	0 (0%)	4 (9.1%)	.121
Hypertension, n (%)	26 (70.3%)	27 (61.4%)	.545
Diabetes mellitus, n (%)	8 (21.6%)	18 (40.9%)	.107
Chronic kidney disease, n (%)	1 (2.7%)	2 (4.5%)	1.000
Positive in urine culture, n (%)	31 (83.8%)	23 (52.3%)	**.006**
Positive in blood culture, n (%)	26 (70.3%)	9 (20.5%)	**<.001**
WBC (/μL), median (IQR)	15,850 (7575, 23,925)	13,190 (9733, 16,775)	.106
Hemoglobin (g/dL), median (IQR)	11.6 (10.8, 13.3)	11.6 (10.6, 13.2)	.663
Platelet (/μL), median (IQR)	136.0 (100.0; 172.0)	208.5 (172.0; 291.0)	**<.001**
Absolute neutrophil counts (/μL), median (IQR)	14,850 (7140, 22,455)	11,080 (7868, 15,003)	**.033**
Absolute lymphocyte counts (/μL), median (IQR)	380.0 (240.0; 630.0)	945.0 (545.0; 1290.0)	**<.001**
Neutrophil-to-lymphocyte ratio, median (IQR)	33.5 (14.6; 46.2)	12.8 (6.4; 21.8)	**<.001**
AST (U/L), median (IQR)	38.0 (28.0; 56.0)	23.0 (17.0; 32.5)	**<.001**
ALT (U/L), median (IQR)	20.0 (13.0; 31.0)	19.5 (14.0; 26.0)	.516
AST-to-ALT ratio, median (IQR)	2.0 (1.6; 3.2)	1.4 (1.0; 1.6)	**<.001**
Albumin (g/dL), median (IQR)	3.00 (2.65, 3.40)	3.75 (3.23, 4.00)	**<.001**
Globulin (g/dL), median (IQR)	2.9 (2.6; 3.4)	3.2 (2.8; 3.5)	.205
Albumin-to-globulin ratio, median (IQR)	1.0 (0.8; 1.2)	1.2 (1.0; 1.4)	**.018**
Total bilirubin (mg/dL), median (IQR)	0.7 (0.5; 1.0)	0.5 (0.4; 1.0)	.143
BUN (mg/dL), median (IQR)	25.6 (22.6; 40.4)	21.6 (14.3; 28.8)	**.003**
Creatinine (mg/dL), median (IQR)	1.8 (1.4; 2.6)	1.4 (0.9; 2.1)	**.011**
eGFR (mL/min/BSA), median (IQR)	28.2 (17.0; 39.2)	53.1 (27.5; 66.8)	**.004**
Sodium (mmol/L), median (IQR)	138.0 (135.0; 141.0)	137.0 (134.0; 139.0)	.313
Potassium (mmol/L), median (IQR)	3.8 (3.4; 4.1)	4.0 (3.7; 4.6)	**.041**
CRP (mg/dL), median (IQR)	16.23 (10.48, 25.63)	12.03 (7.11, 20.46)	.138
Procalcitonin (ng/mL), median (IQR)	57.3 (35.8; 100.0)	0.7 (0.2; 9.1)	**<.001**
PT (S), median (IQR)	14.0 (13.2; 15.2)	12.6 (12.0; 13.2)	**<.001**
aPTT (S), median (IQR)	35.8 (31.3; 42.0)	29.9 (27.1; 32.5)	**<.001**
INR, median (IQR)	1.3 (1.2; 1.4)	1.1 (1.1; 1.2)	**<.001**
*pH, median (IQR)	7.4 (7.3; 7.5)	7.4 (7.4; 7.4)	.609
***pCO2 (mm Hg),** median (IQR)	24.4 (20.9; 30.4)	35.3 (31.7; 40.7)	**<.001**
***pO2 (mm Hg),** median (IQR)	73.2 (44.8; 93.3)	30.9 (25.9; 50.4)	**<.001**
***HCO3 (mmol/L),** median (IQR)	16.7 (13.9; 18.4)	22.5 (20.1; 25.4)	**<.001**
***Baseline excess (mEq),** median (IQR)	–6.0 (–9.3; –3.8)	–0.8 (–3.5; 1.3)	**<.001**
****Lactic acid (mmol/L),** median (IQR)	4.5 (3.5; 5.7)	1.6 (1.0; 2.4)	**<.001**

For normally distributed continuous variables, *t* tests were utilized. For nonnormally distributed variables, we conducted the Kruskal–Wallis rank sum test. For categorical variables, Pearson chi-squared tests were used with Yates' continuity correction.

aPTT = activated partial thromboplastin time, ALT = alanine aminotransferase, AST = aspartate transaminase, BUN = blood urea nitrogen, CRP = C-reactive protein, ECOG = Eastern Cooperative Oncology Group, eGFR = estimated glomerular filtration rate, INR = international normalized ratio, PT = prothrombin time, WBC = white blood cell.

* Eleven patients in the NSS group lacked blood gas analyses data.

** Twenty patients in the NSS group lacked lactic acid data.

in that it not only combines these variables but also identifies the optimal cutoff values for each parameter within the models. In addition, these 3 variables are generally included in routine investigations, which increases their practical utility.

PCT is a precursor of a hormone involved in calcium metabolism. It is elevated in cases of major trauma, elective surgery, and severe burns, as well as in some cancers.[15] However, it is widely used as a biomarker to diagnose sepsis and SS early and to guide treatment.[16] PCT demonstrated higher diagnostic accuracy for sepsis than CRP in a systematic review and meta-analysis that included approximately 1300 patients from 9 studies.[17]

Lymphocytopenia is generally defined as an ALC of fewer than 1000 cells/mm³.[16] In our study, 33 patients (89.2%) in the SS group and 22 patients (50.0%) in the nonseptic shock (NSS) group met this criterion. Previous research has noted that lymphocytopenia can occur during sepsis, burns, trauma, general anesthesia, and major surgery.[18] Several studies have suggested that lymphocytopenia plays a crucial role in severe infections, such as sepsis and SS. Tulzo et al[19] and Venet et al[20] reported a higher rate of lymphocyte apoptosis in patients suffering from SS, as well as decreased counts of CD^{4+}, CD^{8+} T, and natural killer (NK) cells, which further contribute to the development of immunosuppressive conditions. In an analysis of 58,260 hospital admissions, Andreu-Ballester et al[18] identified lymphocytopenia as a predictor of illness severity and mortality. According to our study, lymphocytopenia is a significant contributor to the prediction of SS, consistent with these previous findings.

Disseminated intravascular coagulopathy is associated with prolonged PT and international normalized ratio (INR), as well

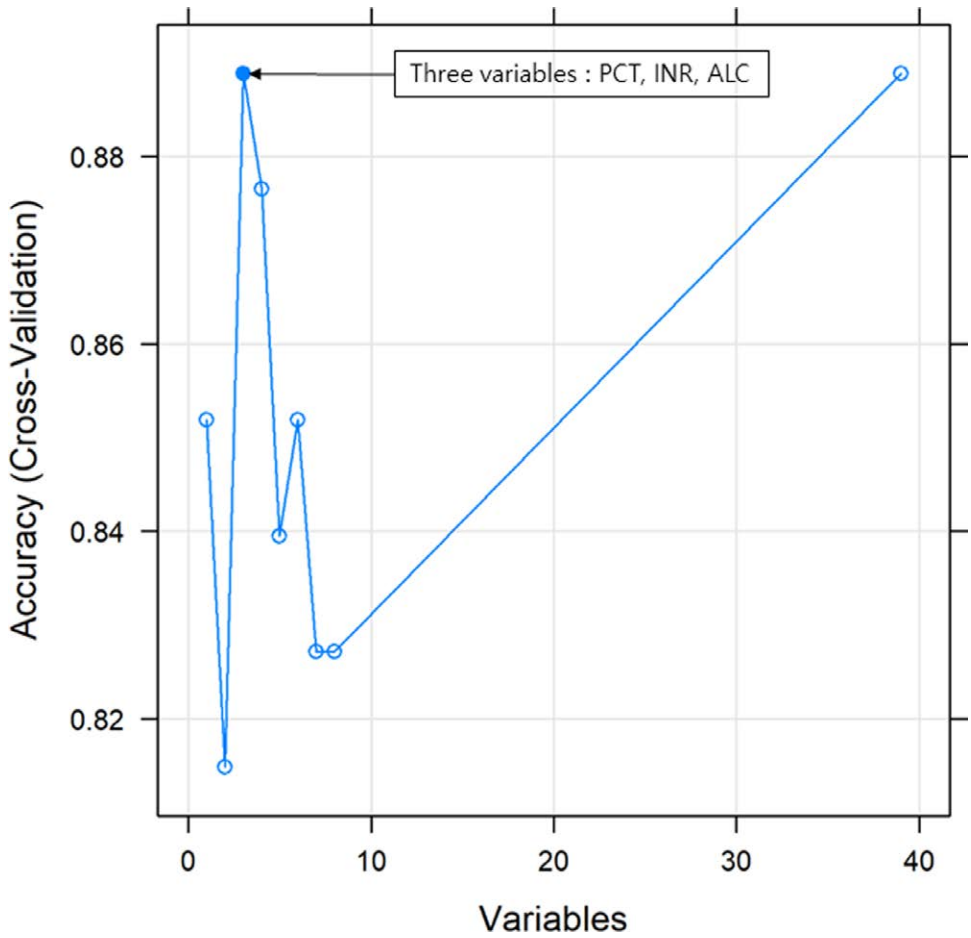

Figure 2. Recursive feature elimination (RFE)-based approach for variable selection. ALC = absolute lymphocyte count, INR = international normalized ratio, PCT = procalcitonin, RFE = recursive feature elimination.

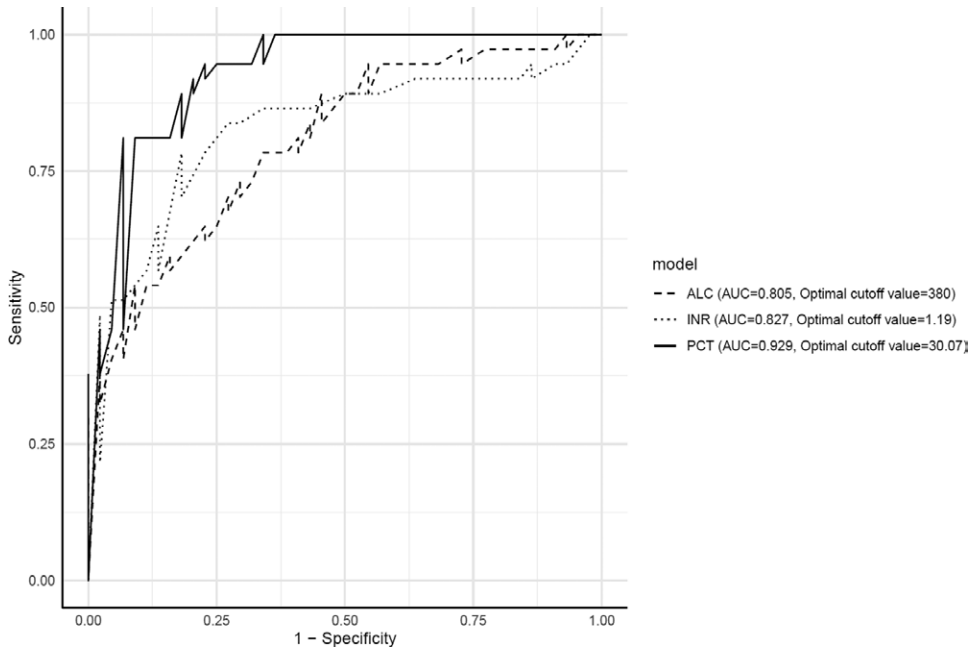

Figure 3. Comparative ROC curves for single-parameter models. ALC = absolute lymphocyte count, INR = international normalized ratio, PCT = procalcitonin, ROC = receiver operating characteristic.

as thrombocytopenia.[21] There is evidence to suggest that thrombocytopenia is linked with poor outcomes in cases of SS, including short overall survival after ICU admission, prolonged length of stay, extended duration of organ support, additional bleeding events, and even mortality.[22–25] These poor outcomes are a result of endothelial dysfunction, coagulopathy, hemodilution, and

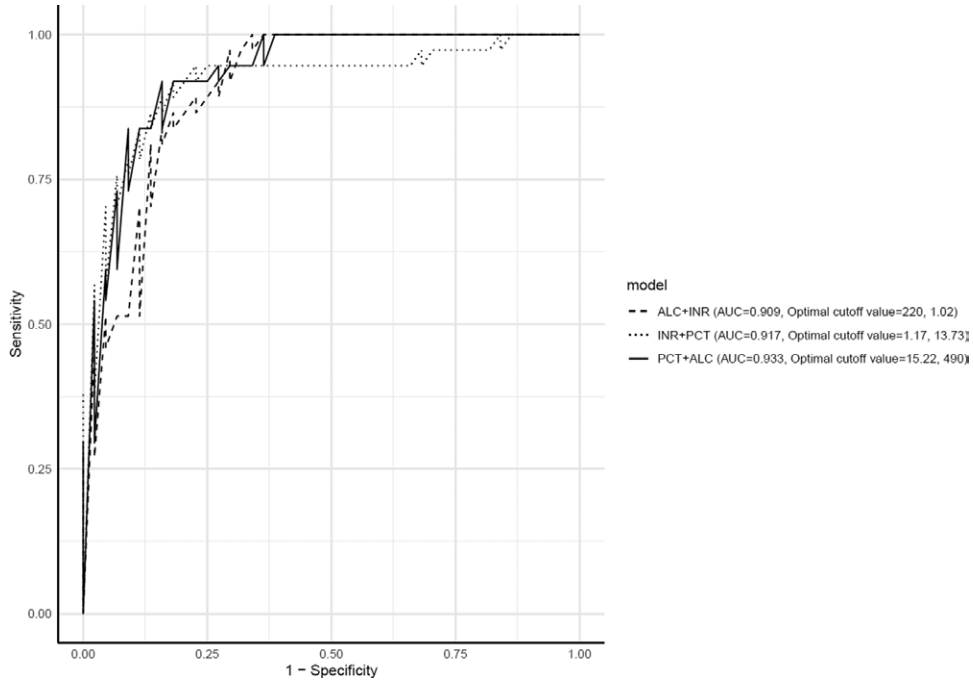

Figure 4. ROC curves analysis for 2-parameter models. ALC = absolute lymphocyte count, INR = international normalized ratio, PCT = procalcitonin, ROC = receiver operating characteristic.

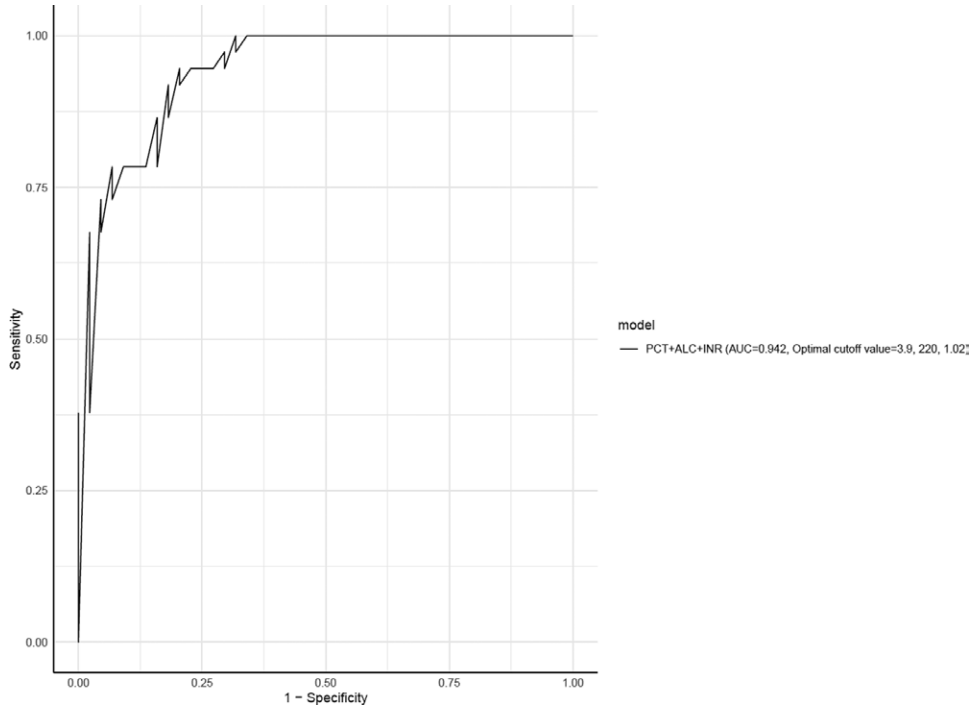

Figure 5. Evaluating a 3-parameter prediction model through ROC curve. ALC = absolute lymphocyte count, INR = international normalized ratio, PCT = procalcitonin, ROC = receiver operating characteristic.

altered thrombopoiesis.[26,27] Although INR alone has not been widely recognized as a prognostic factor, recent studies suggest its effectiveness. According to Ling et al,[28] INR was an important predictor of mortality in patients suffering from necrotizing fasciitis and sepsis. Furthermore, Zhang et al[29] recommended using INR to assess the early stages of nonpulmonary infectious sepsis in adults. Our study also suggests that INR is a better predictor of the severity of infection than platelet count or PT.

In addition to being consistent with the parameters of previous studies, our research aligns with studies on obstructive acute pyelonephritis associated with ureteral stones (OAPN-US). Three studies have employed the Sepsis-3 criteria to predict sepsis and SS in patients with OAPN-US. According to Tambo et al,[9] multiple logistic regression analyses were performed on 50 patients with OAPN-US, including 11 patients who also had sepsis. PCT and presepsin were identified as the most significant predictors of sepsis. Similarly, Baboudjian et al[10] conducted multiple logistic regression analyses on 110 patients with OAPN-US, including 39 patients with SS. Their findings also highlighted PCT, CRP, and DM as major predictors of SS, with PCT levels showing

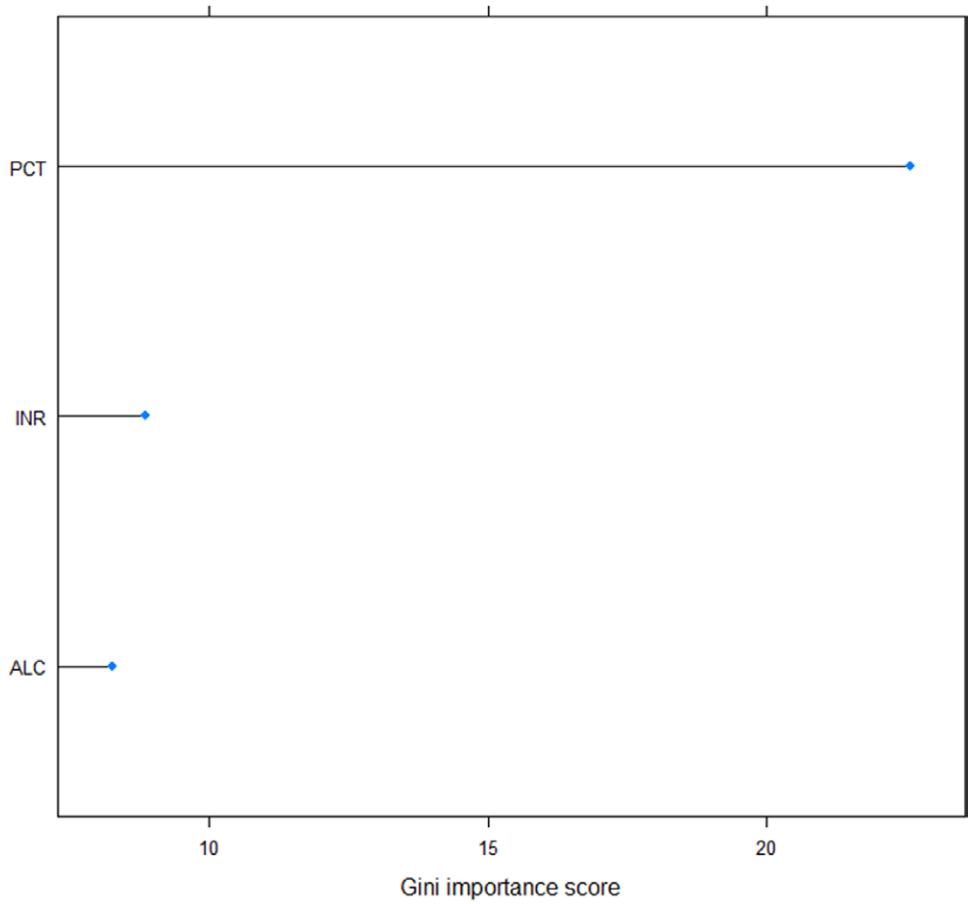

Figure 6. Assessing variable importance in predictive models. ALC = absolute lymphocyte count, INR = international normalized ratio, PCT = procalcitonin.

excellent predictive power with an area under the curve of 0.91. Lastly, Cao et al[11] demonstrated that age over 65, serum Cr >248 mmol/L, and CKD were independently associated with the progression of obstructive urosepsis to severe sepsis or SS. Among these, Tambo et al[9] and Baboudjian et al[10] consistently identified PCT as a crucial prognostic factor for sepsis and SS, findings that are corroborated by our study.

It is important to note that this study has some limitations. Firstly, it was a retrospective study conducted at a single institution with a small number of patients and did not undergo validation in an external cohort. We attempted to find an external cohort for model validation, but no suitable option was available. Secondly, our center did not perform analyses of PCT levels for patients with mild infections, such as uncomplicated acute pyelonephritis. Given that this was not a prospective study, PCT levels were not consistently analyzed across all patients diagnosed with OAPN-US. Consequently, patients lacking PCT level analyses were excluded from the study. This led to the exclusion of more than half of the potential participants, potentially introducing bias.

In conclusion, we have developed a high-performance model for predicting SS in patients with OAPN-US. Utilizing this prediction model at an early stage of an infectious disease enables the provision of timely intensive care, potentially preventing fatal outcomes. However, given the small size of our cohort and the study's inherent limitations, further prospective, larger-scale studies are necessary to refine and validate the model.

Author contributions

Conceptualization: Kyungchan Min, Bum Soo Kim, Hansoo Park.
Data curation: Kyungchan Min, Bum Soo Kim, Yun-Sok Ha, Jae-Wook Chung, Jun Nyung Lee, Hyun Tae Kim, Eun Sang Yoo, Tae Gyun Kwon, So Young Chun.
Formal analysis: Kyungchan Min.
Funding acquisition: Bum Soo Kim.
Investigation: Kyungchan Min, Yun-Sok Ha, Jae-Wook Chung.
Methodology: Kyungchan Min, Yun-Sok Ha, Jae-Wook Chung, Gyuho Jang, Myung-giun Noh, Hyeok Ahn, Hansoo Park.
Project administration: Kyungchan Min.
Resources: Bum Soo Kim, Yun-Sok Ha, Jae-Wook Chung, Jun Nyung Lee, Hyun Tae Kim, Eun Sang Yoo, Tae Gyun Kwon.
Software: Kyungchan Min, Gyuho Jang, Myung-giun Noh, Hyeok Ahn, Hansoo Park.
Supervision: Bum Soo Kim, Yun-Sok Ha, Jae-Wook Chung, Gyuho Jang, Myung-giun Noh, Hyeok Ahn, Jun Nyung Lee, Hyun Tae Kim, Eun Sang Yoo, Tae Gyun Kwon, So Young Chun, Hansoo Park.
Validation: Kyungchan Min, Gyuho Jang, Myung-giun Noh, Hyeok Ahn.
Visualization: Kyungchan Min, Hansoo Park.
Writing – original draft: Kyungchan Min, Bum Soo Kim.
Writing – review & editing: Kyungchan Min, Bum Soo Kim, Yun-Sok Ha, Jae-Wook Chung, Gyuho Jang, Myung-giun Noh, Hyeok Ahn, Jun Nyung Lee, Hyun Tae Kim, Eun Sang Yoo, Tae Gyun Kwon, So Young Chun, Hansoo Park.

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