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Development and validation of prediction scores for the outcome associated with persistent inflammation, immunosuppression, and catabolism syndrome among patients with trauma

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ABSTRACT

Background Persistent inflammation, immunosuppression, and catabolism syndrome (PICS) has impacted on long-term prognosis of patients with trauma. We aimed to identify patients with trauma at risk of PICS-related complications early in the intensive care unit (ICU) course.

Methods A single-center retrospective cohort study was conducted. All consecutive patients with trauma who had stayed in the ICU for >7 days were included in the study. We developed the prediction score for the incidence of PICS-related outcomes in the derivation cohort for the initial period and then evaluated in the validation cohort for the subsequent period. Other outcomes were also assessed using the score.

Results In total, 170 and 133 patients were included in the derivation and validation cohorts, respectively. The prediction score comprised the variables indicating PICS presence, including a maximum value of C-reactive protein >15 mg/dL, minimum value of albumin <2.5 g/dL, and an episode of nosocomial infection for the first 7 days after admission. A score of 1 was assigned to each variable. The area under the receiver operating characteristic curve of the score to predict PICS incidence was 0.74 (95% CI 0.66 to 0.81) and 0.72 (95% CI 0.64 to 0.81) in the derivation and validation cohorts, respectively. The higher score was also significantly associated with a higher Sequential Organ Failure Assessment score at day 14, a longer duration of mechanical ventilation, a longer length of stay in ICU, and experienced multiple episodes of infection. Similar results were obtained in the validation cohort.

Conclusions Our scoring system could predict the outcomes associated with PICS among patients with trauma. Because the score comprised the parameters measured for the first 7 days during the ICU course, it could contribute to identifying patients at a high risk of unfavorable outcome earlier.

Level of evidence Multivariate prediction models; level IV.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Persistent inflammation, immunosuppression, catabolism syndrome (PICS) affects the long-term outcome of patients with trauma. Because the diagnostic criteria of PICS has not been established, clinicians acknowledge only after encountering unfavorable outcomes of patients.

WHAT THIS STUDY ADDS

⇒ The developed scoring system comprising C-reactive protein value, albumin value, and nosocomial infection predicted the outcomes associated with PICS within the 7 days from admission.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Identified patients at risk of unfavorable PICS-related outcome could be the targets for intervention in the future. The scoring system could also be used as a standard reference to diagnose PICS.

BACKGROUND

Trauma remains one of the leading causes of death worldwide.[1] A previous study reported that long-term mortality did not decrease among severely injured patients, despite a decline in early in-hospital mortality.[2] One reason for this is an increase in the number of patients who survived catastrophic injuries but required extended intensive care unit (ICU) stays, prolonged mechanical ventilation (MV), and low-grade organ failure.[3] These clinical trajectories are described as chronic critical illness (CCI).[3] Some patients with CCI exhibit ongoing inflammation, protein catabolism, poor nutritional status, poor wound healing, immunosuppression, and recurrent nosocomial infections.[4] These pathophysiological characteristics have recently been termed as persistent inflammation, immunosuppression, and catabolism syndrome (PICS). According to the previous studies, the criteria for PICS were proposed with multiple parameters, including admission to the ICU >14 days; C-reactive protein (CRP) >150 µg/dL; retinol binding protein <1 mg/dL; total lymphocyte count $<0.80\times10^9$/L; serum albumin <3.0 g/dL; creatinine height index <80%; weight loss >10% or body mass index <18 during hospitalization.[4 5] However, the accuracy of those parameters toward diagnosis has not yet been fully investigated. Additionally, a detailed protocol on how to apply the criteria to clinical practice has not been suggested; thus, clinicians could acknowledge PICS only after patients experienced a complicated in-hospital course. Early identification of patients at high risk of PICS-related outcome could potentially contribute to the development of intervention for PICS.

This study aims to develop a scoring system for injured patients to predict the unfavorable outcomes associated with PICS, and to validate the scoring system over different periods.

METHODS

Study design

A single-center retrospective cohort study for consecutive patients with trauma was conducted. The derivation cohort comprised patients admitted to the hospital between January 2012 and December 2015, whereas the validation cohort comprised those admitted between January 2016 and December 2018. This study complied with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis guidelines.[6] The study was conducted in accordance with the ethical standards of the Helsinki Declaration. The need for informed consent was waived because of the retrospective nature of the study design.

Study participants

This study included adult injured patients who stayed in the ICU for >7 days. Patients ≤15 years, transferred to the ICU from general wards, transferred from other hospitals, admitted to the ICU secondary to non-trauma causes, complicated with burns, implemented do-not-attempt-resuscitation orders within 14 days, and discharged from hospital by any cause, including 'early death',[7] within 14 days were excluded. Moreover, patients with missing data on predictors and outcomes were excluded.

Data collection

Demographic, clinical, and physiological data were collected by medical chart reviews: age, gender, mechanism of trauma, vital signs on arrival at the hospital, coexisting medical condition, Injury Severity Score (ISS), Abbreviated Injury Scale (AIS), days to start nutrition support, and undergoing treatment and organ support. To develop the model, readily available variables presenting PICS were selected. A maximum value of CRP and minimum value of albumin, and an episode of nosocomial

Table 1 Characteristics of patients in the derivation and validation cohorts

Characteristics	Derivation (n=170)	Validation(n=133)
Baseline characteristics		
Age, median (IQR), year	61.5 (44.0–73.0)	68 (49.0–76.0)
Male gender, n (%)	119 (70)	98 (73.7)
Body mass index, median (IQR)	23.2 (20.7–25.1)	22 (19.7–24.5)
Blunt injury, n (%)	168 (98.8)	131 (98.5)
Severity of injuries		
ISS, median (IQR)	34 (25.0–43.0)	29 (20.0–38.0)
Maximum AIS for head, median (IQR)	1 (0–3)	3 (0–4)
Maximum AIS for face, median (IQR)	0 (0–0)	0 (0–0)
Maximum AIS for neck, median (IQR)	0 (0 to 0)	0 (0–0)
Maximum AIS for chest, median (IQR)	4 (3–4)	3 (0–4)
Maximum AIS for abdomen, median (IQR)	0 (0–3)	0 (0–0)
Maximum AIS for spine, median (IQR)	0 (0–3)	0 (0–3)
Maximum AIS for upper extremities, median (IQR)	0 (0–2)	0 (0–2)
Maximum AIS for lower extremities, median (IQR)	0 (0–3)	1 (0–3)
Maximum AIS for external, median (IQR)	0 (0–0)	0 (0–0)
Vital signs on arrival		
Systolic blood pressure on arrival, median (IQR), mm Hg	117 (90.0–151.8)	133 (102.0–156.0)
Heart rate on arrival, median (IQR)/min	100 (82.0–127.0)	95 (78.0–111.0)
Glasgow Coma Scale on arrival, median (IQR)	13.5 (8.0–14.0)	13 (6.0–14.0)
Comorbidities		
Diabetes mellitus, n(%)	24 (14.7)	7 (5.2)
Cancer, n(%)	4 (3.7)	2 (1.5)
Chronic kidney disease, n(%)	3 (1.8)	3 (2.2)
Outcome of event		
Primary outcome		
LOS in ICU >14 days and organ failure* ≥1, or in-hospital mortality, n (%)	67 (39.4)	46 (34.6)
Secondary outcomes		
In-hospital mortality, n (%)	12 (7.1)	4 (3.0)
Episodes of multiple infections, n (%)	67 (39.4)	38 (28.6)
SOFA score at day 14, median (IQR)	4 (2–5)	3 (1–4)
Mechanical ventilation days, median (IQR), days	10 (8.0–16.0)	9 (6.0–12.0)
LOS in ICU, median (IQR), days	11 (9.0–14.0)	12 (9.0–15.0)
LOS in hospital, median (IQR), days	55 (42.0–72.0)	52 (40.0–59.0)

*Organ failure was defined as tracheostomy, the duration of mechanical ventilation ≥96 hours, poor wound healing (complicated with surgical site infections or wound dehiscence) or receiving renal replacement therapy.
AIS, Abbreviated Injury Scale; ICU, intensive care unit; ISS, Injury Severity Score; LOS, length of stay; SOFA, Sequential Organ Failure Assessment.

infection over the 7 days were extracted as surrogate markers of inflammation, catabolism, and immunosuppression, respectively. Nosocomial infection was identified based on the Centers for Disease Control and Prevention/National Healthcare Safety Network criteria.[8] Regarding pneumonia, we omitted the evaluation of chest radiograph findings because interpreting them entailed the subjectivity and variability in patients receiving MV,[9] especially those with chest injuries. Each infection also met the following criteria: infection occurred 48 hours after the admission; the microbiological pathogen was isolated from the culture of the suspected source; and the response to the treatment (eg, antibiotics or drainage) was confirmed by physicians. The treatment decision was based on the physician's discretion.

Definition and outcome

The primary outcome was a composite comprising a prolonged stay in the ICU (≥14 days)[7 10 11] and at least one of the comorbid organ failures during the hospital stay or in-hospital mortality after 14 days from admission. Organ failure was defined as follows: tracheostomy, the duration of MV ≥96 hours, poor wound healing (complicated with surgical site infections or wound dehiscence) or receiving renal replacement therapy. These definitions were derived from the concept of CCI[12 13] based on the assumption that PICS is a subset of CCI.[5] The primary outcome was used to determine the variables of the scoring system. The performance of the scoring system in predicting secondary outcomes was also evaluated, including in-hospital all-cause mortality, Sequential Organ Failure Assessment (SOFA) score at day 14, length of stay (LOS) in the ICU, hospital LOS, duration of MV, and multiple episodes of nosocomial infection during the in-hospital course.

Statistical analysis

In the derivation cohort, multivariate logistic regression for the composite outcome was performed to identify predictive factors. Continuous variables were dichotomized at clinically meaningful and convenient values. The following candidate variables were tested in the model: maximum CRP value >15 mg/dL within 7 days, minimum albumin value <2.5 g/dL within 7 days, and an episode of infection within 7 days. The cut-off values of maximum CRP and minimum albumin were determined by the number close to the median value. Further, age ≥70 years, ISS ≥16, systolic blood pressure (SBP) on arrival ≤90 mm Hg, and Glasgow Coma Scale (GCS) score on arrival ≤8 were also evaluated. We subsequently developed a scoring system using the adjusted coefficients of significantly associated variables with the composite outcome. According to Sullivan's scoring system, the scores were assigned based on a calculation in which all coefficients were divided by the smallest absolute value of the coefficient and rounded to the nearest integer.[14 15]

To evaluate the accuracy of the scoring system, the receiver operating characteristic (ROC) curve and area under the curve (AUC) for predicting the composite outcome were also obtained. Sensitivity, specificity, and positive predictive value (PPV) and negative predictive value (NPV) were calculated. To predict secondary outcomes, multivariate linear regression and logistic regression models were used for continuous and binary outcomes, respectively. Both analyses were adjusted for age, ISS, SBP on arrival, and GCS on arrival. The time to in-hospital death was also assessed by scores using survival analysis. Survival curves were estimated based on the Kaplan-Meier method, and the log-rank test was performed. After deriving the scoring system, the score was evaluated using the same multivariate analyses to predict outcomes in the validation cohort.

As a sensitivity analysis, AUC for the composite outcome was calculated after excluding patients with isolated traumatic brain injuries (TBI). Patients with isolated TBI were defined as those with injuries with AIS score ≥3 for the head and with AIS score between 0 and 2 for other body regions.

For all tests, a two-sided $p<0.05$ was defined as significant. All statistical analyses were performed using R V.4.1.3 (R Foundation for Statistical Computing, Vienna, Australia).

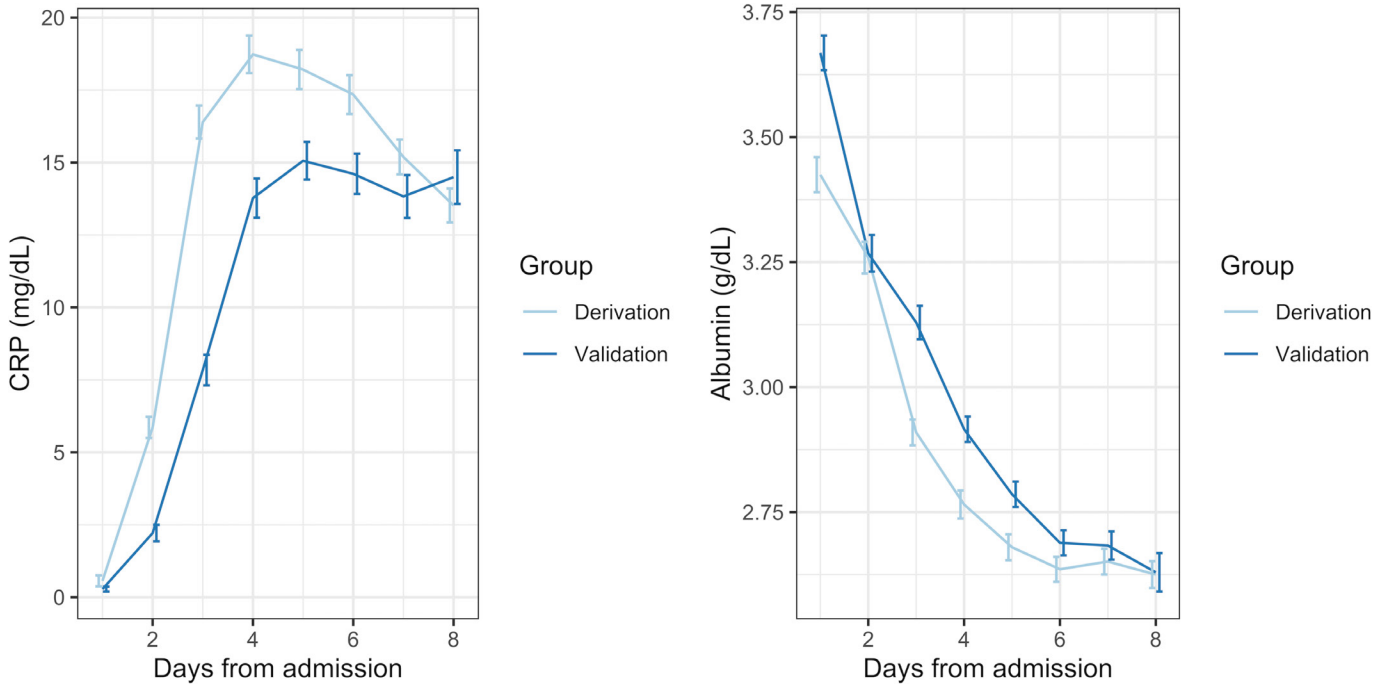

Figure 1 Time course of C-reactive protein (CRP) and albumin from admission into the intensive care unit (ICU). Error bars represent standard errors.

Table 2 Results of multivariate logistic regression for the composite outcome and assignment of developed score

	Logistic regression			Assigned score	
Variable	OR	95% CI	P value	Coefficient	Point score
Maximum CRP >15 mg/dL	2.76	1.02 to 7.49	0.046	0.99	1
Minimum Alb <2.5 g/dL	3.95	1.92 to 8.14	<0.01	1.21	1
Infection within 7 days	2.81	1.37 to 5.78	0.01	0.99	1
Age ≥70 years	0.61	0.28 to 1.34	0.22	–	–
ISS ≥16	3.50	0.66 to 18.53	0.14	–	–
SBP on arrival ≤90 mm Hg	1.07	0.48 to 2.34	0.88	–	–
GCS score on arrival ≤8	0.94	0.42 to 2.11	0.89	–	–

Alb, albumin; CRP, C–reactive protein; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; SBP, systolic blood pressure.

RESULTS

There were 191 and 147 eligible patients between 2012 and 2015, and between 2016 and 2018, respectively. Of these, this study enrolled 170 and 133 patients in the derivation and validation cohorts, respectively (online supplemental figure 1). None of the patients had missing data on predictors and outcomes. Patient characteristics in both cohorts are presented in table 1 and online supplemental table 1. Median age was 61.5 (IQR 44 years to 72.8 years) and 68 years (IQR 49 to 76), and median ISS was 34 (IQR 25 to 43) and 29 (IQR 20.5 to 38), in the derivation and validation cohorts, respectively. Most patients (>98%) in both cohorts had blunt mechanism of injuries (table 1). The trend of observed data for the first 7 days showed that CRP level gradually increased and reached a peak of around 15 mg/dL on day 4, and albumin gradually decreased and reached a bottom of around 2.5 g/dL on day 6 in both cohorts (figure 1). For the initial 7 days from admission, 91 (53.5%) and 52 (39.1%) patients experienced an episode of nosocomial infection, and 75 (44.1%) and 47 (35.3%) patients had pneumonia as a source of infection in the derivation and validation cohorts, respectively (online supplemental table 1).

The logistic regression model to select the variables for the scoring system showed that maximum CRP value >15 mg/dL, minimum albumin value <2.5 g/dL, and the episode of infection within 7 days were associated with the primary composite outcome (table 2). A score of 1 was assigned to each variable (table 2). We named this generated scoring system as 'the ACIDS score' (including the lower value of Albumin, higher value of CRP, and the episode of Infection until Day Seven from admission).

The ACIDS scores distribution in both cohorts had a proportional relationship with the occurrence of primary composite outcome (figure 2). The ROC curves to predict the composite outcome using the ACIDS score are shown in figure 3. The AUC was 0.74 (95% CI 0.66 to 0.81) and 0.72 (95% CI 0.64 to 0.81) in the derivation and validation cohorts, respectively. If the cut-off value was determined as the ACIDS score ≥2, the sensitivity, specificity, PPV and NPV in the derivation cohort were 0.84 (95% CI 0.73 to 0.92), 0.52 (95% CI 0.42 to 0.62), 0.53 (95% CI 0.43 to 0.63), and 0.83 (95% CI 0.72 to 0.91), respectively. If the cut-off value was the score ≥3, the sensitivity, specificity, PPV and NPV in the derivation cohort were 0.48 (95% CI 0.35 to 0.60), 0.86 (95% CI 0.78 to 0.92), 0.70 (95% CI 0.54 to 0.82), and 0.72 (95% CI 0.63 to 0.79), respectively. Similar results were obtained in the validation cohort (online supplemental table 2). In the sensitivity analysis, the AUC after excluding patients with isolated TBI was 0.74 (95% CI 0.66 to 0.81) in the derivation cohort (n=166) and 0.74 (95% CI 0.65 to 0.82) in the validation cohort (n=120).

The results of the analyses of the secondary outcomes are shown in table 3. In the derivation cohort, there was a significant association between the ACIDS score and in-hospital mortality (adjusted OR (aOR) 4.61, 95% CI 1.64 to 12.95; p<0.01) (table 3). Survival curve analysis showed that patients with a higher ACIDS score were associated with lower survival to discharge rate (p=0.03) (online supplemental figure 2). Additionally, a higher ACIDS score was significantly associated with an increased odds of multiple episodes of nosocomial infection (aOR 2.53, 95% CI 1.68 to 3.83; p<0.001), a higher SOFA score at day 14 (adjusted coefficient 0.66, 95% CI 0.25 to 1.08; p<0.01), longer duration of MV (adjusted coefficient 4.42, 95% CI 2.06 to 6.78; p<0.001), ICU LOS (adjusted coefficient 2.26, 95% CI 1.25 to 3.27; p<0.001) and hospital LOS (adjusted coefficient 11.72, 95% CI 3.75 to 19.69; p=0.04). In the validation cohort, the ACIDS score was significantly associated with increased odds of multiple episodes of nosocomial infection (aOR 1.62, 95% CI 1.06 to 2.47; p=0.03), a higher SOFA score at day 14 (adjusted coefficient 0.91, 95% CI 0.50 to 1.32; p<0.01), longer duration of MV (adjusted coefficient 2.82, 95% CI 1.87 to 3.77; p<0.001), and LOS in the ICU (adjusted

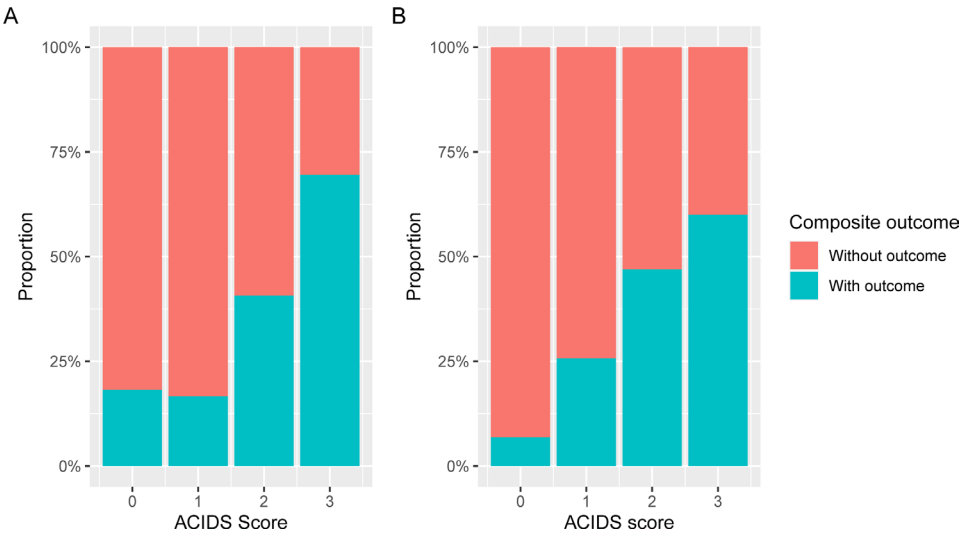

Figure 2 Proportion of the occurrence of the primary outcome for each score (A, derivation cohort, n=170; B, validation cohort, n=133).

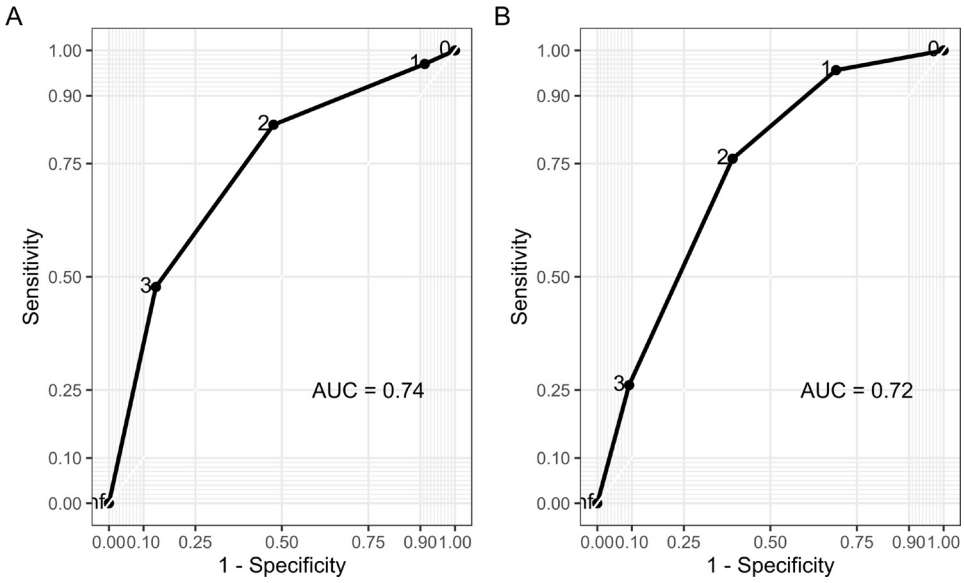

Figure 3 The receiver operating characteristic curve and area under the curve (AUC) to predict the composite outcome using the ACIDS score (A, derivation cohort, n=170; B, validation cohort, n=133).

coefficient 1.82, 95% CI 0.98 to 2.67; p<0.001) (table 3 and online supplemental tables 3–9).

DISCUSSION

We developed a new scoring system and named the ACIDS score, comprising a maximum CRP value >15 mg/dL, a minimum albumin <2.5 g/dL, and an episode of infection during the 7 days from admission. Those variables indicated the presence of PICS and could predict poor outcomes associated with PICS among patients with trauma. Based on the results, the scores of 1, 2, and 3 could be interpreted as 'low risk', 'intermediate risk', and 'high risk' of PICS-related outcomes, respectively.

Severe tissue injury releases damage-associated molecular patterns (DAMPs), activates the innate immune response and increases the production of proinflammatory and anti-inflammatory cytokines.[16] Patients with PICS are characterized to have persistent presence of DAMPs and acute inflammatory response.[17] CRP is produced in response to the stimulation of interleukin-6.[18] Circulating CRP concentration reflects the intensity of ongoing inflammation.[19] Previous studies have reported that a higher CRP level was a diagnostic marker of PICS.[4 20] Recently, Ingels *et al* reported that higher CRP levels on day 3 among critically ill patients were associated with more infections and longer ICU stays.[21] It suggests that early elevation of CRP levels reflects a severe immune response after injury. The enhanced immune response presumably increases susceptibility to infection, leading to further inflammation. The pathophysiology supports that CRP levels in the early phase after injury could be the surrogate markers of the PICS presence. Interestingly, Ingels *et al* also demonstrated that higher CRP levels were associated with the late initiation of nutrition support but not with the serum concentration of cytokines.[21] Thus, CRP may be affected by nutrient deficits as well as immune responses, although this is beyond the scope of the present study.

Persistent inflammation induces myonecrosis and catabolism.[22] In patients with severe critical illness, the protein balance remains negative on day 7 because the intensity of catabolic signaling overwhelms the anabolic process.[23] From our findings, a lower

Table 3 Results of multivariate logistic and linear regression analyses for outcomes

	Derivation			Validation		
Outcome	**Adjusted OR**	**95% CI**	**P value**	**Adjusted OR**	**95% CI**	**P value**
Primary outcome						
LOS in ICU >14 days and organ failure* ≥1, or in-hospital mortality	3.18	2.04 to 4.97	<0.001	2.66	1.66 to 4.24	<0.001
Secondary outcomes						
In-hospital mortality	4.61	1.64 to 12.95	<0.01	5.73	0.87 to 37.6	0.07
Multiple episodes of infection	2.53	1.68 to 3.83	<0.001	1.62	1.06 to 2.47	0.03
	Adjusted coefficient	**95% CI**	**P value**	**Adjusted coefficient**	**95% CI**	**P value**
Secondary outcomes						
SOFA score at day 14	0.66	0.25 to 1.08	<0.01	0.91	0.50 to 1.32	<0.001
Duration of mechanical ventilation	4.42	2.06 to 6.78	<0.001	2.82	1.87 to 3.77	<0.001
LOS, ICU	2.26	1.25 to 3.27	<0.001	1.82	0.98 to 2.67	<0.001
LOS, hospital	11.72	3.75 to 19.69	0.04	3.97	−0.84 to 8.77	0.11

*Organ failure was defined as tracheostomy, the duration of mechanical ventilation ≥96 hours, poor wound healing (complicated with surgical site infections or wound dehiscence) or receiving renal replacement therapy.
ICU, intensive care unit; LOS, length of stay; SOFA, Sequential Organ Failure Assessment.

albumin level for the first 7 days is considered as a proxy for an increased catabolic state after post-trauma inflammatory insult, suggesting the presence of PICS. Additionally, low albumin levels at the onset of infectious disease are associated with mortality.[24] It indicates that the catabolic state suppresses immune competence. Then, secondary infection under the immunosuppressive state contributes to protracting persistent inflammation, exacerbating catabolism.[22] This vicious circle is considered as the process of developing PICS-related outcome.

Inflammatory insult proportionally increases the expansion of myeloid-derived suppressor cells (MDSCs),[4] a heterogenous population of activated immature myeloid cells, to decrease inflammation.[25] However, their persistent expansion causes immunosuppression and is predictive of nosocomial infection.[25] Given this pathophysiology, nosocomial infection can reflect immunological dysfunction in patients with trauma. Mira *et al* reported that patients with CCI experienced more than twice the frequency of nosocomial infection within 7 days compared with those with rapid recovery.[10] In addition, Stortz *et al* described that sepsis with onset after 48 hours of admission secondary to a postsurgical or post-traumatic injury was significantly associated with CCI development.[7] Those studies indicated the association of early nosocomial infection with PICS occurrence, although the causal relationship between them was unclear. In critically ill patients, persistent lymphopenia is also associated with ICU-acquired infection and mortality.[26] Inflammatory insult after trauma initiates the emergency myelopoiesis and proliferates MDSCs at the expense of lymphocyte production, leading to lymphopenia.[17] Therefore, lymphocyte count is considered as another candidate marker of immunosuppression. In fact, it is a constituent of the existing criteria as described earlier.[4] However, this study could not evaluate lymphocyte count in the multivariate analyses because of many missing measurements in our data. The accuracy of the prediction model using lymphocyte counts needs to be compared with that of our model in the future.

To the best of our knowledge, this is the first study to develop and validate a prediction score for the outcome associated with PICS. The score could also be associated with a higher SOFA score on day 14 and a longer duration of MV. Those outcomes were also related to moderate organ dysfunction, which is typically associated with PICS.[4] The results of analyses for the validation cohort were almost consistent with those of the derivation cohort, demonstrating the robustness of the scoring system. Furthermore, the sensitivity analysis developed robustness through consistent accuracy using the scoring system after excluding patients with isolated TBI. The results demonstrated that the poor outcomes were not driven by the severity of TBI alone. Another strength of the score is that it can be applied in the early stages of the ICU course. Vanzant *et al* reported that patients with complicated clinical courses showed significant changes in gene expression suggesting PICS as early as day 7.[11] This indicates that some changes in clinical findings could be identified in the first 7 days after injury in patients complicating PICS. The early prediction of PICS-related outcome might contribute to the development of treatment strategies of PICS for the future. The present study suggested that interventions could be considered if patients have an ACIDS score ≥2 (ie, 'intermediate' or 'high' risk). For instance, early peripheral amino acid infusion reduces inflammatory responses and modifies metabolism in critically ill patients with trauma.[27] Introducing such interventions based on the score is expected to reduce PICS-related outcomes. Lastly, all components of the ACIDS score are easily measured in clinical practice. Therefore, the score can be applied to most ICU settings, even in resource-limited environments.

This study had several limitations. First, the scoring system could not be compared with other models, including existing criteria.[4] However, no established protocol is currently available to diagnose PICS. We think that the ACIDS score could be used as a standard reference. Second, the CCI definition was substituted for the outcome associated with PICS to develop the ACIDS score because of a lack of evidence for established criteria. Nevertheless, this is consistent with the concept that PICS constitutes a subset of CCI.[5] Additionally, CCI has many overlaps with 'post-intensive care syndrome',[22] having a similar term but a different concept from PICS in this context. Given the involvement of multiple issues, CCI could be an optimal target for improvement in modern ICUs. Third, this was a hospital-based study; hence, the long-term prognosis could not be surveyed. PICS encompasses poor functional outcomes, including discharge to long-term acute care facilities or indolent death.[4] Further follow-up investigations are required to assess long-term outcomes. Finally, this study had a single-center trial design. Although the results were validated in two different cohorts, the generalizability of the results remains to be verified. For example, the median age of patients was relatively older in both cohorts (table 1). Those findings reflected the trend that people between 65 and 90 have been the age group with the largest number of patients with trauma in Japan.[28] Therefore, the scoring system needs to be validated in the settings of younger population. As the scoring system can be used without special resources, a multicenter trial is required for external validation in the future.

CONCLUSIONS

In patients with trauma who required a stay in the ICU longer than 7 days, a maximum CRP value >15 mg/dL, minimum albumin <2.5 g/dL, and an episode of nosocomial infection for the first 7 days after admission were associated with PICS-related outcome. A scoring system incorporating these factors suggests the presence of PICS and could be applied to predict unfavorable outcomes.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The Institutional Review Board of Nippon Medical School Chiba Hokusoh Hospital approved this study (registration number 801, approved May 15, 2020).

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terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

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