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Article

Low Prognostic Nutritional Index Predicts In-Hospital Complications and Mortality in Patients with Spontaneous Intracerebral Hemorrhage: A Retrospective Study

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Abstract: Background: The study aimed to explore the association between the prognostic nutrition index (PNI) and in-hospital complication and mortality in patients with spontaneous intracerebral hemorrhage (ICH). Methods: We conducted a retrospective analysis using data from the Changhua Christian Hospital Clinical Research Database (CCHRD) between January 2015 and December 2022. 2402 patients were included, with the median PNI value set at 42.77. The restricted cubic spline model, Kaplan-Meier and ROC analysis for overall survival were used to evaluate the association of PNI with medical complications and mortality. Propensity score matching (PSM) analysis was performed to balance these clinical variables between groups, which could reduce potential bias to some extent. Results: PNI was significantly associated with in-hospital complications and 28-day and 90-day mortality in multivariate analysis. The main finding of our study is that a low PNI score at admission was independently associated with a poor ICH outcome. The Kaplan-Meier curves revealed higher survival rates in the high PNI group. PNI demonstrated sensitivity to predict medical complications and mortality based on ROC analysis. Conclusions Our study suggests that PNI could serve as a valuable marker for predicting medical complications and mortality in patients with spontaneous ICH.

Keywords: prognostic nutrition index (PNI); spontaneous intracerebral hemorrhage (ICH); in-hospital complication; mortality; propensity score matching (PSM)

1. Introduction

In Taiwan, cerebrovascular diseases are the leading cause of death worldwide and have been ranked fifth among the top ten causes of death in 2022 [1]. Approximately 10% of the 795,000 strokes that occur annually in the United States are intracerebral hemorrhages (ICH)[1]. In Taiwan, data from stroke registration indicates that ICH constitutes 15.9% of all stroke cases and is associated with a 30-day mortality rate of 19.8% and a 1-year mortality rate of 29.6% [2]. The incidence of ICH incidence is higher in Taiwan than in Western populations. An analysis of the Taiwan National Health Insurance Research Database from 2011 to 2014, revealed that the odds of death for those with ICH were significantly higher, with an adjusted odds ratio of 5.80 compared to 2.07 for ischemic stroke [4]. Spontaneous intracerebral hemorrhage (ICH) remains one of the most serious subtypes of stroke, characterized by a high mortality rate, higher medical costs, and often resulting in poor functional outcomes[2,3].

Nutritional status is associated with mortality, length of hospitalization, and clinical outcomes with cerebrovascular diseases [4–6]. Previous research has also indicated that acute ICH patient with poor outcomes had a greater degree of undernutrition compared to those without (p<0.001)[7]. A low level of serum albumin can increase the risk of infections and mortality in critically ill patients [10,11]. Hypoalbuminemia is a simple marker of malnutrition that is a major cause of impaired immune response and serves as a reliable predictor of hospital-acquired infections [12]. Previous reports suggested a relationship between hypoalbuminemia and increased mortality in patients with ICH[8,9]. Furthermore, admission lymphopenia is associated with an increased risk of infection and unfavorable outcome in patients with spontaneous ICH[10].

The prognostic nutritional index (PNI) is an objective and convenient biological marker that could evaluate the immunological nutritional status by calculating the serum albumin concentration and the total number of peripheral blood lymphocytes. Thus, PNI is more feasible in clinical work. In recent studies, the lower PNI has been shown to be associated with the worse New York Heart Association classification of coronary heart disease patients [11]. Yang et al. found that PNI was an independent predictor of 30-day, 90-day, and 1-year mortality in critically ill stroke patients [12]. An observational study revealed that preoperative PNI could be associated with the occurrence of postoperative pneumonia in patients with aneurysmal subarachnoid hemorrhage (aSAH) [13].

However, the association and predictive value of PNI in the prognosis of patients with spontaneous intracerebral hemorrhage have not been reported. Therefore, our study aimed to explore the association between PNI and prognosis in patients with spontaneous intracerebral hemorrhage (ICH).

2. Materials and Methods

2.1. Study Populations

This retrospective study was conducted between January 2015 and December 2022, enrolling all patients admitted with spontaneous intracerebral hemorrhage (ICH) who received medical or surgical treatment in our medical unit at Changhua Christian Hospital, Taiwan. The diagnosis of ICH was initially confirmed by brain computed tomography (CT) scans at admission. The institutional review board waived the requirement of informed consent, since no intervention was performed and no personally identifiable information was disclosed.

2.2. Inclusion/Exclusion Criteria

Patients were included if they had spontaneous intracerebral hemorrhage. We excluded (1) patients < 20 years, (2) patients> 100 years, (3) patients with missing vital sign data, or (4) patients with incomplete biochemical data from this study.

2.3. Data Collection and Definition

We included a total of five thousand six hundred thirty-three patients with spontaneous intracerebral hemorrhage at Changhua Christian Hospital between January 2015 and December 2022, and patient data were filtered in the Changhua Christian Hospital Clinical Research Database (CCHRD). We enrolled a total of two thousand four hundred and two cases of ICH in our study (Figure 1). Our study was approved by the Institutional Review Board of CCH (IRB No: 230539).

The following data was collected: demographic variables, comorbidities, laboratory biochemical parameters, vital signs at admission, Charlson Comorbidity Index, and Glasgow Coma Scale from the medical records. Demographic characteristics included age, gender, and body mass index (BMI). The BMI was calculated as weight (kg)/height (m)². Comorbidities included hypertension, diabetes mellitus, and dyslipidemia. Vital signs included temperature, heart rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and percutaneous oxygen saturation (SPO2) at the first admission. Laboratory parameters included red blood cells (RBC), white blood cells (WBC), lymphocytes, hemoglobin concentration, platelet count, red blood cell distribution width (RDW), serum creatinine, blood urea nitrogen (BUN), serum potassium, serum sodium, albumin, and HbA1c

at first admission. The Charlson comorbidity index calculator estimates survival in patients with multiple comorbidities. It consists of 17 items related to various health conditions associated with mortality. Glasgow Coma Scale (GCS) is a neurological scale that is used to assess the level of consciousness and neurological functioning in patients. The GCS evaluates three components of neurological function: eye opening, verbal response, and motor response, with a lower score indicating a higher degree of coma. The PNI was calculated as follows: PNI = albumin (g/L) + 5 × lymphocyte (10^9/L). Patients were divided into low-value groups (PNI < 42.77) and high-value groups (PNI ≥ 42.77) according to the cut-off point.
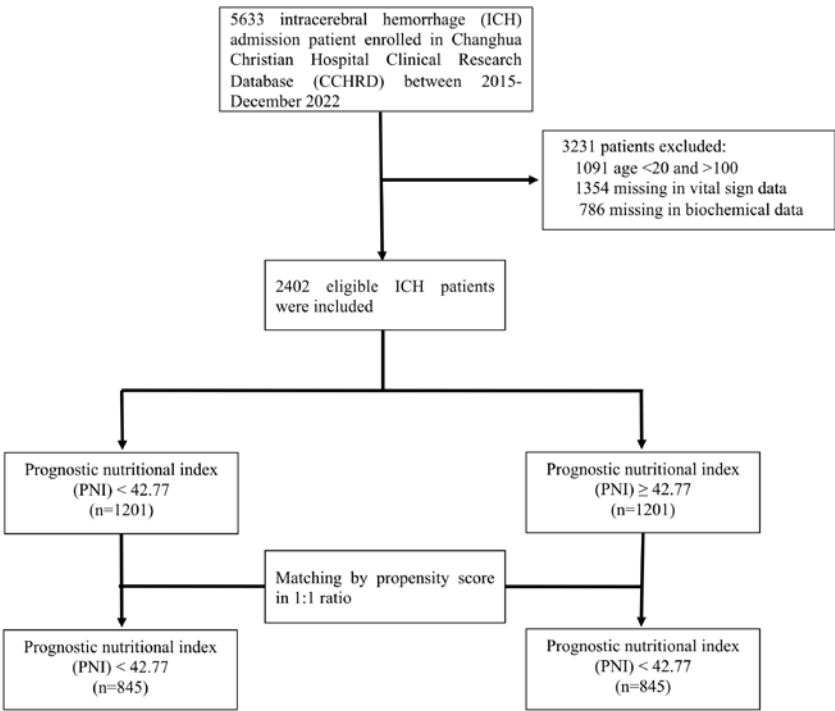

Figure 1. Flow chart of the patient selection.

2.4. Study Results and Definitions

The primary outcome was medical complications that developed during hospitalization, such as acute respiratory failure, stroke-associated pneumonia (SAP), urinary tract infection (UTI), seizures, cardiopulmonary resuscitation (CPR), sepsis, gastrointestinal bleeding, and acute venous thromboembolism, as recorded in the forms of the paper registry. Secondary outcomes were mortality at 28 days and 90 days after ICH. The start date was the date of admission of the patient.

2.5. Statistical Analysis

Categorical variables were presented as numerical proportions, and continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) according to the data distribution. Continuous variables were compared using Student's t test or Mann-Whitney U test and the chi-square test for categorical variables. Confounding factors always diminish the accuracy and objective of retrospective studies. Propensity score matching (PSM) analysis was performed to balance these clinical variables between groups, which could reduce potential bias to some extent. These patients were matched 1:1 using the nearest-neighbor algorithm with a caliper width of 0.017 and without replacement to identify the impact of PNI on ICH. Propensity score matching (PSM) was carried out to adjust for an imbalance of clinical parameters with a p-value of <0.05 in the multivariate analysis.

To investigate the associations between medical complications and PNI level in patients with spontaneous ICH, the logistic regression model was used. In order to investigate the correlation

between 28- and 90- day mortality and the PNI level in patients with spontaneous ICH, we constructed the crude and multivariate Cox's proportional hazard models. To improve the reliability of the results, two different adjustment models were applied before and after the propensity score matching.

Multivariate regression analyzes were performed and adjusted for potential covariates, including sex, age, GCS scores, history of diabetes mellitus, hypertension and hyperlipidemia, temperature, heart rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP) and percutaneous oxygen saturation (SPO2), red blood cells (RBC), white blood cells (WBC), lymphocytes, hemoglobin concentration, platelet count, serum creatinine, blood urea nitrogen (BUN), serum potassium, serum sodium, HbA1c and Charlson comorbidity index. The relationship of PNI level with the 'Odds ratio' of inhospital complications and the 'Hazard ratio' of mortality at 28 and 30 days was evaluated using a restricted cubic spline with 4 knots. The Kaplan–Meier curves and log-rank test were used for survival analysis. Kaplan–Meier analysis was performed to evaluate time-to-event outcomes and the evaluation of discrepancies was assessed by log-rank tests.   A significant log-rank test suggests that there are differences in survival experiences between the compared groups. The predictive value of RAR was evaluated using the receiver operating characteristic (ROC) curve. The results are shown as the area under the curve (AUC). A p-value < 0.05 was considered statistically significant in this study.

All statistical analyzes were performed with SAS and R software (version 4.1.0, accessed on May 18, 2021), and the R Archive Network (http://cran.rproject.org). In this study, we define a p-value below 0.05 as statistically significant.

3. Results

3.1. Patient Characteristics before and after Propensity Score Matching

Among the 5633 patients with spontaneous ICH who were initially enrolled. We excluded 3231 people who (1) <20 years or >100 years (1091 patients), (2) missing vital sign data (1,354 patients) or (3) missing biochemical data (786 patients). Finally, in the present study, 2402 patients who met the screening criteria were included (Figure 1). The comparison of demographic and clinical characteristics between the low PNI (< 42.77) and high PNI (≥ 42.77) groups before and after the propensity-score matching is presented in Table 1.

Table 1. The demographics and clinical characteristics divided by the cut-off value of PNI score = 42.77 before and after the propensity score matching.

Variables	Before Propensity Score Matching N = 2402				After Propensity Score Matching N=1690		
	Total	PNI<42.77	PNI◎42.77	P-value	PNI<42.77	PNI◎42.77	P-value
Characteristics number	2402	1201	1201		845	845	
Ages (years)	63.6±18.6	67.3±17.6	59.9±18.7	<0.001	63.6±17.9	64.4±17.3	0.345
Gender, male , n (%)	1419(59.1%)	705(58.7%)	714(59.5%)	0.709	492(58.2%)	496(58.7%)	0.843
BMI	23.9±7.5	23.5±9.8	24.4±4.2	0.004	23.6±4.2	24±4.1	0.031
GCS at admission [median (IQR)]	13(9,14)	13(7,14)	14(10,14)	<0.001	13(8,14)	13(10,14)	0.044
Vital sign at admission							
SBP (mmHg)	131±16.7	132.4±16.7	129.6±16.6	<0.001	131.5±16.3	131.7±16.5	0.865
DBP (mmHg)	72.9±10.8	72.5±11	73.4±10.7	0.039	73.5±11	73.4±10.8	0.841

	Total	Low PNI	High PNI	P	Matched Low	Matched High	P
Heart rate(bpm)	80.1±14.3	81.9±14.9	78.3±13.6	<0.001	79.8±14.3	79.8±13.9	0.943
Body temperature (° C)	36.6±0.5	36.5±0.6	36.6±0.5	0.023	36.6±0.6	36.6±0.5	0.806
Respiratory rate (bpm)	17.8±2.3	17.9±2.5	17.7±2.1	0.006	17.8±2.2	17.8±2.2	0.694
SPO2 (%)	97.7±2.1	97.7±2	97.7±2.1	0.591	97.7±2.1	97.7±1.9	0.933
Laboratory data at admission							
Creatinine (mg/dl)	1.1±1.3	1.3±1.5	1±1	<0.001	1.1±1.3	1.1±1.1	0.804
Hb (g/dl)	13±2.1	12.3±2.1	13.6±1.9	<0.001	12.8±2	13.3±1.9	<0.001
K (mmol/l)	3.8±0.5	3.8±0.6	3.7±0.5	0.020	3.8±0.5	3.8±0.5	0.876
Na (mmol/l)	137.2±3.8	136.7±4.2	137.7±3.1	<0.001	137.4±3.5	137.3±3.3	0.587
BUN (mg/dl)	18.3±12.1	19.5±13.5	17±10.4	<0.001	17.8±11.4	17.9±11.9	0.779
RBC (10*6/μl)	4.3±0.8	4.1±0.8	4.5±0.7	<0.001	4.3±0.7	4.3±0.7	0.291
RDW (%)	14.1±1.7	14.4±1.9	13.8±1.3	<0.001	14.2±1.7	13.9±1.4	<0.001
Hba1c (%)	6.3±1.1	6.2±1.1	6.3±1	0.246	6.3±1.1	6.3±1	0.647
Albumin (g/dl)	3.4±0.5	3.2±0.4	3.7±0.4	<0.001	3.2±0.4	3.7±0.4	<0.001
Platelet (10*3/μl)	208.5±79.8	199.7±85.9	217.2±72.2	<0.001	206.5±85	211.3±74	0.217
WBC (10*3/μl)	10.1±4.8	10.2±5.1	10±4.5	0.420	10.5±5.3	9.8±4.3	0.001
Lymphocyte (%)	19.6±11.9	13.3±8.6	25.9±11.4	<0.001	13.3±8.2	25.9±11.4	<0.001
Charlson Comorbidity Index	1.9±2.6	2.3±2.9	1.6±2.3	<0.001	2±3	2±2	0.514
Medical history							
Antihypertension treatment, n (%)	795(33.1%)	443(36.9%)	352(29.3%)	<0.001	282(33.4%)	293(34.7%)	0.572
Lipid-lowering treatment, n (%)	331(13.8%)	175(14.6%)	156(13%)	0.261	120(14.2%)	123(14.6%)	0.835
Non-insulin antihyperglycemic treatment, n (%)	281(11.7%)	157(13.1%)	124(10.3%)	0.036	90(10.7%)	96(11.4%)	0.641
Insulin treatment, n (%)	125(5.2%)	80(6.7%)	45(3.7%)	0.001	36(4.3%)	40(4.7%)	0.639
NG insertion during admission, n (%)	409(17%)	211(17.6%)	198(16.5%)	0.480	140(16.6%)	133(15.7%)	0.644
Propensity score	0.5±0.2	0.4±0.2	0.6±0.2	<0.001	0.5±0.1	0.5±0.1	0.962

Data are presented as mean ± SD, n, median [IQR], or n (%). BMI, body mass index; GCS, Glasgow Coma Scale; SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO2, percutaneous oxygen saturation; RBC, red blood cells; Hb, hemoglobin; WBC, white blood cell; RDW, red blood cell distribution width; BUN, blood urea nitrogen; SD, standard deviation; IQR, interquartile range.

Among the 2402 patients included in the present study. There were 1201 (50%) in the low PNI group and 1201(50%) in the high PNI group. The study population was 59.1 % male, and the mean age at diagnosis was 64 years. Before propensity-score matching, spontaneous ICH patients with PNI < 42.77 had lower levels of BMI (P = 0.004), GCS scales (P < 0.001), diastolic blood pressure (P=0.039), body temperature P=0.023), Hb (P < 0.001), Na (P < 0.001), RBC (P < 0.001) , albumin (P < 0.001),

platelet (P < 0.001), and lymphocyte counts (P < 0.001) ; higher levels of ages (P < 0.001), systolic blood pressure (P < 0.001), heart rate (P < 0.001), respiratory rate(P=0.006), creatine (P < 0.001),K (P =0.02), blood urea nitrogen (P < 0.001), red blood cell distribution width (P < 0.001), Charlson Comorbidity Index (P < 0.001), antihypertension treatment (P < 0.001), non-insulin antihyperglycemic treatment (P = 0.036), and insulin treatment (P =0.001). After that, we performed a propensity score matching analysis which divided into a low PNI group (n = 845) and a high PNI group (n = 845). All covariates were well balanced. BMI, GCS, Hb, RDW, albumin, WBC, and lymphocyte counts had statistically significant differences between the low PNI group and the high PNI group (Table 1).

3.2. Association between PNI and in-Hospital Complication

In this study, the patients were subdivided into the following two groups according to the PNI value: < 42.77 (n=1201) and ≥42.77 (n=1201). The reference value for PNI was chosen as the median value, that is, 42.77 (OR=1). Table 2 shows the association between PNI and in-hospital complication. A univariate logistic regression analysis demonstrated that patients in the high PNI group were significantly associated with a reduced risk of in-hospital complications (OR for the high group: 0.64; 95% CI 0.53-0.77; P < 0.001). In other words, the individuals in the high PNI group had a 0.64-fold lower risk of in-hospital complications in the crude logistic regression model. Similar results were also found in multivariate logistic regression and after analysis of propensity-score matching. When we included PNI as a categorical variable in the multivariate analysis, PNI levels were associated with in-hospital complication. (odds ratio, 0.69 ; 95% confidence interval, 0.55–0.87; P = 0.002).The odds ratio of in-hospital complications after propensity-score matching analysis was 0.74 (95% CI 0.58–0.94; p-value = 0.013) (Table 2). We observed a significant association between PNI value and risk of in-hospital complications before and after propensity score-matched analysis.

Table 2. Univariate and multivariate analyses of in-hospital complication in the PNI group using before and after propensity score-matched datasets.

	Univariate Analysis		Multivariate Analysis		Propensity Score Match Analysis	
	crude OR (95% CI)	P-value	adjusted OR (95% CI)	P-value	PSM OR (95% CI)	P-value
Overall complication						
PNI < 42.77	1(reference)		1(reference)		1(reference)	
PNI ≥ 42.77	0.64(0.53,0.77)	<0.001	0.69(0.55,0.87)	0.002	0.74(0.58,0.94)	0.013

PSM propensity score matching, OR odds ratio, CI confidence interval.

Restricted cubic spline analyses illustrate the shapes of the multivariate association between the PNI and in-hospital complications in the single-center study. An elevated risk of complications was observed with decreasing PNI levels (Figure 2)
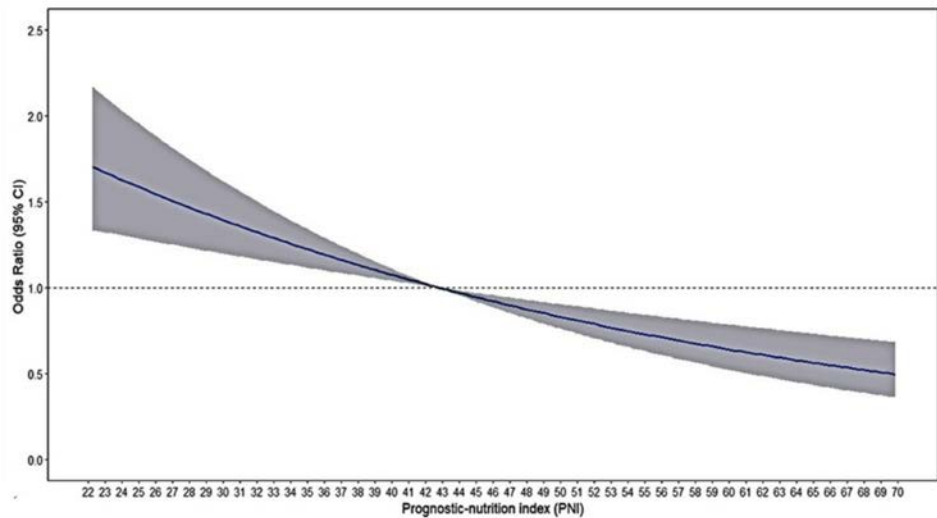
Figure 2. Association between levels of PNI and in-hospital complication using a restricted cubic spline regression model in the total population. The odds ratio (OR) is represented by the solid line, and the 95% confidence interval (CI) by the shaded area.

3.3. Association between PNI and 28- and 90-Day Mortality

We performed a Cox regression analysis to explore the association between PNI and mortality in patients with spontaneous ICH. The results, presented in Table 3, revealed that the PNI serves as an independent predictor of 28- and 90-day mortality in spontaneous ICH patients. In the unadjusted model, the hazard ratio for the high group (PNI ≥ 42.77) was 0.46 (95% CI: 0.36-0.59) and 0.45 (95% CI: 0.35-0.57), respectively, that is, the decreased PNI (PNI < 42.77) was significantly associated with an increased incidence of 30-day and 90-day mortality. After adjustment was made, the hazard ratio (of 30-day and 90-day mortality for the high group) was 0.72 (95% CI: 0.55-0.94) and 0.72 (95% CI: 0.56-0.93), respectively, compared to the lower group. In the multivariate logistic regression analysis after PSM, the HR (of 30-day and 90-day mortality) of the PNI ≥ 42.77 group was 0.71 (95% CI: 0.52-0.98) and 0.69 (95% CI: 0.51-0.94), respectively. (Table 3).

Table 3. Univariate and multivariate Cox proportional hazards regression analysis of PNI level affecting overall survival before and after propensity scores matching.

	Univariate Analysis		Multivariate Analysis		Propensity Score Match Analysis	
	crude HR(95% CI)	P-value	adjusted HR(95% CI)	P-value	PSM HR(95% CI)	P-value
28-day mortality						
PNI<42.77	1(reference)		1(reference)		1(reference)	
PNI≥42.77	0.46(0.36,0.59)	<0.001	0.72(0.55,0.94)	0.015	0.71(0.52,0.98)	0.039
90-day mortality						
PNI<42.77	1(reference)		1(reference)		1(reference)	
PNI≥42.77	0.45(0.35,0.57)	<0.001	0.72(0.56,0.93)	0.011	0.69(0.51,0.94)	0.020

PSM propensity score matching: was a multivariateregression model , HR hazard ratio, CI confidence interval.

We further examined the crude hazard ratio (HR) for 90-day mortality by treating the PNI as a continuous variable, utilizing restricted cubic spline analysis in the Cox model, as shown in Figure 3. The figure illustrates that the increased PNI level,the restricted cubic spline curve showed the trend of monotonic decrease in the risk of 90-days all-cause mortality.
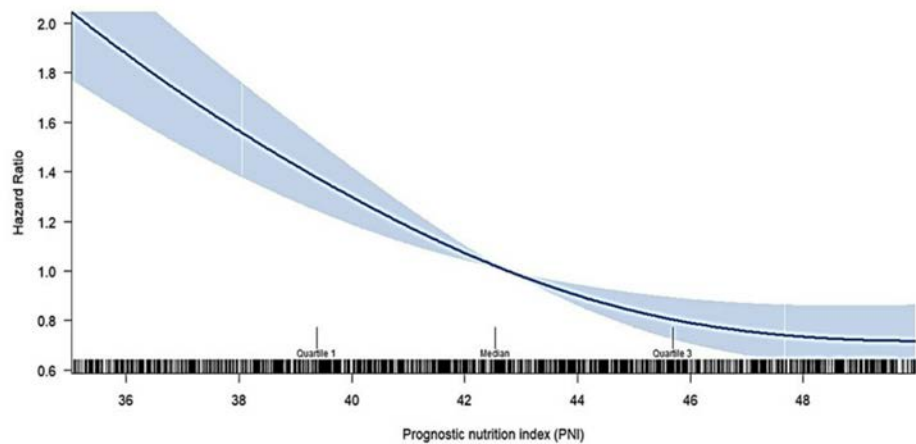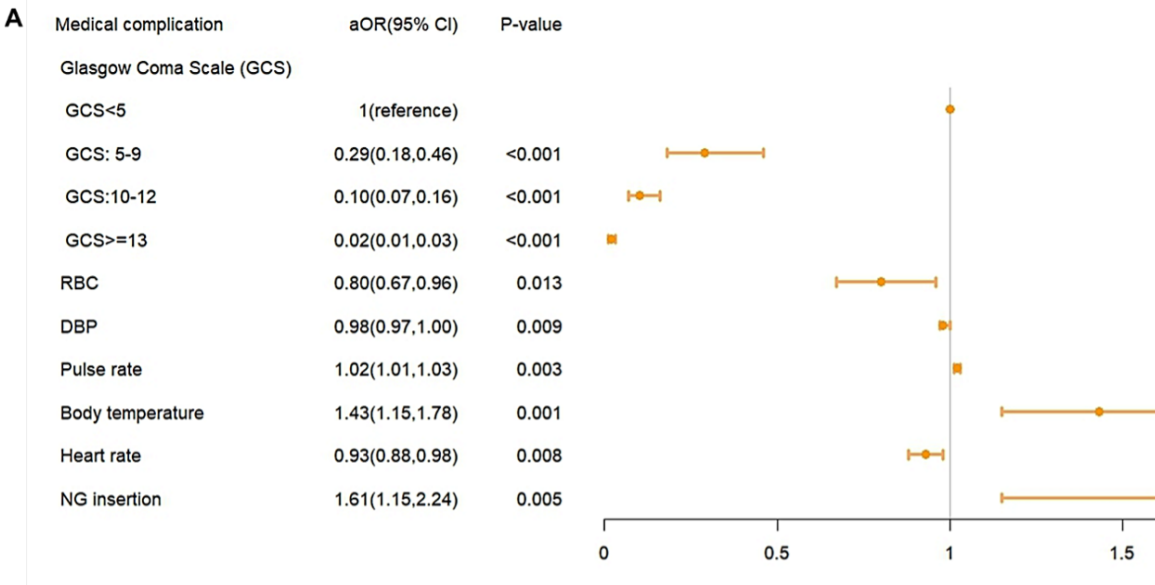

Figure 3. Association between PNI and the risk of 90-days all-cause mortality using a restricted cubic spline regression model in the total population. The hazard ratios (HR) are represented by the solid line and the 95% confidence interval (CI) by the shaded area.

3.4. Risk Factor for In-Hospital Complication and 28- and 90-Day Mortality

In the analysis of risk factors, a higher pulse rate, a higher body temperature, and NG insertion were shown to have a higher risk of in-hospital complications (Figure 4A).Higher GCS level of GCS, RBC, DBP and heart rate were shown to have a lower risk of in-hospital complications. In the risk factor for mortality risk, old age, higher creatine level, and higher pulse rate were shown to have higher mortality risk. A higher level of GCS, SDP, DBP, SPO2 were shown to have a lower risk of mortality. (Figure 4B, Figure 4C).

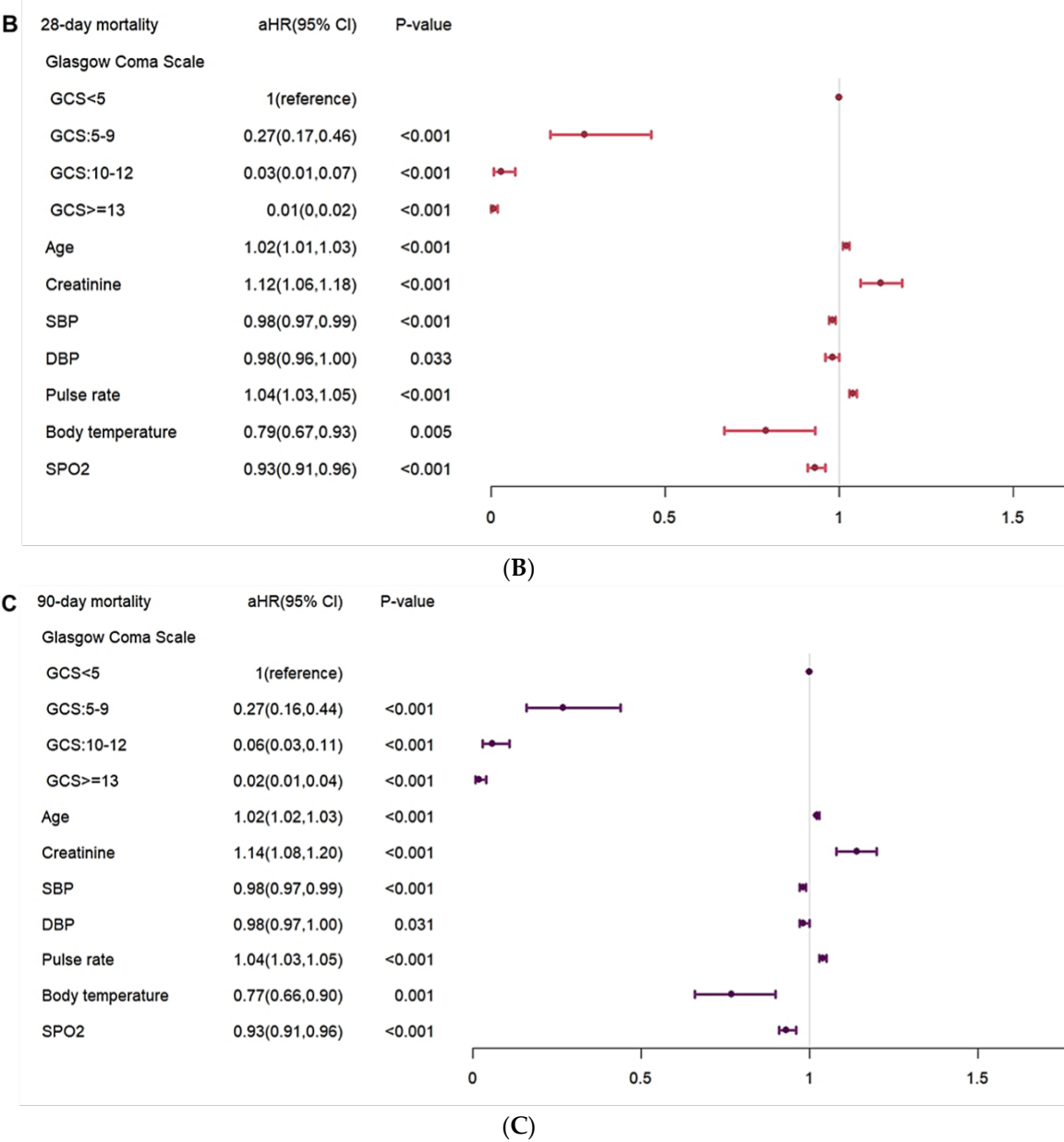| A	Medical complication	aOR(95% CI)	P-value
	Glasgow Coma Scale (GCS)		
	GCS<5	1(reference)	
	GCS: 5-9	0.29(0.18,0.46)	<0.001
	GCS:10-12	0.10(0.07,0.16)	<0.001
	GCS>=13	0.02(0.01,0.03)	<0.001
	RBC	0.80(0.67,0.96)	0.013
	DBP	0.98(0.97,1.00)	0.009
	Pulse rate	1.02(1.01,1.03)	0.003
	Body temperature	1.43(1.15,1.78)	0.001
	Heart rate	0.93(0.88,0.98)	0.008
	NG insertion	1.61(1.15,2.24)	0.005

(A)

Figure 4. The significant risk factor for (A) medical complication, (B)28-day mortality, and (C) 90-day mortality. GCS, Glasgow Coma Scale ;DBP, diastolic blood pressure; SBP, systolic blood pressure; SpO2, percutaneous oxygen saturation; RBC, red blood cells.

3.5. Predictive Value of PNI for 90-Day Mortality in Patients with Spontaneous ICH

In the results of a Kaplan-Meier survival curve analysis, the study population was divided into a high PNI group ($\geq$ 42.77) and a low PNI group (< 42.77) showing that the mortality at 90 days of all causes in the low PNI group was significantly higher than in the high group (log-rank P<0.001; Figure 5).
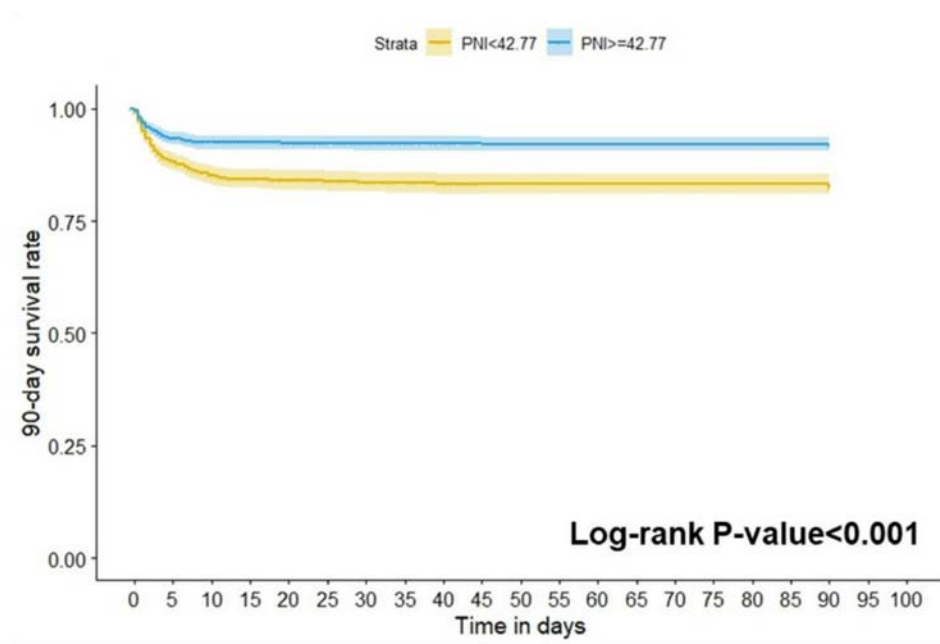
Figure 5. Kaplan-Meier curve for 90-day mortality in relation to PNI estimated using restricted cubic spline models. The survival curve is represented by the solid line and the 95% confidence interval (CI) by the shaded area.

The value of PNI for predicting in-hospital complications, 28-day and 90-day mortality in patients with spontaneous ICH was analyzed using the ROC curve. As shown in the ROC curve, PNI had a good ability to predict in-hospital complications in patients with ICH with an AUC of 0.575 (95% CI: 0.547–0.604) (Figure 6A).Furthermore, the time-dependent ROC curve for the prediction of mortality at 28- and 90-day mortality and the AUC value of PNI in all patients was 0.637(95% CI: 0.597-0.676) and 0.645 (95% CI: 0.607-0.683) respectively (Figure 6B and Figure 6C). The above results showed that PNI was a valuable predictive biomarker of the risk of in-hospital complication, 28-day and 90-day mortality in patients with spontaneous ICH.

As shown in the ROC curve, PNI had a good ability to predict in-hospital complications in patients with ICH with an AUC of 0.575 (95% CI: 0.547–0.604) (Figure 5A). The AUC for the PNI to predict 28-day and 90-day mortality was 0.637 (95% CI: 0.597–0.676, Figure 5B), 0.645 (95% CI: 0.607–0.683, Figure 5C), respectively.
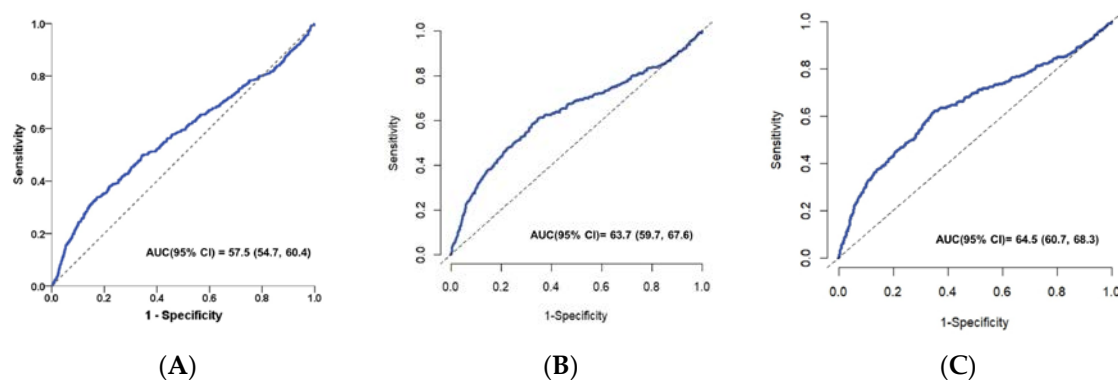

| (A) | (B) | (C) |

Figure 6. (A) Receiver operating characteristics curve (ROC) of the PNI for prediction of in-hospital complications. (B) Time-dependent ROC curve for prediction of mortality at 28-day. (C) Time-dependent ROC curve for prediction of mortality at 90-day.

4. Discussion

To the best of our knowledge, this is the first study to compare all-cause in-hospital complications and 28- and 90-day mortality between high and low PNI groups with spontaneous ICH patients. In our study, propensity score matching (PSM) was carried out to adjust for an imbalance of clinical parameters with a p-value of <0.05 in the multivariate analysis to reduce the interference of confounders with survival outcomes. The main finding of our study is that a low PNI score at admission was independently associated with a poor ICH outcome. After intracerebral hemorrhage, neuroinflammation plays a significant role in causing damage to brain tissue[14–16] and downregulates the immune system, which may result in immunodepression [15–18]. Recent evidence showed that post-ICH neuroinflammation is a major contributor to secondary-induced brain damage and is often associated with a poor clinical prognosis [17,18]. In recent decades, blood-based biomarkers upon admission have demonstrated substantial promise for the diagnosis and prognosis of ICH[10,14,19–21]. Stroke-induced immunosuppression decreases immune capacity as lymphocyte numbers reduce, which increases the risk of infection and is strongly associated with an unfavorable functional outcome[22,23]. Another study reported that ICH patients with lower lymphocyte counts are associated with poor outcomes[21].Furthermore, malnutrition is associated with impaired immunological function and can increase the risk of infections and mortality in critically ill patient[24,25]. Previous reports suggested a relationship between hypoalbuminemia and increased mortality in patients with ICH[8,9]. Rui et al. showed that a poor outcome ICH group had worse nutritional and inflammatory status[21]. Thus, the prognosis of patients with ICH is related not only to inflammation levels, but also to nutritional status. Consequently, PNI combined with serum albumin and lymphocytes can well predict the efficacy of spontaneous ICH and it can be easily calculated from parameters that are routinely measured in blood parameters at admission.

In this study, we confirmed that the PNI score was an independent biomarker to predict complications and overall survival in spontaneous ICH patients. Our study showed that a low PNI score was associated with a higher risk of in-hospital complication, 28-day and 90-day mortality. We first used univariate logistic analysis to investigate the association between in-hospital complications and PNI as categorical variable with a median value of 42.77(OR=1) and PNI ≥ 42.77 was significantly associated with a reduced risk of in-hospital complications (OR = 0.64; 95% CI 0.53-0.77; P < 0.001). We then performed a multivariate logistic regression analysis to further explore the association between in-hospital complications and PNI. In a similar way, the results revealed PNI ≥ 42.77 to be an independent decrease risk for in-hospital complications (OR = 0.69, 95% CI: 0.55-0.87, P = 0.002). To eliminate potential residual confounding variables, we subsequently performed PSM analysis to further identify the relationship between in-hospital complication and PNI using multivariate logistic regression analyses. After matching, the results revealed that the low PNI group was significantly associated with in-hospital complications. Its significant finding was that PNI was an independent predictor of complications, 30- and 90-day mortality among patients with spontaneous ICH.

In the present study, a low GCS level, anemia, low blood pressure, high fever, and NG insertion have been shown to have a higher risk of in-hospital complications. Langmore et al. identified the need for tube feeding as a predictor of pneumonia, because patients who cannot tolerate oral feeding due to impaired consciousness or severe dysphagia.[26–28].One meta-analysis showed that anemia at admission was associated with increased mortality and an increased risk of poor outcomes in patients with ICH[29]. Schwarz S report that the incidence of fever in patients with hemorrhagic stroke is high and the duration of fever is associated with poor outcome[30]. The findings of our study are consistent with the previous literature.

Based on the findings of the study, it is important to take action to minimize the nutritional and immune decline of ICH patients. Early identification of potentially modified risk factors can provide an alternative approach to reduce the risk of complications and improve the outcome. PNI scores can better reflect the balance between nutrition and inflammation than single markers.

We identified some limitations in our study: First, this is a retrospective cohort study conducted in a single center, which leads to inevitable selection bias. In this regard, we adjusted various variables to enhance the accuracy of the results. More validation through prospective multicenter

studies is necessary to corroborate our findings. Second, the PNI was evaluated only at admission, neglecting the changes in the laboratory over time. The potential of dynamic PNI to predict the poor prognosis of spontaneous ICH patients requires further exploration. Third, since our study was confined to Taiwan, the generalizability of our results to other populations remains uncertain. Future research conducted in different countries is essential to validate our conclusions.

5. Conclusions

This retrospective study revealed that PNI may be valuable markers to predict the outcomes of patients with spontaneous ICH.

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