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The predictive value of the CONUT score combined with the A²DS² scale for post-ischemic stroke infection

Vrednost skora CONUT u kombinaciji sa skalom A²DS² za predikciju infekcije posle ishemijskog moždanog udara

Yongqing Zhang, Wei Zhang, Yiwu Zhou

Sichuan University, West China Hospital, Department of Emergency Medicine, Emergency Medical Laboratory, Chengdu, Sichuan, China

Abstract

Background/Aim. Stroke-associated infection is the most common and most serious complication of ischemic stroke (IS), which is the most important cause of death and disability in humans. The aim of the study was to determine the predictive value of nutrition risk score – Controlling Nutritional Status (CONUT) combined with Age, Atrial Fibrillation, Dysphagia, Sex, Stroke Severity (A²DS²) scale for post-IS infection (PISI) in IS patients. **Methods.** This retrospective study analyzed the clinical data of 333 IS patients admitted to the Emergency Department of West China Hospital of Sichuan University from December 2017 to April 2019. Patients were divided into the No-PISI group (244 cases) and the PISI group (89 cases) based on whether they had a PISI. Multivariate logistic regression analysis was used to identify independent risk factors for PISI. Receiver operating characteristic (ROC) curve analysis was used to evaluate the accuracy of different variables in predicting the outcome. **Results.** Multivariable logistic regression analysis showed that the CONUT score [odds ratio (OR) = 1.321, 95% confidence interval (CI): 1.040–1.677, $p < 0.05$] and age (OR = 1.026, 95%CI: 1.004–1.048, $p < 0.05$) were independent influencing factors for PISI. With the increase of the CONUT score, the proportion of PISI increased. Area under the ROC curve for predicting PISI was 0.651, 0.696, and 0.725 for CONUT, A²DS², and CONUT plus A²DS², respectively. **Conclusion.** Combining the CONUT score and A²DS² scale enhances their predictability of PISI, thereby serving as a valuable tool for early risk assessment and clinical intervention.

Key words:
age factors; infections; nutritional status; prognosis; risk factors; stroke.

Apstrakt

Uvod/Cilj. Infekcija povezana sa moždanim udarom je najčešća i najozbiljnija komplikacija ishemijskog moždanog udara (IMU), koji je najvažniji uzrok smrti i invalidnosti kod ljudi. Cilj rada bio je da se utvrdi vrednost skora nutritivnog rizika – kombinacije skora *Controlling Nutritional Status* (CONUT) i skale *Age, Atrial Fibrillation, Dysphagia, Sex, Stroke Severity* (A²DS²) za predikciju infekcije posle IMU (IPIMU) kod bolesnika sa IMU. **Metode.** Ovom retrospektivnom studijom analizirani su podaci 333 bolesnika sa IMU, primljenih na Odeljenje hitne pomoći Zapadnokineske bolnice Univerziteta Sičuan od decembra 2017. do aprila 2019. godine. Bolesnici su bili podeljeni na osnovu toga da li su imali ili ne IPIMU u dve grupe: grupu bez-IPIMU (244 bolesnika) i grupu IPIMU (89 bolesnika). Za identifikaciju nezavisnih faktora rizika od IPIMU, korišćena je multivarijantna logistička regresiona analiza. Za procenu tačnosti različitih varijabli u predviđanju ishoda, korišćena je analiza *receiver operating characteristic* (ROC) krive. **Rezultati.** Multivarijantna logistička regresiona analiza pokazala je da su skor CONUT [*odds ratio* (OR) = 1,321, 95% interval poverenja (IP): 1,040–1,677, $p < 0,05$] i životno doba (OR=1,026, 95% IP: 1,004–1,048, $p < 0,05$) bili nezavisni faktori koji su uticali na IPIMU. Sa porastom CONUT skora, proporcija IPIMU se povećavala. Površina ispod ROC krive za predikciju IPIMU iznosila je 0,651, 0,696 i 0,725 za CONUT skor, A²DS² skalu i CONUT skor sa A²DS² skalom, redom. **Zaključak.** Kombinovanje skora CONUT i skale A²DS² povećava njihovu prediktabilnost IPIMU, i služi kao dragoceno sredstvo za ranu procenu rizika i kliničko delovanje.

Ključne reči:
životno doba, faktor; infekcija; nutritivni status; prognoza; faktori rizika; moždani udar.

Correspondence to: Yiwu Zhou, Sichuan University, West China Hospital, Department of Emergency Medicine, Emergency Medical Laboratory, No.37 Guoxue Road, Chengdu, Sichuan 610041, China. E-mail: 456zyw@163.com

Introduction

Stroke is a neurologic dysfunction caused by acute focal injury of the central nervous system due to vascular reasons. It currently ranks second among global human causes of death and is the leading cause in China [1, 2]. Ischemic stroke (IS) is the most important cause of human death and disability, with stroke-associated infection (SAI) being the most common and most serious complication, occurring at a rate of 23%–65% [3]. Research has shown that post-stroke infection (PSI) is an important factor that affects the recovery and mortality of stroke patients; hence, early diagnosis is crucial [4]. Pneumonia and urinary tract infections are common after IS. They are difficult to control clinically and often lead to rapid deterioration or even death of patients, thus seriously affecting early control and functional recovery of stroke patients, bringing a heavy economic burden to families and society [5]. It has become a major clinical problem that urgently needs to be solved in the field of cerebrovascular disease.

Currently, there have been studies on the Age, Atrial Fibrillation, Dysphagia, Sex, Stroke Severity (A^2DS^2) scale for predicting PSI, but the sensitivity and specificity of the prediction are unsatisfactory [6, 7]. Therefore, there is a lack of accurate early predictive indicators and effective prevention and treatment strategies for PSI, such as prophylactic antibiotics, prevention of aspiration, and management of the respiratory tract. These measures have been proven to be ineffective in reducing the incidence of PSI and improving the clinical prognosis of PSI patients. Therefore, exploring early specific warning diagnostic factors for PSI can achieve early clinical intervention and treatment and reduce the mortality and disability caused by stroke.

Malnutrition-related diseases are the most common challenge in healthcare, whether in developed or developing countries. The relationship between nutritional status and prognosis of cardiovascular disease patients has increasingly gained interest among scholars. The Controlling Nutritional Status (CONUT) score, proposed by Ignacio et al. [8] in 2005, is a new nutritional assessment system that comprehensively evaluates patients' nutritional and immune status based on serum albumin concentration, total lymphocyte count, and total cholesterol concentration. The CONUT score is the most effective method among various nutritional assessment indicators and can assist in evaluating patients' nutritional status during hospitalization. Previous studies have shown that CONUT is associated with the prognosis of various malignancies [9–11], but there are few reports on its application in predicting infections after IS. Therefore, the aim of the study was to evaluate the predictive value of the CONUT score combined with the A^2DS^2 scale for post-IS infection (PISI) in IS patients.

Methods

Patients

This retrospective observational study included a total of 333 patients (216 males and 117 females) diagnosed with IS and admitted to the Emergency Department of the West China Hospital of Sichuan University between December 2017 and April 2019. The study was approved by the Ethics Committee of West China Hospital of Sichuan University and the Ethics Committee of the Wuhan Red Cross Hospital of Hubei Province (No. 1175, 2021).

The inclusion criteria for the study were age ≥ 18 years, onset time < 12 hrs and the patients had to meet the diagnostic criteria for acute IS in the "Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke 2018" formulated by the Neurology Branch of the Chinese Medical Association in 2018 [12]. The exclusion criteria (one must be met) were as follows: concurrent infectious diseases before admission; recent use of steroids or long-term use of immunosuppressive agents; incomplete clinical data or laboratory data; previous blood system diseases; history of severe trauma or surgery within one month; patients with a history of ischemic or hemorrhagic cerebrovascular disease and residual sequelae; patients who refuse to participate in this study.

Data

General clinical data of the study subjects, such as gender, age, hypertension, diabetes mellitus, heart rate, blood pressure, and body temperature, were collected through follow-up and electronic medical records. Laboratory indicators on admission (within 2 hrs) were collected, and the A^2DS^2 score and the CONUT score were calculated.

After providing institutional review board approval at each institution, written informed consent was obtained from each patient or the patient's legally authorized guardian before conducting study-specific procedures.

Score scales

The A^2DS^2 score scale was proposed by Hofmann et al. [13] and assesses the risk of early-onset pneumonia in patients with acute IS based on age, atrial fibrillation, dysphagia, sex, and stroke severity. The sensitivity and specificity of the Hoffmann scale in China are 69% and 73%, respectively, with a total score of 10 points. Scores of 0–4 indicate low risk, while scores of 5–10 indicate high risk.

Reference for the CONUT score standard was as follows: serum albumin levels of 3.5–4.5 g/dL, 3.0–3.49 g/dL, 2.5–2.9 g/dL, and < 2.5 g/dL are assigned scores of 0, 2, 4, and 6 points, respectively. Serum total cholesterol levels of > 180 mg/dL, 140–180 mg/dL, 100–139 mg/dL, and < 100 mg/dL are assigned scores of 0, 1, 2, and 3 points, respectively. Peripheral blood total lymphocyte counts of > 1,600 $\times 10^3$/mL, 1,200–1,599 $\times 10^3$/mL, 800–1,199 $\times 10^3$/mL, and < 800 $\times 10^3$/mL are assigned scores of 0, 1, 2, and 3 points, respectively. The sum of these three items is the CONUT score. Scores of 0–1 indicate normal nutritional status, scores of 2–4 indicate mild malnutrition, scores of 5–8 indicate moderate malnutrition, and scores of 9–12 indicate severe malnutrition.

Definition of outcomes and grouping

The main indicator observed in this study is PSI, also known as SAI [14]. This refers to an infection that occurs within seven days of stroke onset in patients who did not have any symptoms of infection or were not, at the time of stroke, in the latent period of infection, such as pulmonary or urinary tract infections or fever of unknown origin. Patients were divided into two groups based on whether they had a PISI: No-PISI group, with 244 patients, and the PISI group, with 89 patients. Baseline data and clinical indicators were compared among the two groups of patients. Finally, independent risk factors for PISI were screened through multivariate analysis.

Statistical analysis

Statistical analysis was performed using SPSS 26.0 software. Normally distributed continuous variables were expressed as mean ± standard deviation, while non-normally distributed continuous variables were expressed as median and interquartile range. Group comparisons were performed using analysis of variance (for normally distributed data) or the Mann-Whitney *U* test (for non-normally distributed data). Categorical variables were expressed as frequency (percentage) and compared using a Chi-square test. Receiver operating characteristic (ROC) curve analysis was used to evaluate the accuracy of different variables in predicting the outcome. Multivariate logistic regression analysis was used to identify independent risk factors for PISI. A *p*-value < 0.05 was considered statistically significant.

Results

The average age in the No-PISI group was 63 years, while in the PISI group, it was 68. The male proportion in the No-PISI group was 64.8%, while it was 65.2% in the PISI group. The study found that hemoglobin, albumin, and absolute lymphocyte count were significantly higher in the No-PISI group compared with the PISI group (141 g/L vs. 138 g/L, 43.2 g/L vs. 40.6 g/L, 1.66 $\times 10^9$/L vs. 1.26 $\times 10^9$/L, respectively). On the other hand, white blood cell count, total bilirubin, A^2DS^2, and CONUT were significantly higher in the PISI than in the No-PISI group (6.72 $\times 10^9$/L vs. 7.82 $\times 10^9$/L, 12.7 ± 5.85 μmol/L vs. 14.5 ± 7.22 μmol/L, 3.0 ± 2.0 vs. 5.0 ± 2.00, 1.00 vs. 2.00), as shown in Table 1.

After adjusting for potential confounding factors, multifactor logistic regression analysis revealed that the CONUT score and age were independent variables significantly associated with PISI, as shown in Table 2.

The ROC curve analysis showed that the area under the curve (AUC) for predicting PISI was 0.651, 0.696, and 0.725 for CONUT, A^2DS^2, and CONUT plus A^2DS^2, respectively. The combined prediction of CONUT plus A^2DS^2 had a larger

Table 1

Baseline characteristics of included patients with and without post-ischemic stroke infection (PISI)

Characteristic	Group		*p*
	No-PISI (n = 244)	PISI (n = 89)	
Age, years	63.0 (51.0–72.0)	68.0 (59.0–78.0)	0.001
Male gender	158 (64.8)	58 (65.2)	0.997
Body mass index, kg/m²	24.3 ± 3.1	23.1 ± 3.3	0.015
Drinking	70 (28.7)	31 (34.8)	0.345
Smoking	111 (45.5)	41 (46.1)	0.998
Hypertension	150 (61.5)	48 (53.9)	0.265
Diabetes	52 (21.3)	29 (32.6)	0.048
Admission vital signs			
systolic blood pressure, mmHg	85.0 (76.0–97.0)	85.0 (75.0–100)	0.556
diastolic blood pressure, mmHg	78.0 (67.0–87.0)	81.0 (68.0–93.0)	0.294
temperature, °C	36.5 (36.3–36.6)	36.5 (36.3–36.7)	0.009
heart rate, beats/min	20.0 (19.0–20.0)	20.0 (19.0–20.0)	0.329
Hemoglobin, g/L	141 (129–152)	138 (122–146)	0.015
Albumin, mmol/L	43.2 (40.9–45.2)	40.6 (36.2–43.1)	< 0.001
White blood cell count, $\times 10^9$/L	6.72 (5.68–8.07)	7.82 (6.50–9.84)	< 0.001
Absolute lymphocyte count, $\times 10^9$/L	1.66 (1.25–2.12)	1.26 (0.94–1.75)	< 0.001
Absolute neutrophil count, $\times 10^9$/L	4.31 (3.34–5.79)	5.95 (4.43–7.76)	< 0.001
Low-density lipoprotein, mmol/L	2.42 (1.88–3.04)	2.32 (1.83–2.83)	0.323
High-density lipoprotein, mmol/L	1.21 (0.97–1.43)	1.12 (0.92–1.43)	0.217
Triglycerides, mmol/L	1.76 ± 1.39	1.47 ± 1.06	0.054
Alanine aminotransferase, U/L	25.8 ± 17.8	28.9 ± 38.4	0.473
Aspartate aminotransferase, U/L	21.0 (17.0–27.0)	23.0 (17.5–31.5)	0.060
Creatinine, μmol/L	73.0 (61.0–87.0)	76.0 (62.5–97.0)	0.390
Urea nitrogen, mmol/L	5.10 (4.20–6.40)	5.60 (3.95–6.75)	0.335
Total bilirubin, μmol/L	12.7 ± 5.85	14.5 ± 7.22	0.036
A^2DS^2 scale	3.0 ± 2.0	5.0 ± 2.00	< 0.001
CONUT	1.00 (0.00–2.00)	2.00 (1.00–3.00)	< 0.001

A^2DS^2 – Age, Atrial fibrillation, Dysphagia, Sex, Stroke Severity; CONUT – Controlling Nutritional Status. Values are given as mean ± standard deviation, mean (minimum-maximum), or numbers (percentages).

AUC than CONUT and A^2DS^2 alone (Figure 1). Through the decision curve analysis of CONUT, A^2DS^2, and COUNT plus A^2DS^2, it can be found that the net return rate of all factors is greater than 0 during a certain risk threshold. The results showed that three factors had a certain impact on the outcome of PISI, and COUNT plus A^2DS^2 had the best benefit (Figure 2).

Table 2

Logistic regression analysis of influencing factors of post-ischemic stroke infection

Factor	Univariate			Multifactor		
	OR	95% CI	*p*	OR	95% CI	*p*
CONUT	1.517	1.278–1.799	< 0.001	1.321	1.040–1.677	0.023
Age	1.035	1.015–1.055	0.001	1.026	1.004–1.048	0.018
White blood cell count	1.246	1.120–1.385	< 0.001	0.999	0.996–1.003	0.790
Diabetes mellitus	1.785	1.041–3.059	0.035	0.588	0.319–1.083	0.089
Lymphocyte absolute value	1.353	1.205–1.519	< 0.001	0.740	0.416–1.316	0.305
Aspartate transaminase	1.384	1.241–1.601	< 0.001	1.020	0.999–1.041	0.057

CONUT – Controlling Nutritional Status. OR – odds ratio; CI – confidence interval.

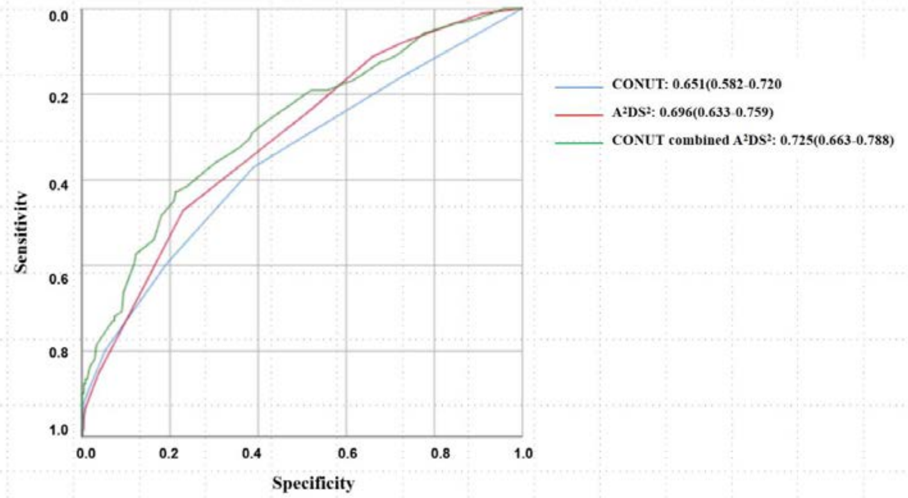

Fig. 1 – The receiver operating characteristic curve of nutritional risk score for post-ischemic stroke infection.
For abbreviations, see Table 1.

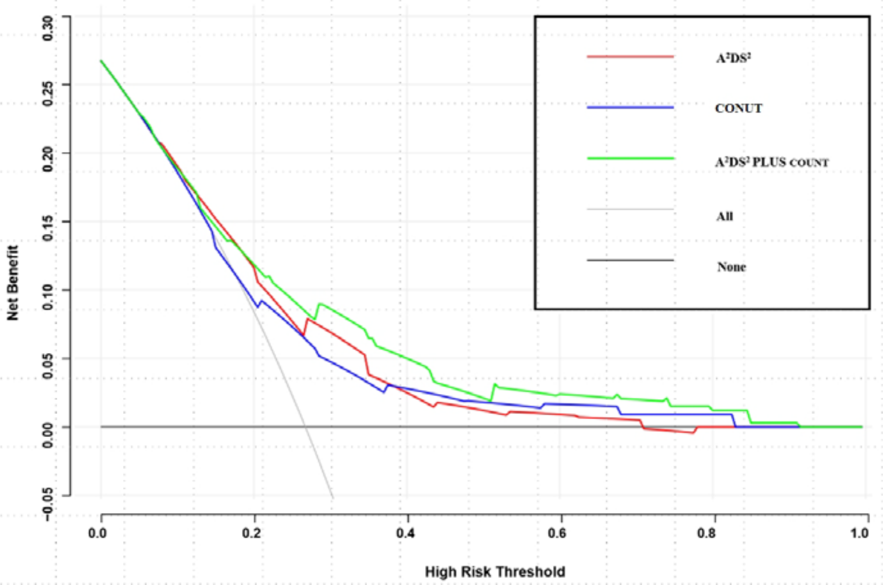

Fig. 2 – Decision curve analysis of nutritional risk score for post-ischemic stroke infection.
For abbreviations, see Table 1.

Discussion

Infection is a frequent complication during the early stages of a stroke, with reported rates ranging from 5–65%. However, discrepancies in patient demographics, study methodology, and infection definition may contribute to the wide range of reported rates [15–17]. Early prediction of PISI to guide clinical interventions can help reduce disability and mortality rates. The A^2DS^2 scale is one of the most widely used rankings and has been extensively used in the clinic [6]. Multivariate analysis was employed to identify the risk factors and assign scores for the A^2DS^2 scale [7, 18]. Different studies have reported different sensitivities and specificities, which may be related to race, incidence, study methodology, and optimal cut-off for the scale [19–21]. With the improvement of people's living standards, the impact of nutritional balance and supplementation on diseases has increasingly received attention from clinical doctors. Patients' nutritional status has attracted more and more attention in various clinical fields, and studies have shown that early nutritional support can improve the prognosis of stroke patients. The CONUT score is one of the tools for objectively evaluating nutritional status [22]. The score is calculated using three factors: serum albumin levels, white blood cell counts, and body mass index. Compared with the currently recognized subjective global assessment and Full Nutrition Assessment subjective nutritional evaluation tools, the CONUT score has high sensitivity and specificity, is easy to operate and popularize, and is suitable for early screening and dynamic monitoring of population nutrition [23, 24]. There are no studies that combine two scores to predict the occurrence of PISI.

The CONUT score has also been suggested as a tool to predict SAIs [25]. Several studies have investigated the use of the CONUT score in predicting the risk of infections following acute IS. A study investigated the relationship between nutritional scales and prognosis in elderly patients after acute IS [26]. The study included 218 patients and found that a lower CONUT score was significantly associated with an increased risk of pneumonia. The authors concluded that the CONUT score appeared to be more useful than Geriatric Nutritional Risk Index (UNR-GNRI) scores for predicting the prognosis of elderly patients with acute IS at discharge [26]. Our study also found that the CONUT score was more sensitive than the A^2DS^2 score in predicting the incidence of PISI. If the two scores are combined, they can increase the efficiency of predicting PISI. Another study indicated that a high CONUT score was associated with an increased risk of 90-day mortality in patients with pleural infection and can be considered for clinical evaluations in practice [27].

The limitation of the CONUT score is that the optimal cut-off values have not been established. Different studies have used different cut-off values, ranging from 4 to 6, and it is unclear which cut-off value is the most accurate in predicting infections [28, 29]. This lack of standardization makes it challenging for clinicians to use the score consistently across different patient populations [30]. Furthermore, the CONUT score may be less useful in patients with pre-existing conditions that affect their immune or nutritional status [31, 32]. For instance, patients with chronic kidney or liver disease may have abnormal serum albumin levels that do not accurately reflect their overall nutritional status [33, 34]. In these cases, the CONUT score may not provide an accurate prediction of the risk of infection, and clinical decision-making should consider additional factors beyond the CONUT score.

Despite these limitations, the CONUT score has potential as a tool for predicting SAIs. Future research should investigate whether incorporating additional laboratory markers into the score improves its predictive ability. Studies should also compare the accuracy of the CONUT score with other commonly used tools for predicting infections, such as the Glasgow Coma Scale and the National Institutes of Health Stroke Scale. Furthermore, additional research is needed to determine the optimal cut-off values for the CONUT score in different patient populations.

The A^2DS^2 scale is an effective tool for evaluating SAIs, but the CONUT score is also a potential tool for predicting SAIs, especially pneumonia. Combining both scoring tools improves their clinical predictive efficacy. Clinicians should consider additional factors beyond the CONUT score, particularly in patients with pre-existing conditions that affect their immune or nutritional status. Further research is needed to establish the clinical utility of the CONUT score in predicting infections and guiding clinical decision-making in patients with acute stroke.

Limitations of the study

The study had several limitations. First, this study is a retrospective observational study. Second, the sample size was quite small. Third and final, there was a lack of dynamic assessment of the CONUT score during hospitalization.

Conclusion

The study suggests that combining the CONUT score and A^2DS^2 scale enhances their predictability of post-ischemic stroke infection, thereby serving as a valuable tool for early risk assessment and clinical intervention.

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Availability of data and materials

The datasets used and/or analyzed in the present study are available from the corresponding author upon reasonable request.

Conflict of interest

The authors declare no conflict of interest.

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