Relationship Between Atrial Fibrillation and Controlling Nutritional Status Score in Acute Ischemic Stroke Patients

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ABSTRACT

Objective: To determine the relationship between nutritional status evaluated *via* the COntrolling NUTritional Status (CONUT) score and in-hospital mortality in acute ischemic stroke (AIS) patients.
Study Design: Observational study.
Place and Duration of Study: Department of Cardiology, University of Health Sciences, Sancaktepe Sehit Prof. Ilhan Varank Training and Research Hospital, Turkey, between September 2019 and January 2022.
Methodology: Four hundred and seventy-one consecutive patients with AIS (age 18–90 years) were retrospectively enrolled. Exclusion criteria were age under 18 years, changes in inflammatory or immune markers other than a cerebrovascular event (*e.g.*, autoimmune diseases, sepsis, trauma, recent major surgery, active malignancy), glomerular filtration rate <30 ml/min, severe hepatic failure, receiving thrombolytic therapy, paroxysmal atrial fibrillation (PAF), and pregnancy. After the exclusion of patients, 400 of cases were included in this study. The patients were divided into two groups: CONUT <2, group 1 included 262 patients; CONUT ≥2, group 2 included 138 patients. The presence of chronic AF and its relationship with CONUT were also evaluated.
Results: Group 2 (18, 12.3%) exhibited higher in-hospital mortality than group 1 (12, 4.7%), (p=0.006). In addition, group 2 had higher chronic AF rates. Chronic AF was an independent predictor of in-hospital mortality in group 2 (p= 0.026).
Conclusion: AIS patients with CONUT score>2 may have a greater in-hospital mortality. Chronic AF may be used as one of the predictors of in-hospital mortality in AIS patients with higher CONUT.

Key Words: *Malnutrition, Atrial fibrillation, Stroke.*

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INTRODUCTION

Stroke is the fifth leading group reason for death worldwide and the main reason for long-run incapacity leading to a world economic health burden.[1] Mortality and morbidity of acute ischemic stroke (AIS) have decreased in recent years as a result of developments in thrombolytic therapy and emergency interventional therapies. Atrial fibrillation (AF) is one of the most frequent arrhythmias and is related to an increased risk of stroke. Recent studies showed, that untreated or undertreated AF causes most of these strokes, which are often fatal or debilitating.[1,2]

Nutritional deficiency is common in AIS and is related to poor prognosis.[3] Malnutrition in AIS is related to dysphagia, senility, restricted upper extremity movement, visuospatial impairment, and poor mood.[4]

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Nutritional status screening applications are important to detect potential or manifest malnutrition in different clinical situations. Some nutritional status screening tools can be used to predict undernutrition in AIS patients like controlling nutritional status (CONUT), GNRI, MUST, NRS-2002, and ESPEN-DCM.[5] There is no clear consensus on how to screen for nutritional deficiency in this group of patients.

CONUT is calculated from albumin, lymphocyte, and total cholesterol levels, and indicates a nutritional deficiency.[6] Albumin helps account for the total protein level, while the total cholesterol represents the calorie intake, and the lymphocyte level dictates the immune response. The reduction in each of these three components is associated with high CONUT, which is an indicative of poor nutrition. CONUT displays both the inflammatory status and nutritional status and is an easy-to-use score for clinicians. CONUT was mostly studied in conjunction with malignancies and has been widely accepted as an accurate predictor for prognoses of patients with cancer.[7,8] A recent study has shown that nutritional status can be used to predict prognosis in patients with AIS.[9] Therefore, the aim of this study was to determine whether or not implementing CONUT at hospital admission might predict in-hospital prognosis and the presence of AF in patients with AIS.

METHODOLOGY

Between September 2019 and January 2022, 471 consecutive adult patients hospitalised, at the Department of Cardiology, University of Health Sciences, Sancaktepe Sehit Prof. Ilhan Varank Training and Research Hospital, Turkey, with the diagnosis of AIS and consulted with cardiology, were enrolled retrospectively. AIS was diagnosed as a new neurologic deficit lasting for at least 24 hours (h) with finding of cranial imaging (magnetic resonance imaging and/or computed tomography) scans. The national institutes of health stroke scale (NIHSS) was used to assess the severity of the stroke during admission to the hospital. Demographic characteristics of the study population were obtained from the hospital records. Exclusion criteria were age under 18 years, changes in inflammatory or immune markers other than a cerebrovascular event (*e.g.*, autoimmune diseases, sepsis, trauma, recent major surgery, active malignancy), glomerular filtration rate <30 ml/min, severe hepatic failure, receiving thrombolytic therapy, paroxysmal atrial fibrillation (PAF), and pregnancy.

After the exclusion of patients with incomplete data, a total of 400 cases were accepted for study. The patients were divided into 2 groups based on their CONUT (CONUT <2, g 1 *vs*. CONUT ≥2, g 2). The institutional review board approved the study (No. E-46059653-020/45). Informed consent were obtained from the patients.

Blood samples (fasting glucose level, cholesterol panel, total protein, albumin, renal function tests, and hemogram) were obtained at 24-hours intervals after the AIS. Fasting glucose level, cholesterol panel, total protein, albumin, and renal function tests were analysed in the central laboratory (Cobas 6000 Roche) while hemogram parameters were measured by an auto haematology analyser (BC6800 Mindray Medical Electronics Co. Shenzhen, China). CONUT was calculated according to the admission serum albumin level, total cholesterol level, and lymphocyte count. A decrease in lymphocyte counts and total cholesterol was assigned with 0, 1, 2, and 3 points, and the decrease in albumin was assigned with 0, 2, 4, and 6 points according to the severity.[6] Prognostic nutrition index (PNI) was calculated using the following equation: 10x serum albumin (g/dl) + 0.005 x total lymphocyte count (mm^3).[10]

All patients underwent 24-h rhythm Holter monitoring. During the recording, patients performed their normal daily activities. Continuous ECG recordings of 400 patients were obtained by experienced doctors using a 3-channel 24-h Holter system (SEER Light, GE Healthcare, Chicago, IL, USA). The definition of AF was diagnosed according to the current guideline of AF. Patients with paroxysmal AF were excluded from the study.[11]

Echocardiographic measurements were performed using the Philips Affinitti 70 ultrasound system (Medical Healthcare Solutions, Inc.; Andover, MA, USA) with an S4-2 transducer probe. The transthoracic echocardiographic analyses were performed by two cardiologists, blinded to the groups of patients according to current guidelines.[12] Single-lead echocardiographic recordings were simultaneously obtained during the echocardiographic recordings. Left ventricular (LV) end-diastolic dimensions and left ventricular anterior-posterior wall thicknesses were measured from parasternal long-axis, apical four- and five-chamber views and averaged. LV ejection fraction (EF) was measured using the Biplane Simpson method.

All patients underwent MRI at intervals 24-hours intervals after the AIS. MRIs were performed on an Achieva 3.0-Tesla scanner (Philips Healthcare, Amsterdam, The Netherlands) with an eight-channel phased-array coil for brain imaging. Brain CTs were also performed at intervals of 24-hours.

All-cause mortality was defined as death from any cause in-hospital follow-up and this was the primary endpoint. Patients' data were recorded by reaching the medical records of the cases.

The statistical analyses of data were conducted using IBM SPSS Statistics 18.0 for Windows, (IBM Corp, Armonk, NY, USA). The determination of normally distributed data was done using the Kolmogorov-Smirnov test. The normal distributions were expressed as the mean ± standard deviation, while those with non-normally distribution were expressed as median (25%-75% percentile). Mann-Whitney U and student's t-tests were used to compare continuous variables. Categorical variables were shown as numbers and percentage values and were analysed with a chi-square test. Logistic (univariate and multivariate) regression analysis was performed using age, gender, cerebrovascular events, chronic AF, total cholesterol, EF, and PNI. Survival plot of the effect of AF on in-hospital mortality in patients with high CONUT was made by Kaplan-Meier analysis. A p-value <0.005 was considered statistically significant.

RESULTS

G 1 with low CONUT <2 included 262 patients and group 2 with high CONUT ≥2 included 138 AIS patients. Mean CONUT scores in group 1 and group 2 were 0.34±0.04 and 2.94±0.74, respectively.

The average age in group 1 was 68.91±12.42 years, and it was 71.62±11.86 years for group 2. The groups were similar regarding age (p>0.05). Baseline demographic characteristics, laboratory, and transthoracic echocardiographic findings of both groups are presented in Tables I and II. The groups were similar regarding baseline clinical and demographic characteristics. Previous cerebrovascular events, chronic AF, and in-hospital mortality were more frequent in group 2 (p =0.007; p=0.019, and p=0.006, respectively). Fasting glucose, body mass index, and EF were similar in both groups. Total cholesterol, lymphocyte count, median values of PNI, and albumin were significantly higher in group 2 (Tables I and II, and values of all p<0.001).

Logistic regression analyses were performed in one model, including continuous values of age, total cholesterol, ejection fraction, and categorical values of CVE, AF, PNI, and gender to detect independent predictors of in-hospital mortality in group 2 is presented in Table III.

Table I: Demographic and clinical characteristics of the groups.

	Total	Group 1 (n=262)	Group 2 (n=138)	p
Gender				
Male	222(55.5%)	142 (54.2%)	80 (58%)	0.269*
Female	178 (44.5%)	120 (45.8%)	58 (42%)	
Age	69.69±12.24	68.91±12.42	71.62±11.86	0.081**
Smoking	97 (24.3%)	58(22.1%)	39 (28.3%)	0.109*
History of CAD	56 (14%)	32 (12.2%)	24 (17.4%)	0.104*
HT	280 (70%)	182 (69.5%)	98 (71%)	0.420*
HL	38 (9.5%)	28 (10.7%)	10 (7.2%)	0.175*
DM	178 (44.5%)	124 (47.3%)	54 (39.1%)	0.072*
CHF	34 (8.5%)	18 (6.9%)	16 (11.6)	0.079*
CVE	76 (19%)	40 (15.3 %)	36 (26.1%)	0.007*
CRF	2 (0.5%)	0	2 (1.4%)	0.120*
Carotid artery lesion	62 (17.7%)	46 (17.7%)	16 (11.6%)	0.071*
Atrial fibrillation	90 (22.6%)	50 (19.2%)	40 (29%)	0.019*
NIHSS	8 (3.25-17)	9 (5-14)	6.5 (2-21)	0.343***
In-hospital mortality	30 (7.5%)	12 (4.7%)	18 (12.3%)	0.006*
In-hospital mortality day	6.06 ± 1.8	6.48±0.79	4.33±0.51	0.029**
CONUT score	1.24 ± 0.31	0.34± 0.04	2.94±0.74	<0.001**
PNI	50.97 (46.28-55.13)	53.15 (50.00-56.75)	45.65 (42.67-49.56)	<0.001***

Table II: Laboratory tests and transthoracic echocardiography results of the groups.

	Group 1 (n=262)	Group 2 (n=138)	p
Glucose (mg/dL)	129.56 ± 50.52	140.76±68.83	0.375*
Total cholesterol (mg/dL)	204 (177-225)	149 (128-176)	<0.001**
Serum creatinine (mg/dL)	0.92 ±0.26	0.94±0.32	0.303*
Lymphocyte (L) count (×10^3/μL)	2.44±0.75	1.77±0.8	<0.001*
BMI	28.19±5.02	27.08±5.22	0.102*
Albumin (group/L)	41.36±3.06	38.3±5.28	<0.001*
Ejection Fraction (%)	60 (60-60)	60 (57-60)	0.102**

*BMI: Body mass index; dL: Decilitre; group: Gram; L: Liter; LDL: Low density lipoprotein; mg: Miligram; uL: microliter. p<0.05 indicates statistical significance; *Student's t-test; **Mann Whitney U test*

Table III: Predictors of in-hospital mortality in group 2 by logistic regression analysis.

Variables	Univariate OR (95 % CI)	p-value	Multivariate OR (95 % CI)	p-value
Age (years)	0.989 (0.950-1.030)	0.599		
Gender	1.972 (0.753-5.167)	0.181		
CVE	0.659 (0.259-1.677)	0.367		
Chronic AF	1.338 (0.123-2.928)	0.035	1.268 (1.084-1.854)	0.026
Total cholesterol (mg/dL)	1.002 (0.992-1.012)	0.729		
Ejection Fraction (%)	1.009 (0.966-1.054)	0.675		
PNI	0.963 (0.889-1.043)	0.340		

AF: Atrial fibrillation; CI: Confident interval; CVE: Cerebrovascular event; dL: Deciliter; mg: milligram; PNI: Prognostic nutrition index.

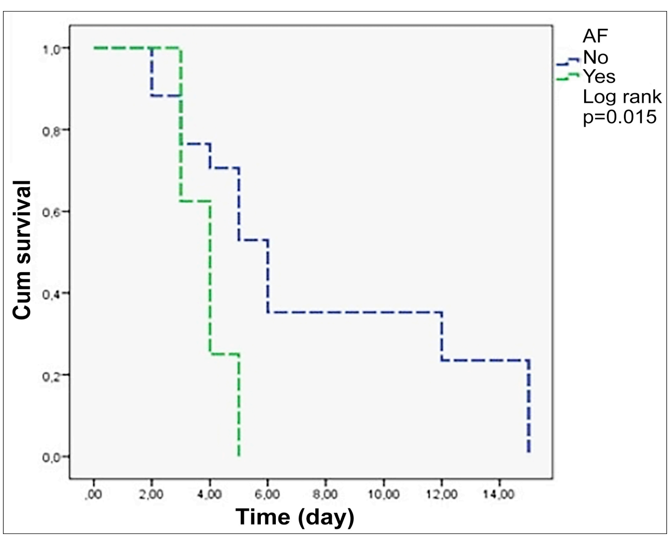

Figure 1: Kaplan-Meier survival curve for in-hospital mortality day in g 2 patients with atrial fibrillation (AF).

According to univariate and multivariate logistic regression analyses, chronic AF (p=0.035 and 0.026, respectively) remained an independent predictor of in-hospital mortality in group 2 (Table III). In Figure 1, the effect of AF on in-hospital mortality in patients with high CONUT was demonstrated *via* Kaplan-Meier analysis. Mortality occurs earlier in high CONUT patients with AF (p=0.015).

DISCUSSION

In the study, the prognostic role of the CONUT was researched on in-hospital mortality in AIS patients. This study demonstrated that the in-hospital mortality rates were greater in AIS patients with a high CONUT score. The study also established that AF was more frequent in AIS patients with higher CONUT.

The results of this study support previous studies showing a link between CONUT score and adverse outcomes in patients with AIS. In this study, the degree of malnutrition might be lower compared to other studies. Because the CONUT was calculated at the time of admission. In a study of 164 AIS patients, a high CONUT was found to be associated with increased in-hospital and post-hospital first 3-month mortality.[13] Naito *et al*. demonstrated in their study that a high CONUT was independently related to poor outcomes in AIS patients.[14] Kokura *et al*. investigated the link between motor functions and CONUT in patients with AIS at admission. They found that high CONUT was an independent predictor of poor motor functions.[15] In another study, it was shown that CONUT at admission may help to predict the functional status of stroke patients.[16]

In ischemic stroke patients, malnutrition was found to be associated with the increased mortality rate in long-term follow-up.[17] Moreover, a high CONUT was related to worse clinical outcomes in patients with haemorrhagic stroke.[18] In contrast to this study, CONUT was not found superior to predict poor outcomes in AIS patients compared to other nutritional risk screening tools.[19]

Since inflammation is important in the occurrence of AF, this study sought to investigate whether a high CONUT could be a predictor of AF coexistence in AIS patients, and the results did suggest a correlation. The literature seemed to show no other study comparing this relationship. AF recurrence rates were found higher in undernourished, post-ablation patients assessed with CONUT.[20] In another study, moderate and severe malnutrition were found as independent predictors of adverse outcomes among very elderly patients with non-valvular AF.[21]

AIS occurs as a result of atherosclerosis such as acute coronary syndromes (ACS) and higher CONUT is linked with increased adverse events in patients with ACS.[22,23] In a study including 1028 cases with acute myocardial infarction, nutrition status was assessed through the use of CONUT, and it was demonstrated that higher CONUT was related to adverse events.[24] In cases with stable coronary artery disease, high CONUT is significantly linked with worse long-term clinical outcomes.[25] Also, there appeared to be a link between in-hospital mortality, and high CONUT in hospitalised patients because of acute heart failure.[25]

The study had some limitations. First, it was a single-centred and the retrospective sample was small. In addition, blood samples were only taken during admission. The malnutrition status can change during time in AIS patients. Only the CONUT score was used to assess nutritional status. No other measures were included to assess nutritional status such as muscle mass and food intake.

CONCLUSION

Stroke is one of the common causes of malnutrition, and the CONUT score is an easy usable nutritional screening tool in AIS patients. The CONUT score at admission might be used to predict in-hospital mortality in these patients. The presence of AF in AIS patients changes both prognosis and treatment and the CONUT score can be used to predict the presence of AF.

ETHICAL APPROVAL:
This retrospective observational study was reviewed and approved by the Institutional Review Board of the University of Health Sciences, Sancaktepe Sehit Prof. Ilhan Varank Training and Research Hospital Ethical Committee for Clinical Investigations (Approval No. E-46059653-020).

PATIENTS' CONSENT:
Informed consent were taken from the patient.

COMPETING INTEREST:
The authors declared that they have no competing interests.

AUTHORS' CONTRIBUTION:
EA: Conceptualisation, design, literature review, methodology, project administration, data curation, visualisation, and writing the original draft.
FOK: Data curation, statistical analysis, supervision, writing the original draft, and methodology.
SC, SD: Data curation, literature review, writing original draft, and methodology.
All the authors have approved the final version of the manuscript to be published.

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