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Prognostic significance of controlling nutritional status (CONUT) score in hemodialysis patients

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ABSTRACT

Introduction: Malnutrition is a common and important problem in HD Hemodialysis (HD) patients. Malnutrition occurs due to various factors increases the risk of morbidity and mortality in HD patients. The Controlling Nutritional Status (CONUT) score has been designed to assess the nutritional status in patients. In addition, the relationship between the CONUT score and mortality has been investigated. We aimed to investigate the effectiveness of the CONUT score in predicting mortality in HD patients.

Material and Method: The data of 110 patients who started HD between 2017-2021 were analyzed retrospectively. From the laboratory parameters were evaluated before starting the first hemodialysis treatment. The CONUT score was calculated based on lymphocyte count, total cholesterol levels, and serum albumin levels. The patients were divided into two groups as CONUT score ≤4 and CONUT score ≥5. The groups were compared regarding these parameters.

Results: The data of 110 hemodialysis patients were analyzed. 58 (52.7%) of these patients were male. The mean age of the patients was 53.18±17.10 years. There were 49 (44.5%) patients with a CONUT score of ≤4 and 61 (55.5%) patients with a CONUT score of ≥5. 35 patients (13.9%) died. Among 35 all-cause deaths, 4 (11.4%) were occurred in the low CONUT group, and 31 (88.6%) were occurred in the high CONUT group ($p<0.001$). According to Kaplan-Meier analysis, the high CONUT group had significantly higher all-cause mortality ($p<0.001$) than the low CONUT group. According to the correlation analysis, there was a positive correlation between the CONUT score and mortality ($p<0.001$). In the multivariate Cox regression analysis, all cause of mortality was independently correlated to age, gender (male) and CONUT score (p: 0.010, p: 0.038 and $p < 0.001$, respectively). According to the ROC curve analysis, the optimal cut-off value of CONUT score in Hemodialysis HD patients was found at 4.5.

Conclusion: We concluded that the higher the CONUT score, the worse the nutritional status in hemodialysis patients, and may be associated with worse clinical outcomes. It is extremely important to evaluate the nutritional status at regular intervals, to detect malnutrition early and to follow up the results in HD patients. We think that CONUT score can be useful in predicting mortality risk for HD patients in clinical practice.

Keywords: Malnutrition, hemodialysis, mortality, CONUT score

INTRODUCTION

Hemodialysis (HD) is the most preferred renal replacement therapy (RRT) method for patients with end-stage renal disease (ESRD). Worldwide, HD forms for 89% of RRTs (1). Nutrition is an important issue in patients undergoing HD. While malnutrition is detected in approximately one third of these patients, the probability of encountering malnutrition increases as the duration of hemodialysis increases (2). Malnutrition occurs due to various factors reduces the quality of life (3) and increases the risk of morbidity and mortality in HD patients. The guidelines recommend frequent assessment of nutritional status in patients with ESRD (4).

It is important to evaluate the nutritional status at regular intervals and to determine malnutrition in the early period in HD patients. To establish the risk of malnutrition, a simple, inexpensive, and rapid screening tool should be used. Controlling Nutritional Status (CONUT) score is a screening tool calculated with laboratory parameters. These parameters are serum albumin level, total cholesterol level and lymphocyte count. CONUT score has been used to detect malnutrition in many diseases. In addition,

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studies have shown that the CONUT score can be used as an independent predictor of mortality (5,6).

Malnutrition is a common and important problem in HD patients. Early screening of malnutrition and implementation of necessary nutritional interventions in this population are very important since reducing morbidity and mortality rates (2). To the best of our knowledge, no study has been performed on the prognostic significance of the CONUT score in HD patients. In our study, we aimed to investigate the effectiveness of the CONUT score in predicting mortality in HD patients.

MATERIAL AND METHOD

The data of patients with ESRD initially undergoing HD at two different hemodialysis units between January 2017 and December 2021 were analyzed retrospectively. Patients under the age of 18, with missing data, malignancy or hematological disease were excluded from the study. 110 patients over the age of 18 were included in the study, regardless of gender. Demographic characteristics of the patients (age, gender), laboratory parameters were collected from the hospital database. From the laboratory parameters before starting the first hemodialysis treatment; leukocyte count, lymphocyte count, hemoglobin, serum urea, creatinine, albumin, corrected calcium, phosphorus, uric acid, total cholesterol, HDL High Density Lipoprotein (HDL) cholesterol, LDL Low Density Lipoprotein (LDL) cholesterol, triglyceride, Parathormone parathormone, CRP C reactive protein (CRP) levels were evaluated. The CONUT score was calculated based on lymphocyte count, total cholesterol levels, and serum albumin levels (**Table 1**) (7). The optimal CONUT score cut-off value for the survival was determined by the Receiver operating characteristics (ROC) curve analysis to be 4. The patients were divided into two groups as CONUT score ≤4 and CONUT score ≥5. The groups were compared regarding these parameters. This study was approved by the Ethics Committee of Gazi Yaşargil Training and Research Hospital (Date:11.02.2022, Decision No: 19). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Table 1. Definition of CONUT score

Parameters	CONUT			
	Normal	Mild	Moderate	Severe
Serum albumin (g/dL)	≥3.5	3.00-3.49	2.50-2.99	<2.50
Albumin score	0	2	4	6
Lymphocyte (count/mm³)	≥1600	1200-1599	800-1199	<800
Lymphocyte score	0	1	2	3
Total Cholesterol (mg/dL)	≥180	140-179	100-139	<100
Total Cholesterol score	0	1	2	3
CONUT score (total)	0-1	2-4	5-8	9-12

Statistical Analysis

Statistical analysis of the results obtained in the study was performed using the SPSS (Statistical Package for Social Sciences) 28 program. Descriptive statistics were used for demographic data. The normal distribution suitability of the variables was examined using visual (histogram and probability plots) and analytical methods (Kolmogrov-Simirnov/Shapiro-Wilk tests). Results are given as numbers and percentages for categorical variables and as mean±standard deviations for continuous variables. Spearman rank correlation analysis was performed to analyze the correlation between CONUT score and selected characteristics or parameters. The Kaplan-Meier method was used for survival analysis and compared using log rank analysis. Univariate and multivariate Cox Regression analysis was used for the analysis of variables related to mortality. The cut-off value of the CONUT score was analyzed with the ROC curve. A p value of less than 0.05 was considered statistically significant.

RESULTS

The data of 110 hemodialysis patients were analyzed. 58 (52.7%) of these patients were male. The mean age of the patients was 53.18±17.10 years. During the median follow-up period of 15.50 (1-58) months, 35 patients (13.9%) died. 20 (57%) of the patients who died were female (p:0.157). The median CONUT score was 4 (0-11) and the mean CONUT score was 4.51±3.196.

According to the cut-off value of 4, the enrolled patients were divided into two groups: Low CONUT group (CONUT score ≤4; 49 patients, 44.5%) and high CONUT group (CONUT score ≥5; 61 patients, 55.5%). There was no statistical difference between the groups and gender (p:0.900). The demographic and baseline laboratory parameters of the study population are shown in **Table 2**. Among 35 all-cause deaths, 4 (11.4%) were occurred in the low CONUT group, and 31 (88.6%) were occurred in the high CONUT group (p<0.001). The Kaplan-Meier analysis of all-cause mortality in hemodialysis patients according to the cut-off CONUT score is shown in **Figure. 1**. The high CONUT group had significantly higher all-cause mortality (p<0.001) than the low CONUT group.

A correlation analysis between CONUT score and variables in the hemodialysis patients were carried out using the Spearman correlation test (**Table 3**). CONUT scores showed a significant positive correlation to age and mortality, and a significant negative correlation to hemoglobin level, lymphocyte count, serum albumin, total cholesterol, HDL cholesterol, LDL cholesterol and parathormone level (p<0.05). There was a significant negative correlation between mortality and serum albumin and lymphocyte count (r: -0.569, p<0.001 and r: -0.388, p<0.001 respectively). Although there was a negative correlation between mortality and total cholesterol, it was not statistically significant (r: -0.146, p:0.127)

The univariate and multivariate Cox regression analyses were performed to confirm the independent predictors of all cause of mortality (**Table 4**). In the univariate Cox regression analysis, age and CONUT score were found to be correlated to all cause of mortality. In the multivariate Cox regression analysis, all cause of mortality was independently correlated to age, gender (male) and CONUT score (p: 0.010, p: 0.038 and p < 0.001, respectively).

According to the ROC curve analysis, the optimal cut-off value of CONUT score in Hemodialysis patients was found at 4.5. CONUT score had an AUC of 0.858 (95% CI, 0.788 -0.928, p < 0.001), with a sensitivity of 88.6% and a specificity of 76% (**Figure 2**).

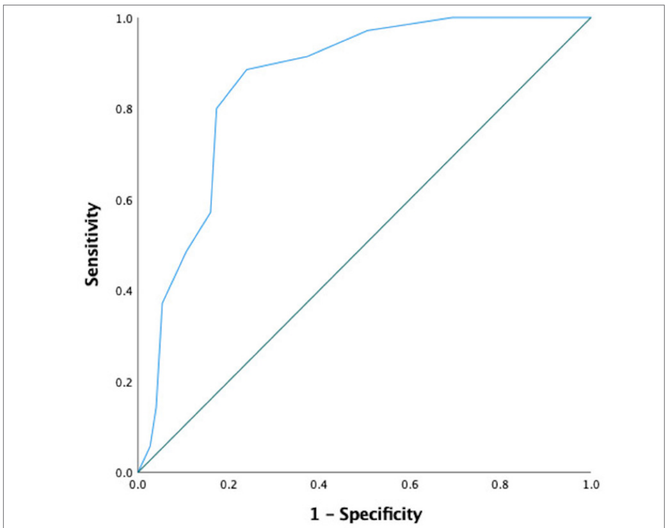

Figure 2. ROC analysis of CONUT score

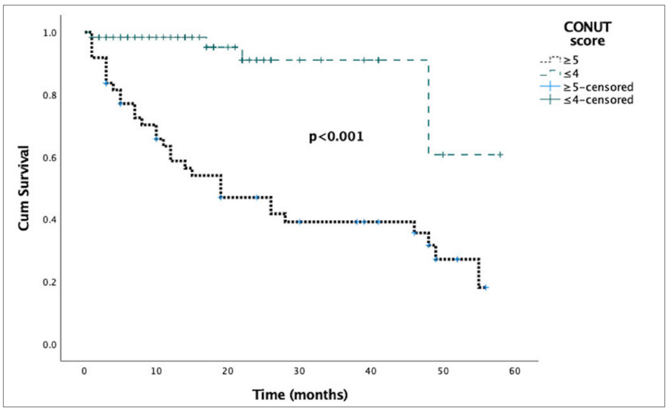

Figure 1. Kaplan-Meier analysis of all-cause mortality in Hemodialysis patients

Table 3. Spearman correlation between CONUT score and variables.

Variables	Correlation Coefficient	p
Age	0.189	0.048
Gender	-0.008	0.933
WBC	-0.121	0.209
Hemoglobin	-0.215	0.024
Lymphocyte	-0.639	<0.001
Urea	0.126	0.189
Creatinine	-0.072	0.452
Uric Acid	-0.002	0.984
Corrected Calcium	0.085	0.377
Phosphate	0.061	0.528
Albumin	-0.846	<0.001
Total Cholesterol	-0.432	<0.001
HDL Cholesterol	-0.305	0.001
LDL Cholesterol	-0.363	<0.001
Triglycerides	-0.148	0.124
CRP	0.075	0.436
Parathormone	-0.268	0.005
Mortality	0.581	<0.001

WBC: White Blood Cell, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, CRP: C Reactive Protein

Table 2. Demographic and baseline laboratory parameters of hemodialysis patients

Characteristics	All patients (n:110)	CONUT score ≤4 (n:61)	CONUT score ≥5 (n:49)	p
Age (years)	53.18±17.10	50.13±16.42	56.98±17.33	0.043
Gender				
Male	58 (52.7%)	29 (47.5%)	23 (46.9%)	0.900
Female	52 (47.3%)	32 (52.5%)	26 (53.1%)	
WBC (count/mm³)	7672.26±2442.20	7817.54±2326.88	7491.41 ±2591.50	0.975
Hemoglobin (g/dL)	9.09±1.85	9.44±1.94	8.65 ±1.65	0.290
Total Lymphocyte (count/mm³)	1534.00±573.43	1746.39±489.46	1269.59±564.40	0.563
Urea (mg/dL)	129.89±54.60	123.84±52.27	137.43 ±57.00	0.988
Creatinine (mg/dL)	6.47±2.64	6.61±2.57	6.14±2.73	0.829
Uric Acid (mg/dL)	6.36±1.52	6.36±1.60	6.37±1.44	0.499
Corrected Calcium (mg/dL)	8.91±0.90	8.89±0.76	8.92 ±1.06	0.019
Phosphate (mg/dL)	4.71±1.25	4.62±1.16	4.81±1.36	0.538
Albumin (g/dL)	3.10±0.61	3.56 ±0.31	2.53±0.38	0.042
Total Cholesterol (mg/dL)	163.69±46.05	169.87±38.38	156.00±53.52	0.112
HDL Cholesterol (mg/dL)	42.45±36.33	47.00±46.75	36.78±14.39	0.334
LDL Cholesterol (mg/dL)	98.51±36.80	102.44±31.39	93.61±42.42	0.106
Triglycerides (mg/dL)	127.98±63.50	131.84±59.29	123.18±68.70	0.987
CRP (mg/dL)	1.37±1.76	1.27±1.66	1.51±1.89	0.388
Parathormone (pg/mL)	441.91±311.258	495.30±338.04	375.45±262.73	0.244
CONUT Score				
Mean±std	4.51±3.196	2.03±1.32	7.59±1.87	0.002
Median (min-max)	4 (0-11)	2 (0-4)	8 (5-11)	

WBC: White Blood Cell, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, CRP: C Reactive Protein

Table 4. Univariate and multivariate Cox analysis of patient survival in hemodialysis dialysis patients

Characteristics	Univariate		Multivariate	
	HR (95%CI)	p	HR (95%CI)	p
Age	1.036 (1.014-1.059)	0.001	1.029 (1.007-1.051)	0.010
Gender (male)	0.536 (0.273-1.054)	0.071	0.480 (0.239-0.961)	0.038
Hemoglobin	0.959 (0.808-1.140)	0.636		
Urea	1.000 (0.994-1.007)	0.938		
Creatinine	0.944 (0.828-1.075)	0.383		
Uric Acid	0.963 (0.769-1.205)	0.740		
Corrected Calcium	1.068 (0.760-1.501)	0.703		
Phosphate	1.080 (0.859-1.358)	0.508		
HDL Cholesterol	0.971 (0.941-1.002)	0.065		
LDL Cholesterol	0.997 (0.987-1.006)	0.496		
Triglycerides	1.001 (0.996-1.006)	0.799		
CRP	0.930 (0.745-1.163)	0.525		
Parathormone	1.000 (0.999-1.001)	0.568		
CONUT score (≥5)	1.328 (1.177-1.500)	<0.001	1.313 (1.162-1.484)	<0.001

DISCUSSION

To the best our knowledge, there is no study comparing the CONUT score and prognosis in HD patients. In this study, we investigated the effectiveness of the CONUT score in predicting mortality. Our results show that malnutrition is associated with all-cause mortality in hemodialysis patients, and a high CONUT score at admission is an independent prognostic factor for mortality. We think that CONUT score can be useful in predicting mortality risk and diagnose malnutrition for HD patients in clinical practice.

Malnutrition has been shown to be associated with increased morbidity and mortality in patients with ESRD (8). Many scoring systems are used for the diagnosis of malnutrition. The CONUT score is one of the tests used to determine nutritional status and has been accepted as an important prognostic marker in many diseases. The CONUT score, calculated using total cholesterol level, serum albumin level and lymphocyte count, accurately reflects the patient's nutritional status by evaluating protein reserve, lipid metabolism and immune status (6,9). Albumin, lymphocytes, and total cholesterol are potential markers of malnutrition. Lower levels of these parameters represent a higher CONUT score (10). In the studies, in hemodialysis patients; It has been shown that low serum total cholesterol level, low lymphocyte count and low albumin level, are associated with malnutrition and are independent predictors of mortality (11,12). In the HEMO study, low serum albumin and low serum total cholesterol levels have been shown to have a relatively higher risk of mortality (13). In our study, there was a significant negative correlation between serum albumin and lymphocyte count and mortality, although there was a negative correlation with total cholesterol, it was not statistically significant.

In the literature, the relationship between the CONUT score and mortality in many diseases has been compared. Especially in cancer patients, there are many studies on the CONUT score. The results of these studies have been shown that the CONUT score is significantly associated with outcomes, including overall survival, in cancer patients, and that a high CONUT score adversely affects overall survival (14-16). It has been reported that a high CONUT score may be an independent prognostic factor for morbidity and overall survival in hematological diseases such as lymphoma (17), multiple myeloma (18), and thalassemia (19). In another study, 2466 patients with a diagnosis of acute heart failure were evaluated and a higher mortality and infection rate was found in patients with a CONUT score ≥5 at the time of hospitalization (20). CONUT score was investigated in patients with contrast-related acute kidney injury, ANCA-related vasculitis, and hypertension, and it was found that an increased CONUT score was associated with all-cause mortality (21-23).

Malnutrition is common in dialysis patients. There are few studies evaluating the CONUT score in dialysis patients. All these studies were conducted in peritoneal dialysis patients. Yang et al. (10) showed in their study that a CONUT score of >3 is associated with technique failure in PD patients. In another study, nutritional indexes were evaluated in PD patients, and it was stated that a CONUT score >3 may be an independent predictor of all-cause mortality (5). Zhou et al. (24), on the other hand, analyzed the relationship of the CONUT score at the onset of PD with technique failure, cardiovascular disease and mortality and reported that a CONUT score of >3 may be a prognostic marker. In our study, we found that a CONUT score of ≥5 increased all-cause mortality 1.3 times. When we reviewed the studies, different cut-off values were used for the CONUT score to predict mortality. This may be due to the fact that since it has been used to in different diseases and in different populations. In our study, we found the cut-off value of the CONUT score of 4.5 according to the ROC curve analysis and divided our patients into 2 groups as CONUT score ≤4 and ≥5. We found high mortality in the group with a CONUT score of ≥5. Similar to previous studies, our findings suggest that a high CONUT score may be an independent predictor of mortality.

Our study had several limitations. First, it is a retrospective study. Second, the number of patients was limited since there were only two centers. Third, we did not investigate how the CONUT score changes over time after dialysis and its relationship to outcomes.

CONCLUSION

It is extremely important to follow up the nutritional status at regular intervals, to detect malnutrition early and to follow up the results in HD patients. Our study includes important clinical findings as it evaluated the relationship between the CONUT score, which indicates nutritional status, and mortality in HD patients. In our study, we concluded that higher CONUT score is associated with worse nutritional status in HD patients and may lead to worse clinical outcomes. CONUT score is a simple and inexpensive scoring system, and we think that it can be useful in predicting mortality risk for HD patients in clinical practice. However, prospective studies with larger population are necessary.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the ethics committee of Gazi Yaşargil Training and Research Hospital (Date: 11.02.2022, Decision No: 19).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer- reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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