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THE CONTROLLING NUTRITIONAL STATUS (CONUT) SCORE MIGHT PREDICT SURVIVAL IN MAINTENANCE HEMODIALYSIS PATIENTS

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Malnutrition causes substantial morbidity in maintenance hemodialysis (HD) patients. The Controlling Nutritional Status (CONUT) has emerged as a simple and an easily obtainable tool to comprehensively assess nutrition as it consists of serum albumin levels, absolute lymphocyte counts, and total cholesterol levels. The CONUT has been shown to predict overall survival (OS) in peritoneal dialysis patients. This study investigated whether CONUT might also predict OS in maintenance HD patients. Clinical and laboratory data were retrospectively collected. Survival time was calculated from the first HD until death or last follow-up; survival analyses were performed using the methods of Kaplan-Meier and Cox regression analysis. Eighty-nine patients were included; mean age was 65.76 years (±14), 35 (39.3%) were female, and the mean CONUT was 3. Higher CONUT score correlated with lower low-density liproprotein, higher serum creatinine, higher serum C-reactive protein and higher neutrophil-to-lymphocyte ratio, as well as with a higher incidence of nephrotic proteinuria (p<0.050 for all analyses). Univariately, patients with higher CONUT (≥5) had an inferior OS (median 54 vs. 112 months, HR 2.27; p=0.013). In the Cox regression analysis, higher CONUT remained independently associated with inferior OS (HR 9.50; p=0.002) when adjusted to age, sex, diabetes mellitus and nephrotic proteinuria. Therefore, the CONUT score might identify HD patients at an increased risk of death; however, future studies are needed to elucidate whether CONUT score might be able to guide nutritional support in HD patients.

Key words: **malnutrition, inflammation, survival, CONUT, hemodialysis**

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INTRODUCTION

Malnutrition and hypoalbuminemia cause substantial morbidity and mortality in hemodialysis (HD) patients (1-4). For this reason, current guidelines recommend nutritional screening for these patients; however, limited evidence exists as to which tool performs best (5).The Controlling Nutritional Status (CONUT) score has emerged as a simple and an easily obtainable tool to comprehensively assess nutrition, as it consists of albumin concentration (indicator of protein reserves), absolute lymphocyte count (indicator of weak immune defense due to malnutrition) and total cholesterol level (indicator of caloric depletion) in peripheral blood (6). This particular index has been shown to be an independent prognostic factor in several cancers (7-10). Moreover, the CONUT score has been recently shown to accurately predict mortality in patients undergoing peritoneal dialysis (11). In this study, we investigated the ability of the CONUT score to predict overall survival (OS) in patients with kidney failure.

PATIENTS AND METHODS

Study design

This was a single-center retrospective study conducted at the Department of Internal Medicine, General Hospital of Šibenik-Knin County, Croatia, in the period between July 2007 and May 2019. Patients undergoing maintenance HD due to kidney failure as defined by the Kidney Disease Improving Global Outcomes (KDIGO) 2012 criteria (12) were retrospectively included. Baseline demographic, clinical and laboratory data were recorded at the time of first HD. Excluded from participation were pregnant women, subjects <18 years of age, and patients with acute kidney injuries requiring HD.

The use of medications was considered significant if prescribed for ≥3 months during the follow-up. Arterial hypertension was defined as the regular use of antihypertensive drugs to control blood pressure or at least two blood pressure measurements of >140/90 mm Hg. Nephrotic proteinuria was defined as >3.5 g/24 h. Erythropoietin was administered to all patients with hemoglobin level <90 g/L despite adequate parenteral iron supplementation (transferrin saturation ≥30%) as *per* KDIGO 2012 guideline 13).

The CONUT score was calculated as described in the original study (6) and in accordance with a tool presented in Table 1. We also evaluated whether this tool might provide additional prognostic information when compared to the Geriatric Nutritional Risk Index (GNRI) and Prognostic Nutritional Index (PNI). The GNRI can be used to assess nutrition in HD patients and was shown to predict OS in these patients (14-16). It can be calculated using body weight, height and serum albumin levels with the formula: GNRI=[1.489×albumin (g/L)]+[41.7×(weight/ideal weight)]. The PNI is a nutritional risk index which also takes into account serum albumin levels and absolute lymphocyte counts, thereby indicating the nutritional and immune status of a patient. It was originally developed to stratify perioperative risk (17) and was shown to predict outcomes in patients with chronic kidney disease (18-20). The PNI can be calculated using the formula: (10 x serum albumin [g/dL]) + (0.005 x lymphocytes/μL).

Statistical analyses

Statistical calculations were performed with MedCalc Statistical Software® (Ostend, Belgium, version 19.7). The Shapiro-Wilk test was used to check for data distribution. Categorical variables were compared using the χ^2-test, whereas the one-way analysis of variance (ANOVA), Mann-Whitney U or Kruskal Wallis test were used to compare continuous variables between patient groups, as appropriate. The Jonckheere-Terpstra trend test was used to test trends for increase in C-reactive protein (CRP) levels and neutrophil-to-lymphocyte ratios (NLR) accross the CONUT scores. Receiver operating curve (ROC) analysis was used for sensitivity and specificity testing. The OS was measured as the time from the first HD until death or the last follow-up visit. Survival analyses were performed using the Kaplan-Meier and Cox regression analysis. Significant p-values were set at <0.050 for all analyses presented.

Ethics

The study was performed in accordance with the Declaration of Helsinki and was approved by the institutional Review Board.

RESULTS

Correlations of the CONUT score with clinical characteristics

Eighty-nine patients were included; mean age was 65.76 years (±14) and 35 (39.3%) were female. The mean CONUT score was 3 (±2) and a total of 25 (28.1%) patients had normal (0-1), 44 (49.4%) had light (2-4) and 20 (22.5%) had moderate (5-8) CONUT score, whereas none of the patients included in this study had severe (9-12) CONUT score.

Patients were then stratified according to the mean CONUT score (0-3 *vs*. 4-8). Clinical characteristics were well balanced, with no differences between the two groups regarding demographics (age and sex), HD-related variables (body weight, body height, body mass index, location of arteriovenous fistula, and presence of central venous catheter), comorbidities (presence of polycystic kidney disease or obstructive uropathy, arterial hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, systemic autoimmune disorders or concomitant cancers), use of medications (statins, uricosurics, aspirin, warfarin, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ARB), steroids and erythropoetins), and the majority of blood cell count components (p<0.050 for all analyses). Expectedly, patients with higher CONUT score had statistically significantly lower serum albumin levels (median 32.7 *vs*. 38 g/L; p<0.001), total cholesterol levels (mean 3.64 *vs*. 4.71 mmol/L; p<0.001) and absolute lymphocyte counts (mean 1280 *vs*. 1500/mm^3; p=0.036), as these three variables are integrated into the CONUT score (Table 1). Similarly, higher CONUT score correlated with lower PNI (median 30.30 *vs*. 37.15; p<0.001). Differences in serum albumin levels might also explain the lower serum calcium levels in patients with higher CONUT score (mean 2.19 *vs*. 2.32 mmol/L; p=0.019). Interestingly, no differences were found in absolute lymphocyte counts between low and moderate CONUT score risk groups (mean 1.273 *vs*. 1.286/mm³; p>0.050) and only two (2.2%) study patients had absolute lymphocyte count <800/mm³ (these patients had CONUT scores of 5 and 6). Patients with higher CONUT score also had lower low-density lipoprotein (median 1.86 *vs*. 2.50 mmol/L; p<0.001), but there were no differences with respect to high-density lipoprotein (p=0.135) and serum triglycerides (p=0.068). Even though the proportion of patients receiving erythropoetin despite adequate iron supplementation was similar in both risk groups (82.7% *vs*. 86.4%), patients with higher CONUT score had lower serum hemoglobin levels (mean 94.72 *vs*. 101.76 g/L; p=0.036). Notably, patients with higher CONUT score had lower serum creatinine (median 498 *vs*. 638 μmol/L; p=0.003), most probably reflecting their lower muscle mass. Also, patients with higher CONUT score more often had nephrotic proteinuria (35.1% *vs*. 9.6%, p=0.003), suggesting a glomerular albumin loss (median serum albumin levels was 33 *vs*. 36.9 g/L; p=0.002 for patients with and without nephrotic-range proteinuria, respectively).

Table 1.
The Controlling Nutritional Status (CONUT) score (6).

Variable	Normal	Light	Moderate	Severe
Serum albumin (g/dL)	3.5-4.5	3.0-3.49	2.5-2.9	<2.5
Albumin score	0	2	4	6
Total lymphocyte count (mm³)	≥1600	1200-1599	800-1199	<800
Total lymphocyte count score	0	1	2	3
Total cholesterol (mg/dL)	>180	140-180	100-139	<100
Total cholesterol score	0	1	2	3
CONUT score	0-1	2-4	5-8	9-12
Assessment	Normal	Light	Moderate	Severe

The CONUT score is calculated as the sum of albumin score, total lymphocyte count score and total cholesterol score.

With respect to inflammatory biomarkers, there were no differences in serum CRP levels (p=0.626) and NLR (p=0.123) between the two groups. However, there was a trend for increase in serum CRP levels (median 1.8 *vs*. 3.45 vs. 3.90 mg/L; p=0.039) and NLR (median 2.45 *vs*. 3.17 *vs*. 3.20; p=0.016) with rising CONUT scores, as shown in Figure 1. Finally, patients with a higher CONUT score also had higher serum immunoglobulin G (mean 13.10 *vs*. 5.87 g/L; p=0.038) and immunoglobulin M levels (mean 0.92 *vs*. 0.33 g/L; p=0.046), whereas there were no differences in serum IgA levels (p=0.288). Statistically significant differences in clinical and laboratory variables between the two groups are summarized in Table 2.

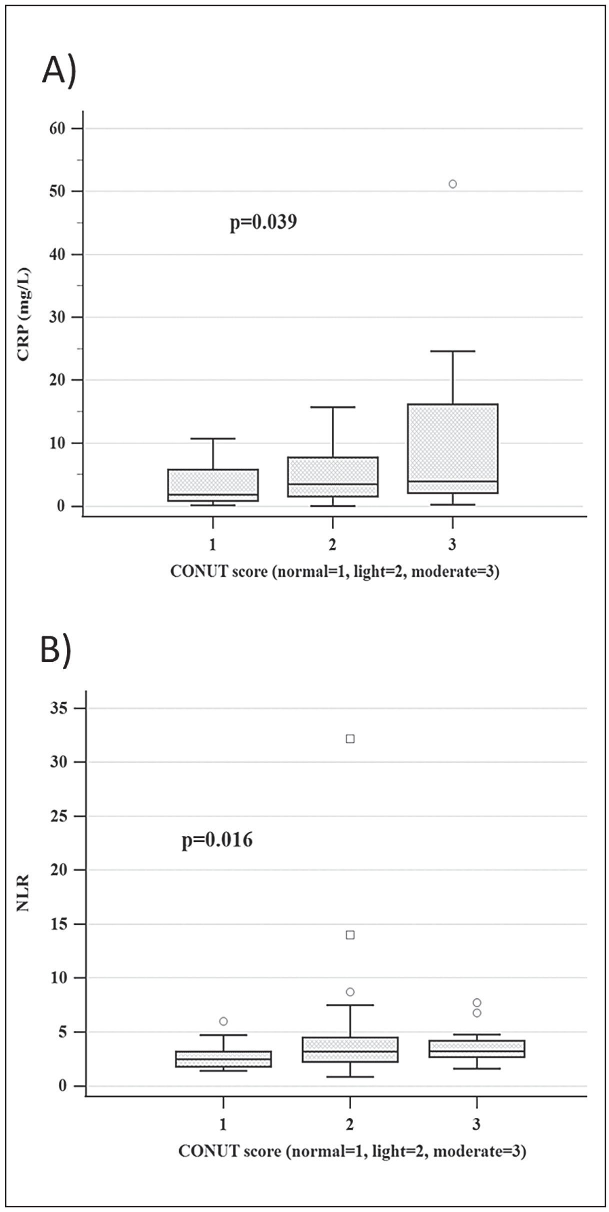

Fig. 1. *An increasing trend in serum C-reactive protein (CRP) levels and neutrophil to lymphocyte ratio (NLR) was found with rising CONUT scores. The Jonckheere-Terpstra trend test was used*

Table 2.
Patient'clinical and laboratory variables that significantly differed according to CONUT score.

Variable	Overall (n=89)	CONUT score 0-3 (n=52, 58.5%)	CONUT score 4-8 (n=37, 41.5%)	p value
Nephrotic proteinuria	18 (20.2%)	5 (9.6%)	13 (35.1%)	**0.003**
Creatinine (μmol/)	584 (IQR 187-1251)	638 (IQR 187-1251)	498 (IQR 227-1091)	**0.003**
Lymphocytes (x10⁹/L)	1.41 (SD ±0.50)	1.50 (SD (±0.55)	1.28 (SD ±0.38)	**0.036**
Hemoglobin (g/L)	98.84 (SD ±15.69)	101.76 (SD ±14.91)	94.72 (SD ±16.04)	**0.036**
Serum albumin (g/L)	36 (IQR 24-46.6)	38.1 (IQR 30-46.6)	32.7 (IQR 24-42)	**<0.001**
Total cholesterol (mmol/L)	4.26 (SD ±1.09)	4.71 (SD ±0.93)	3.64 (SD ±1.01)	**<0.001**
LDL (mmol/L)	2.3 (IQR 0.1-4.75)	2.50 (0.1-4.75)	1.86 (IQR 0.3-4.45)	**<0.001**
Serum calcium (mmol/L)	2.27 (SD ±0.26)	2.32 (SD ±0.27)	2.19 (SD ±0.21)	**0.019**
Immunoglobulin G (g/L)	8.97 (SD ±4.93)	5.87 (SD ±3.45)	13.10 (SD ±3.24)	**0.038**
Immunoglobulin M (g/L)	0.59 (SD ±0.41)	0.33 (SD ±0.37)	0.92 (SD ±0.05)	**0.046**

The χ^2, ANOVA one-way analysis of variance, and Mann-Whitney U tests were used. Significant p values are bold and were set at <0.050; CONUT = Controlling Nutritional Status score; LDL = low-density lipoprotein; SD = standard deviation; IQR = interquartile range.

Survival analyses

The median follow-up was 54 (range 6-146) months; 35 (44.3%) patients died during this time. For the purpose of survival analyses, ROC curve with death as a classification variable was created to search for the optimal cut-off value of the CONUT score. The approximate area under the ROC curve (AUC) for the CONUT score ≥5 was 0.667 (±0.061, 95% CI 0.559-0.764; p=0.009). Univariately, patients with a CONUT score of 5-8 had an inferior OS (median OS 54 *vs*. 112 months, HR 2.27; p=0.013), as shown in Figure 2. Additionally, diabetes mellitus (median OS 79 *vs*. 125 months, HR 1.82; p=0.070), age >54 years (median 85 months *vs*. not reached, HR 3.76; p=0.018), lower (<35 g/L) serum albumin levels (HR median 58 *vs*. 112 months, HR 2.04; p=0.031) and lower (≤4.9 mmol/L) total cholesterol levels (HR median 90 months *vs*. not reached, HR 5.0; p=0.010) were associated with inferior OS. In the multivariate Cox regression model, higher CONUT score (5-8) remained statistically significantly associated with inferior OS (HR 9.50; p=0.002), when adjusted to age, sex, diabetes mellitus and nephrotic proteinuria, as shown in Table 3. Of note, using the ROC curve analyses, we could not establish the optimal cut-off values of absolute lymphocyte counts and low-density lipoprotein levels which could have been associated with an inferior OS.

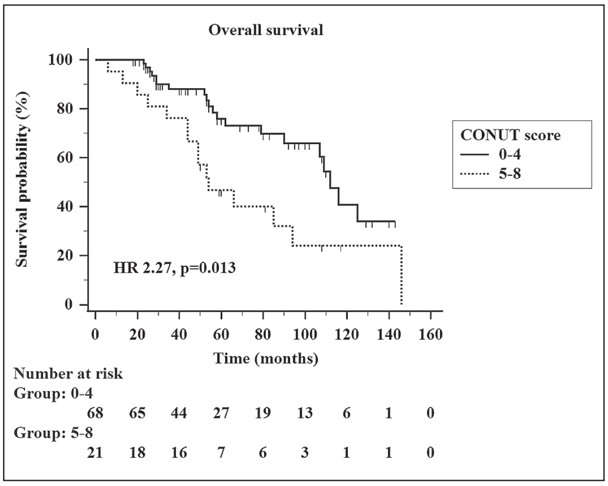

Fig. 2. *Patients presenting with higher Controlling Nutritional Status (CONUT) score had an inferior overall survival. The Kaplan-Meier log-rank test was used*

Table 3.
Prognostic impact of high CONUT score on overall survival remained statistically significant in the multivariate Cox regression model.

Variable	HR	95% CI	p value
CONUT 5-8	9.50	1.54-7.02	**0.002**
Age >54 years	4.53	1.11-13.52	**0.033**
Diabetes mellitus	0.97	0.66-3.48	0.324
Nephrotic proteinuria	0.93	0.24-1.61	0.333
Male sex	2.03	0.24-1.24	0.153

Significant p values are bold and were set at <0.050; CONUT = Controlling Nutritional Status score; HR = hazard ratio, CI = confidence interval.

For final analyses, we set the optimal cut-off levels of the PNI and GNRI at 37.9 and 86, respectively. Univariately, patients having low (<86) GNRI demonstrated inferior OS (median 85 *vs*. 116 months, HR 2.31; p=0.041), whereas patients with low (<37.9) PNI had a trend towards an inferior OS, which barely failed to reach statistical significance (median 79 *vs*. 116 months; HR 1.87; p 0.072). Using the Cox multivariate regression models, we tested performance of the CONUT score when compared to the GNRI and PNI. In the first model, the CONUT score was shown to accurately predict survival (HR 5.63; p=0.017) when adjusted to low (<86) GNRI (HR 1.86; p=0.174), age >54 years (HR 4.72; p=0.029), male sex (4.09; p=0.049), diabetes mellitus and nephrotic proteinuria (p not significant). In the second model, the CONUT score (HR 5.54; p=0.018) and age >54 years (HR 4.98; p=0.025) remained independently associated with inferior OS, whereas low (<37.9) PNI (HR 2.25; p=0.133), sex, diabetes mellitus and nephrotic proteinuria were not (p not significant). Finally, the ROC analysis with death as a classification variable demonstrated no statistically significant differences in the predictive abilities of the GNRI, PNI and CONUT score with respect to OS (p>0.050 for all pairwise comparisons), as shown in Figure 3. However, the AUC for the CONUT score (0.667, 95% CI 0.559-0.764) was higher than that of the GNRI (0.617, 95% CI 0.507-0.718) and PNI (0.593, 95% CI 0.483-0.696).

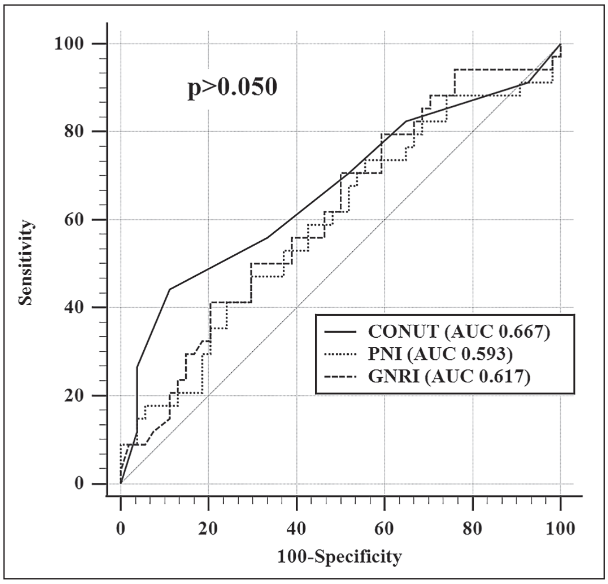

Fig. 3. *There were no statistically significant differences in the predictive abilities of the Geriatric Nutritional Risk Index (GNRI), Prognostic Nutritional Index (PNI) and Controlling Nutritional Status (CONUT) score with respect to overall survival. The receiver operating curve analysis was used.*

DISCUSSION

To our knowledge, this is the first study to report that higher CONUT score might be prognostic of an inferior OS in kidney failure patients undergoing maintenance HD. Malnutrition has been recognized as a late complication of kidney failure. More importantly, several studies have shown that protein-energy malnutrition in maintenance HD patients is associated with increased morbidity and mortality (1-4); thus, routine nutrition screening is recommended at least bianually in order to identify those at a high nutritional risk (5). For this reason, several risk scores have been developed; however, limited evidence exists to suggest the use of one tool over others. In addition, some indexes can be quite time-consuming as they include a wide set of clinical and laboratory variables (21,22). On the other hand, our study suggests that CONUT score, a comprehensive, yet a simple and an easily obtainable tool, could also be used to rapidly screen maintenance HD patients for nutrition. More importantly, this tool was able to correctly identify HD patients at an increased risk of death. Interestingly, in the multivariate Cox regression models, the CONUT score was associated with an inferior OS when adjusted to the GNRI and PNI rendering them insignificant. This is most probably due to their overlapping prognostic properties as all three risk scores include a related set of variables (i.e. serum albumin levels and lymphocyte counts) and were shown to be similarly prognostic (Figure 3). Nevertheless, the CONUT score includes low total cholesterol levels, a risk factor associated with inferior OS in our study. In addition, the AUC of the CONUT score was higher than that of the GNRI and PNI; thus, it seems that the CONUT score might provide additional information and perhaps identify an additional proportion of HD patients at an increased risk of death. However, future studies on a larger number of patients are needed to confirm our observations. Also, as this study only assessed baseline nutritional status, longitudinal assessment of nutrition is lacking and prospective studies are needed to elucidate whether the CONUT score might be able to guide nutritional support in order to improve outcomes in maintenance HD patients.

Besides nutrition, higher CONUT score might also reflect a higher degree of systemic inflammation, as it is derived from serum albumin concentration and absolute lymphocyte counts. Studies have shown that proinflammatory cytokines (such as interleukin-6 or tumor necrosis factor-alpha) can cause decreased serum albumin concentrations through the increased consumption and *via* down-regulation of albumin synthesis in hepatocytes (23,24). Furthermore, elevated NLR has been shown to correlate with higher inflammation, lower hemoglobin and serum creatinine levels, and to accurately predict mortality among HD patients (25,26). Interestingly, higher CONUT score was associated with lower hemoglobin, higher CRP, elevated NLR and higher serum immunoglobulin levels in our study as well; therefore, higher CONUT score could also reflect on another adverse pathophysiological process in HD patients, systemic inflammation (1-4).

Interestingly, higher CONUT score in our HD patients seemed to be mostly caused by lower protein reserves and caloric depletion (as indicated by markedly lower serum albumin and total cholesterol levels in the higher CONUT score risk groups). More importantly, both lower serum albumin and total cholesterol levels were associated with inferior OS. This paradoxical association of hypocholesterolemia and OS in maintenance HD patients was recognized a decade ago and was most pronounced in hypoalbuminemic patients and in those with a low dietary protein intake, indicating a detrimental effect of malnutrition on survival (27). On the other hand, absolute lymphocyte counts were similar between the light and moderate risk groups (in both groups, the mean lymphocyte count was >1200/mm^3, assigning only 0 or 1 points to the majority of patients). Of note, only two patients in our study had absolute lymphocyte count <800/mm^3; none of them had a severe CONUT score. This might represent a selection bias with exclusion of the severely malnourished patients who could have experienced unfavorable outcomes prior to study entry. In addition, during the study period, patients might have been exposed to different enteral supplements (i.e. patients with cancers, systemic autoimmune disorders or nephrotic-range proteinuria) that could have modulated different patient characteristics (such as serum albumin and total cholesterol levels), as well as patient outcomes. For this reason, future studies are needed to analyze clinical correlations and outcomes of severely malnourished patients (according to the CONUT score), as well as the ability of the CONUT score to identify HD patients at an increased risk of infection due to secondary lymphocyte depletion.

Other notable limitations of this study were its single-center retrospective design and small number of patients included. Due to the retrospective design of the study, we were also unable to assess other important anthropometric measures at baseline, i.e. body composition or waist circumference (5).

CONCLUSION

The results of this study suggest that the CONUT score might be used for rapid nutritional screening and for prediction of mortality in maintenance HD patients; however, our observations need confirmation on larger datasets, or even better, in a prospective trial.

R E F E R E N C E S

1. Zyga S, Christopoulou G, Malliarou M. Malnutrition-inflammation-atherosclerosis syndrome in patients with end-stage renal disease. J Ren Care 2011; 37(1): 12-5. doi: 10.1111/j.1755-6686.2011.00201.x

2. Kalantar-Zadeh K, Ikizler TA, Block G, Avram MM, Kopple JD. Malnutrition-inflammation complex syndrome in dialysis patients: causes and consequences. Am J Kidney Dis 2003; 42: 864-81. doi: 10.1016/j.ajkd.2003.07.016

3. Obi Y, Qader H, Kovesdy CP, Kalantar-Zadeh K. Latest consensus and update on protein-energy wasting in chronic kidney disease. Curr Opin Clin Nutr Metab Care 2015; 18: 254-62. doi: 0.1097/MCO.0000000000000171

4. Maraj M, Kuśnierz-Cabala B, Dumnicka P *et al.* Malnutrition, inflammation, atherosclerosis syndrome (MIA) and diet recommendations among end-stage renal disease patients treated with maintenance hemodialysis. Nutrients 2018; 10(1): 69. doi: 10.1097/MCO.0000000000000171

5. Ikizler TA, Burrowes JD, Byham-Gray LD *et al.* KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update. Am J Kidney Dis 2020; 76(3 Suppl 1): S1-S107. doi: 10.1053/j.ajkd.2020.05.006

6. Ignacio de Ulíbarri J, González-Madroño A, de Villar NG *et al.* CONUT: a tool for controlling nutritional status. First validation in a hospital population. Nutr Hosp 2005; 20(1): 38-45. PMID: 15762418

7. Kuroda D, Sawayama H, Kurashige J *et al.* Controlling Nutritional Status (CONUT) score is a prognostic marker for gastric cancer patients after curative resection. Gastric Cancer 2018; 21(2) :204-12. doi: 10.1007/s10120-017-0744-3

8. Takamori S, Toyokawa G, Taguchi K *et al.* The Controlling Nutritional Status score is a significant independent predictor of poor prognosis in patients with malignant pleural mesothelioma. Clin Lung Cancer 2017; 18(4): e303-e313. doi: 10.1016/j.cllc.2017.01.008

9. Toyokawa G, Kozuma Y, Matsubara T *et al.* Prognostic impact of Controlling Nutritional Status score in resected lung squamous cell carcinoma. J Thorac Dis 2017; 9(9): 2942-51. doi: 10.21037/jtd.2017.07.108

10. Kono T, Sakamoto K, Shinden S, Ogawa K. Pre-therapeutic nutritional assessment for predicting severe adverse events in patients with head and neck cancer treated by radiotherapy. Clin Nutr 2017; 36(6): 1681-5. doi: 10.1016/j.clnu.2016.10.021

11. Zhou H, Chao W, Cui L, Li M, Zou Y, Yang M. Controlling Nutritional Status (CONUT) score as immune-nutritional predictor of outcomes in patients undergoing peritoneal dialysis. Clin Nutr 2019; 39(8): 2564-70. doi: 10.1016/j.clnu.2019.11.018

12. Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward. Kidney Int 2014; 85: 49-61. doi: 10.1038/ki.2013.444

13. Locatelli F, Nissenson AR, Barrett BJ *et al.* Clinical practice guidelines for anemia in chronic kidney disease: problems and solutions. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2008; 74(10): 1237-40. doi: 10.1038/ki.2008.299

14. Xiong J, Wang M, Zhang Y *et al.* Association of Geriatric Nutritional Risk Index with mortality in hemodialysis patients: a meta-analysis of cohort studies. Kidney Blood Press Res 2018; 43(6): 1878-91: doi: 10.1159/000495999

15. Takahashi H, Ito Y, Ishii H *et al*. Geriatric Nutritional Risk Index accurately predicts cardiovascular mortality in incident hemodialysis patients. J Cardiol 2014; 64(1): 32-6. doi: 10.1016/j.jjcc.2013.10.018

16. Hwang W, Cho MS, Oh JE *et al*. Comparison of creatinine index and Geriatric Nutritional Risk Index for nutritional evaluation of patients with hemodialysis. Hemodial Int 2018; 22(4): 507-14. doi: 10.1111/hdi.12674

17. Onodera T, Goseki N, Nosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nihon Geka Gakkai Zasshi 1984; 85: 1001-5. PMID: 6438478

18. Zhang H, Tao Y, Wang Z, Lu J. Evaluation of nutritional status and prognostic impact assessed by the prognostic nutritional index in children with chronic kidney disease. Medicine (Baltimore) 2019; 98(34): e16713. doi: 10.1097/MD.0000000000016713

19. Kurumisawa S, Kawahito K. Risk analysis using the prognostic nutritional index in hemodialysis-dependent patients undergoing cardiac surgery. J Artif Organs 2018; 21(4): 443-9. doi: 10.1007/s10047-018-1056-z

20. Kang SH, Cho KH, Park JW, Yoon KW, Do JY. Onodera's prognostic nutritional index as a risk factor for mortality in peritoneal dialysis patients. J Korean Med Sci 2012; 27(11): 1354-8. doi: 10.3346/jkms.2012.27.11.1354

21. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. A malnutrition-inflammation score is correlated with morbidity and mortality in maintenance hemodialysis patients. Am J Kidney Dis 2001; 38(6): 1251-63. doi: 10.1053/ajkd.2001.29222

22. Beto JA, Bansal VK, Hart J, McCarthy M, Roberts D. Hemodialysis prognostic nutrition index as a predictor for morbidity and mortality in hemodialysis patients and its correlation to adequacy of dialysis. Council on Renal Nutrition National Research Question Collaborative Study Group. J Ren Nutr 1999; 9(1): 2-8. doi: 10.1016/s1051-2276(99)90015-8

23. Honda H, Qureshi AR, Heimbürger O *et al*. Serum albumin, C-reactive protein, interleukin 6, and fetuin A as predictors of malnutrition, cardiovascular disease, and mortality in patients with ESRD. Am J Kidney Dis 2006; 47(1): 139-48. doi: 10.1053/j.ajkd.2005.09.014

24. Peters SJ, Vanhaecke T, Papeleu P *et al.* Co-culture of primary rat hepatocytes with rat liver epithelial cells enhances interleukin-6-induced acute-phase protein response. Cell Tissue Res 2010; 340(3): 451-7. doi: 10.1007/s00441-010-0955-y

25. Ouellet G, Malhotra R, Penne EL *et al*. Neutrophil-lymphocyte ratio as a novel predictor of survival in chronic hemodialysis patients. Clin Nephrol 2016; 85(4): 191-8. doi: 10.5414/CN108745

26. Catabay C, Obi Y, Streja E *et al.* Lymphocyte cell ratios and mortality among incident hemodialysis patients. Am J Nephrol 2017; 46(5): 408-16. doi: 10.1159/000484177

27. Kilpatrick RD, McAllister CJ, Kovesdy CP *et al.* Association between serum lipids and survival in hemodialysis patients and impact of race. J Am Soc Nephrol 2007; 18(1): 293-303. doi: 10.1681/ASN.2006070795

SAŽETAK

NUTRITIVNI ZBROJ *(CONTROLLING NUTRITIONAL STATUS – CONUT)* MOŽE PREDVIDJETI PREŽIVLJENJE BOLESNIKA NA HEMODIJALIZI

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Pothranjenost uzrokuje značajan pobol i smrtnost bolesnika na hemodijalizi (HD). *Controlling Nutritional Status* (CONUT) je jednostavan nutritivni zbroj koji cjelovito procjenjuje uhranjenost, a sastoji se od serumske koncentracije albumina, apsolutnog broja limfocita i koncentracije serumskog kolesterola. Ova unicentrična retrospektivna studija analizirala je prediktivnu sposobnost zbroja CONUT da procijeni preživljenje bolesnika na HD. Ukupno preživljenje mjereno je kao vrijeme od prve HD do smrti ili posljednjeg pregleda bolesnika, a krivulje preživljenja uspoređene su Kaplan-Meirovom metodom, dok je Coxova regresijska metoda primijenjena u multivarijatnim analizama. Uključeno je 89 bolesnika, od toga 35 (39,3 %) žena; srednja dob bila je 65,76 godina (±14). Srednji zbroj CONUT bio je 3. Viši zbroj CONUT korelirao je s nižim koncentracijama serumskog lipoproteina niske gustoće, višim serumskim kreatininom, višim serumskim C-reaktivnim proteinom i višim omjerom neutrofila/limfocita, kao i s većom učestalošću nefrotske proteinurije (p<0,050 za sve analize). U univarijatnoj analizi je viši zbroj CONUT (≥5) bio povezan s lošijim preživljenjem (medijan 54 prema 112 mjeseci, HR 2,27; p=0,013). U multivarijatnoj Coxovoj regresijskoj analizi je viši CONUT ostao nezavisno povezan s lošijim preživljenjem (HR 9,50; p=0,002) kada je bio ispravljen za dob, spol, šećernu bolest i nefrotsku proteinuriju. Zaključno, zbroj CONUT može identificirati bolesnike na HD s povišenim rizikom od smrti. Potrebne su dodatna istraživanja kako bi se analizirala sposobnost zbroja CONUT da usmjeri nutritivnu potporu u bolesnika na HD.

Ključne riječi: pothranjenost, upala, preživljenje, CONUT, hemodijaliza