Research Article

Pamukkale Medical Journal
doi:https://dx.doi.org/10.31362/patd.1497044

Controlling nutritional (CONUT) score for nutritional screening in kidney transplant recipients

Böbrek transplantli bireylerde beslenme takibi için CONUT skoru

Esin Avcı, Belda Dursun, Rukiye Nar, Süleyman Demir

Posted date:05.07.2024 Acceptance date:09.09.2024

Abstract

Purpose: Nutrition is severely impaired in individuals with renal impairment, and transplant often ameliorates this condition. In this study, we aimed to evaluate the controlling nutritional status (CONUT) score of kidney transplant (KT) recipients.

Materials and methods: Using the data from the nephrology transplant unit, we analyzed 188 patients whose data on the constituents of the CONUT score were available. We included KT individuals with at least one lymphocyte count and total cholesterol and albumin concentrations. This data has been used to calculate the CONUT score. The decrease of lymphocyte counts, and total cholesterol was determined with 0, 1, 2, and 3 points, and the reduction of albumin was assigned with 0, 2, 4, and 6 points in agreement with disease severity. Patients were classified according to this score: normal, light, moderate, and severe.

Results: There were 130 patients in normal, 54 in light, and three in moderate and one in severe group. The CONUT score was good for regular-weight patients both before and after transplantation. All laboratory findings revealed significant differences between CONUT groups (p<0.05).

Conclusion: After transplantation, the number of patients in the underweight group decreased when normal weight and obesity increased. However, some patients' nutrition was not ameliorated. The CONUT score may be a useful tool for monitoring transplant patients' nutritional status.

Keywords: Kidney transplantation, nutrition process, clinical laboratory test, risk scores.

Avci E, Dursun B, Nar R, Demir S. Controlling nutritional (CONUT) score for nutritional screening in kidney transplant recipients. Pam Med J 2024;17:714-720.

Öz

Amaç: Kronik böbrek hastalığı hastanın nutrisyonel durumunu bozmaktadır. Nakil bu tabloyu sıklıkla düzeltir. Çalışmamızda böbrek transplantı olan bireylerde nutrisyonel durumu değerlendirmek için kontrol beslenme durumu (CONUT) skorunu değerlendirmeyi amaçladık.

Gereç ve yöntem: Böbrek nakli olan bireyleri takip eden Nefroloji bilim dalından gelen verileri kullanarak, 188 bireyin CONUT skorunu hesaplamayı amaçladık. Laboratuvar bilgi sisteminde en az bir kez ölçülmüş, lenfosit sayısı, total kolesterol ve albümin düzeyleri olan nakilli bireylerini dahil ettik. Lenfosit sayısı ve toplam kolesteroldeki azalma 0, 1, 2 ve 3 puanla, albümin azalması ise hastalığın şiddetine göre 0, 2, 4 ve 6 puanla belirlendi. Hastalar bu skora göre normal, hafif, orta ve ağır olarak sınıflandırıldı.

Bulgular: Normal grupta 130, hafif grupta 54, orta grupta 3 ve ağır grupta bir hasta vardı. CONUT skoru normal kilolu hastalar için hem nakil öncesinde hem de sonrasında iyiydi. Tüm laboratuvar bulguları CONUT grupları arasında anlamlı fark olduğunu ortaya koydu (p<0,05).

Sonuç: Transplantasyon sonrası normal kilolu ve obez birey sayısı artarken, az kilolu hasta sayısı azaldı. CONUT skoru transplante hastaların beslenme durumunu izlemede etkin bir araç olarak öne sürülebilir.

Anahtar kelimeler: Böbrek nakli, nutrisyonel durum, klinik laboratuvar testleri, risk skorlama.

Avcı E, Dursun B, Nar R, Demir S. Böbrek transplantli bireylerde beslenme takibi için CONUT skoru. Pam Tıp Derg 2024;17:714-720.

Esin Avcı, Assoc. Prof. Department of Medical Biochemistry, Medicine Faculty of Pamukkale University, Kınıklı, Denizli, Türkiye, e-mail: eavci@pau.edu.tr (https://orcid.org/0000-0002-5366-2572) (Corresponding Author)

Belda Dursun, Prof. Department of Nephrology, Medicine Faculty of Pamukkale University, Kınıklı, Denizli, Türkiye, e-mail: bdursun@pau.edu.tr (https://orcid.org/0000-0003-3235-0577)

Rukiye Nar, Assoc. Prof. Department of Medical Biochemistry, Medicine Faculty of Pamukkale University, Kınıklı, Denizli, Türkiye, e-mail: rnar@pau.edu.tr (https://orcid.org/0000-0002-1062-0217)

Süleyman Demir, Prof. Department of Medical Biochemistry, Medicine Faculty of Pamukkale University, Kınıklı, Denizli, Türkiye, e-mail: suleyman@pau.edu.tr (https://orcid.org/0000-0003-4156-4040)

Introduction

Chronic kidney disease (CKD) is characterized with loss of kidney function or structural alterations that have been determined more than three months and have health implications [1]. In CKD, irreversible abnormalities in kidney structure are due to ischemic, toxic, or metabolic damage. Inflammation and malnutrition may cause severe complications and increase the mortality rate in CKD patients [2, 3].

Recently, dialysis and kidney transplantation (KT) have been the applicable treatment modalities. KT is the best proper treatment for individuals with end-stage renal disease [4]. Nutritional status of patients is important after KT. The patient's nutrition after kidney transplantation is affected by many factors, such as the period after transplantation, the stage of deterioration in kidney function (chronic kidney disease stages 1-5), side effects of immunosuppressants and other drugs, interactions of drugs with foods, and the immune- regulating effects of some food additives. The patient's metabolic homeostasis after transplant surgery is affected by many factors, for example time after surgery, renal function, side effects of drugs, possible food-drug interferences, especially side effects of immune-suppressive [4, 5].

About 25% of transplanted patients are overweight/obese with hypertension, hyperglycaemia, and more extended hospitalization periods [6]. On the other hand, malnutrition is usually related to an increased morbidity ratio after organ transplantation [7].

Therefore, predicting prognosis using pre-treatment clinical variables is important to ensure recovery and offer an optimal monitoring strategy. In the literature, hs-CRP, IL-6 and TNF-α are the most known inflammation markers and they have potential role in the prognosis of chronic diseases. Many nutritional scores have been used to monitor the prognosis of this clinical situation. The CONtrolling NUTritional status (CONUT) score is widely used to control nutritional status in chronic diseases and malignancies [8]. This index has so many advantages for monitoring nutritional status in inflammatory diseases because it is cost-effective, simple to calculate, and non-invasive [9, 10]. However, the usefulness of CONUT in assessing patients who underwent KT has not been determined yet. We initiate to evaluate the CONUT score to determine whether protein-energy metabolism is valuable for monitoring nutritional situations in kidney transplant patients in present study.

Materials and methods

We included 188 kidney transplant recipients who underwent KT surgery and followed up at Pamukkale University Nephrology Department. We collected gender, age, etiology of CKD, hypertension, immune suppressive agent, donor relationship, diabetes mellitus status, weight and height findings before-after transplantation, transplantation date, and laboratory results from the Hospital Information System (HIS) between February 2018 and February 2019. The study was done with the approval of the ethical board of the Pamukkale University Medicine Faculty, Denizli, Türkiye (16.01.2018/02).

We used serum total cholesterol and albumin levels, and total lymphocyte counts for this nutritional score. We showed calculating this score in detail in Table 1 [10].

Table 1. Scoring system for the CONUT

Parameter	Undernutrition degree			
	None	Light	Moderate	Severe
Serum albumin (g/dL)	≥3.50	3.00-3.49	2.50-2.99	<2.50
Score	0	2	4	6
Total lymphocyte count (K/uL)	≥1600	1200-1599	800-1199	<800
Score	0	1	2	3
Total cholesterol (mg/dL)	≥180	140-179	100-139	<100
Score	0	1	2	3

CONUT score= Serum albumin score + Total lymphocyte count score + Total cholesterol score
The risk of malnutrition is classified as normal (score 0-1), light (2-4), moderate (5-8) and severe

All analyses were performed by a IBM SPSS Statistics 25 software. Continuous variables were indicated as mean ± standard deviation; qualitative variables were meant as counts. Shapiro–Wilk and Kolmogorov Smirnov tests revealed test normality. We used the independent samples t-test when parametric test hypotheses were for independent groups' comparisons. The Mann-Whitney U test was used when parametric test hypotheses were not provided. Spearman correlation analysis were used to analyse the relationships between continuous variables. Statistical significance was determined as $p<0.05$.

Results

The sample consisted of 71 males and 117 females, with a mean age of 45.68±13.02 years, ranging from 19 to 72 years old. One hundred forty-four subjects had received their kidneys from living donors (76.5%), and 44 from cadaver donors (23.5%). The causes of CKD were as follows: diabetic nephropathy (n=84, 45%), chronic glomerulonephritis (n=73, 39%), genetic disorders (n=11, 6%), hypertensive nephrosclerosis (n=8, 4%) and idiopathic (n=12, 6%). A total of 26 out of all subjects were given cyclosporine, and 162 were tacrolimus therapy. The average time after transplantation was 84 months (24-120 months). According to CONUT score calculation; there were 130 patients in the normal group; 54 were in light, three were in moderate, and one was in severe. There was one KT recipient in the severe group, so we merged moderate and severe under one heading as "moderate". By taking into consideration CONUT, we compared patients body mass index (BMI) before and after transplant. The results revealed CONUT was well related to normal weight patients in both periods. Most patients were included in the overweight group after the transplant.

The moderate group was not included in the comparisons due to an insufficient number of subjects. We only compared normal and light groups; there is a statistical difference between two groups on behalf of routine laboratory analytes (Table 2). Spearmean's correlation coefficients between indices patients' characteristics are shown in Table 3. Our data revealed strong negative correlation between total cholesterol and CONUT score (r=-0.75). All other coefficients were <0.7 could be accepted as moderate relations, all the statistical significance.

Table 2. All rotuine parameters of individuals and the comparison of normal and light groups

	Normal (n=130)	Light (n=54)	Moderate (n=4)	*p*
White blood cell(K/uL)	8.47 (4.99-21.15)	6.72 (1.69-13.65)	4.38 (3.01-9.11)	0.0001* (z=-3.722)
Red blood cell(M/uL)	4.74±0.78	4.4±0.8	3.02±0.4	0.01* (t=2.602)
Hemoglobin (g/dL)	13.23±1.98	12.49±2.13	9.18±1.63	0.028* (t=2.214)
Hematocrit (%)	40.54±5.88	38.24±6.62	26.98±4.81	0.023* (t=2.285)
Platelet(K/uL)	245.5 (14.2-514)	220.5 (110-415)	183.5 (37-216)	0.024* (z=-2.262)
Lymphocyte (K/uL)	2.37 (1.12-54.6)	1.47 (0.61-3.33)	0.83 (0.57-2.14)	0.0001* (z=-5.758)
Monocyte(K/uL)	0.62 (0.32-2.95)	0.51 (0.25-1.14)	0.5 (0.24-1.05)	0.004* (z=-2.854)
Basophile(K/uL)	0.03 (0.01-0.7)	0.03 (0-0.6)	0.02 (0.01-0.03)	0.007* (z=-2.688)
Neutrophil(K/uL)	4.98 (0.04-15.16)	4.32 (0.47-11.43)	2.98 (1.63-5.71)	0.043* (z=-2.02)
Urea (mg/dl)	39 (18-153)	48.5 (20-162)	62.5 (54-136)	0.041* (z=-2.041)
BUN (mg/dl)	18 (8-71)	22.5 (9-76)	29 (25-64)	0.037* (z=-2.09)
Creatinine (mg/dl)	1.26 (0.58-9.87)	1.6 (0.7-9.86)	3.18 (0.6-13.16)	0.009* (z=-2.627)
Calcium (mg/dl)	9.66 (7.69-11.92)	9.32 (7.61-10.3)	9.12 (7.78-12.8)	0.0001* (z=-3.966)
Phosphorus (mg/dl)	3.27 (1.98-7.04)	3.57 (2.4-5.67)	4.07 (1.86-5.25)	0.013* (z=-2.495)
ALT (IU/L)	16 (5.8-88)	12 (4-90)	17 (12-37)	0.002* (z=-3.116)
AST (IU/L)	17 (8-37)	15 (8-86)	28 (9-57)	0.035* (z=-2.109)

Table 2. All rotuine parameters of individuals and the comparison of normal and light groups (contunied)

Triglyceride (mg/dl)	148.5 (53-464)	117 (40-218)	138 (83-213)	0.0001* (z=-3.816)
Cholesterol (mg/dl)	197 (141-295)	137.5 (86-230)	142 (131-161)	0.0001* (z=-7.994)
HDL cholesterol(mg/dl)	49.5 (22-108)	43.5 (21-113)	33 (20-50)	0.001* (z=-3.457)
LDL cholesterol (mg/dl)	114 (61-206)	73 (37-152)	86.5 (51-101)	0.0001* (z=-6.944)
VLDL (mg/dl)	30 (11-73)	23.5 (8-44)	27.5 (17-43)	0.0001* (z=-3.867)
GFR_CKD_EPI (ml/dk)	63.8±23.44	52.88±31.81	10±5.66	0.048* (t=2.027)

*p<0.05 statistically significant; t: Independent Samples t test; z: Mann Whitney U test; Descriptive statistics are shown as Mean ± Standart Deviation; Moderate group was not included in the comparisons due to insufficient number of subjects

Table 3. Relations between CONUT, laboratory parameters, and clinical findings

	CONUT	
	r	***p***
BMI (After Tx)	-0.276	0.0001*
BMI (Before Tx)	-0.201	0.006*
White Blood Cell	-0.363	0.0001*
Red Blood Cell	-0.276	0.0001*
Hemoglobin	-0.197	0.006*
Hematocrit	-0.208	0.004*
Mean corpuscular volume	0.153	0.034*
Mean corpuscular hemoglobin	0.153	0.035*
Platelet	-0.244	0.001*
Lymphocyte	-0.508	0.0001*
Monocyte	-0.287	0.0001*
Basophile	-0.329	0.0001*
Urea	0.163	0.024*
Creatinine	0.174	0.016*
Calcium	-0.26	0.0001*
Phosphorus	0.167	0.021*
ALT	-0.209	0.004*
Triglyceride	-0.348	0.0001*
Cholesterol	-0.75	0.0001*
HDL cholesterol	-0.235	0.001*
LDL cholesterol	-0.651	0.0001*
VLDL cholesterol	-0.34	0.0001*
Creatinine clearance	-0.167	0.025*

*statistically significant correlation; r: Spearman Correlation Coefficient

Discussion

Our study suggested that CONUT is a rapid and quick-to-use screening tool for kidney transplant patients, requiring only three laboratory parameters for estimation. Our study showed that the transplant ameliorated patients' nutrition. After transplantation, the number of patients in the underweight group decreased when normal weight and obesity increased.

When we classified KT patients into three groups with reference to CONUT estimation, some hemogram parameters, calcium, phosphorus, cholesterol panel tests, and liver and kidney function tests were better in the normal group.

CONUT was first validated by De Ulibarri et al. [11] in a sample of 53 individuals from different service hospitals in Spain. The authors computed a nutritional formula estimated with albumin, lymphocyte, and cholesterol and revealed that CONUT seemed to be an efficient tool for early detection and continuous control of hospital under nutrition. After this validation, the CONUT score was managed in many studies to evaluate nutritional situations and clinical outcomes. Literature revealed that in both cancers and chronic situations, CONUT can be an independent predictor of all-cause mortality.

Liu et al. [12] and his friends set up a study with 9764 participants, this score may serve as a valuable biomarker in foreseeing clinical consequences in patients with gastric cancer. Di Vincenzo et al. [13] revealed CONUT is an independent prognostic score by evaluating 15 studies including 16 929 stroke patients, and it is not also related with nutrition but also could be independent risk factor for infections and major disabilities authors suggested.

Fukushima et al. [14] revealed that CONUT helps predict the long-term prognosis of 58 patients with end-stage liver diseases. By assessing five models, the authors revealed the patient had a higher risk factor for mortality with high CONUT scores. Narumi et al. [15], patients with high CONUT score with chronic heart failure. Harimoto et al. [16] estimated the CONUT score in hepatocellular carcinoma patients, and Toyokawa et al. [9] established CONUT in patients with resectable thoracic esophageal squamous cell carcinoma.

In our study, CONUT score was not only well correlated with nutritional parameters in transplant but also related to the 24-hour creatinine clearance test (-0.167, p=0.025), which was a gold standard test showing CKD stage. An increased CONUT score was related to low creatinine clearance, high creatinine, and urea levels.

Lower GFR_CKD_EPI is a lousy indicator not only of all-cause morbidity/mortality but also of worsening nutrition. Takagi et al. [17] evaluated CONUT in 311 end stage CKD patients who stably initiated dialysis. During the following period, 100 patients died because of some complications and the patients with higher CONUT scores. Likely Takagi et al. [17], Huo et al. [18] studied this score in diabetic kidney disease and showed CONUT was an independent risk factor for development of end stage renal disease. Zhou et al. [19] assessed the CONUT score, in total of 252 patients with ESRD initially undergoing peritoneal dialysis. In the 1.9-year period, 35 patients died who had a high score of CONUT.

In our study, our kidney transplant patients have low CONUT scores, and there weren't any deaths, so we showed that we can use this score, an independent indicator of death in chronic diseases, to monitor well-being. As life expectancy with a transplanted kidney increase, the nutritional score also improves.

This study has some limitations because it is a retrospective study and a single hospital experience. On the other hand, one patient is in the severe group and four patients are in the moderate group; so, we can only compare two groups, light and normal. By increasing the number of patients monitored and extending the period, the relationship between high CONUT values and mortality can be evaluated by including more patients in these groups. This point showed us that CONUT is more valuable for monitoring kidney transplant recipients before and after surgery. A prospective study by Zarifi et al. [20], conducted among 40 kidney transplant recipients and 40 healthy adults, revealed that transplantation improved clinical and nutritional status. They showed that the malnutrition index percentage gradually decreased in the following period.

This study aimed to evaluate kidney transplant patients' nutrition with CONUT score. Our study will shed light on other studies conducted on kidney transplant patients.

In conclusion, nutritional status has been shown to be a relevant clinical factor in patients with kidney transplant patients. This comprehensive analysis showed that the CONUT score is a valuable monitoring tool for kidney transplant patients, which is an objective and non-invasive approach.

Conflict of interest: No conflict of interest was declared by the authors.

References

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl 2013;3:4. https://doi.org/10.1038/kisup.2012.76
2. Çiçek EA, Rota S, Dursun B, Kavalci E. Evaluation of serum NGAL and hepcidin levels in chronic kidney disease patients. Ren Fail 2016;38:35-39. https://doi.org/10.3109/0886022X.2015.1107823
3. Munib S, Ahmed T, Ahmed R, Din NU. Renal allograft biopsy findings in live-related renal transplant recipients. J Coll Physicians Surg Pak 2021;31:197-201. https://doi.org/10.29271/jcpsp.2021.02.197
4. Allawi AAD. Malnutrition, inflamation and atherosclerosis (MIA syndrome) in patients with end stage renal disease on maintenance hemodialysis (a single centre experience). Diabetes Metab Syndr 2017;12:91-97. https://doi.org/10.1016/j.dsx.2017.09.003
5. Keshavarz Shahbaz S, Pourrezagholi F, Nafar M, et al. Dynamic variation of kidney injury molecule-1 mRNA and protein expression in blood and urine of renal transplant recipients: a cohort study. Clin Exp Nephrol 2019;23:1235-1249. https://doi.org/10.1007/s10157-019-01765-y
6. Veroux M, Corona D, Sinagra N, et al. Nutrition in kidney transplantation. Int J Artif Organs 2013;36:677-686. https://doi.org/10.5301/ijao.5000234
7. Marino LV, Romão EA, Chiarello PG. Nutritional status, energy expenditure, and protein oxidative stress after kidney transplantation. Redox Rep. 2017;22:439-444. https://doi.org/10.1080/13510002.2017.1325572
8. Hwang JH, Ryu J, An JN, et al. Pretransplant malnutrition, inflammation, and atherosclerosis affect cardiovascular outcomes after kidney transplantation. BMC Nephrol 2015;16:1-12. https://doi.org/10.1186/s12882-015-0108-3
9. Toyokawa T, Kubo N, Tamura T, et al. The pretreatment Controlling Nutritional Status (CONUT) score is an independent prognostic factor in patients with resectable thoracic esophageal squamous cell carcinoma: results from a retrospective study. BMC Cancer 2016;16:1-4. https://doi.org/10.1186/s12885-016-2696-0
10. Yoshihisa A, Kanno Y, Watanabe S, et al. Impact of nutritional indices on mortality in patients with heart failure. Open Heart 2018;5:1-8. https://doi.org/10.1136/openhrt-2017-000730
11. De Ulíbarri JI, Gonzalez Madrono A, De Villar NGP, et al. CONUT: a tool for controlling nutritional status. Nutr Hosp 2005;20:38-45.
12. Liu H, Yang XC, Liu DC, Tong C, Wen W, Chen RH. Clinical significance of the controlling nutritional status (CONUT) score in gastric cancer patients: a meta-analysis of 9,764 participants. Front Nutr 2023;10:1156006(e1-11). https://doi.org/10.3389/fnut.2023.1156006
13. Di Vincenzo O, D'Elia L, Ballarin G, Pasanisi F, Scalfi L. Controlling Nutritional Status (CONUT) score and the risk of mortality or impaired physical function in stroke patients: a systematic review and meta-analysis. Nutr Metab Cardiovasc Dis 2023;33:1501-1510. https://doi.org/10.1016/j.numecd.2023.05.012
14. Fukushima K, Ueno Y, Kawagishi N, et al. The nutritional index 'CONUT' is useful for predicting long-term prognosis of patients with end-stage liver diseases. Tohoku J Exp Med 2011;224:215-219. https://doi.org/10.1620/tjem.224.215
15. Narumi T, Arimoto T, Funayama A, et al. Prognostic importance of objective nutritional indexes in patients with chronic heart failure. J Cardiol 2013;62:307-313. https://doi.org/10.1016/j.jjcc.2013.05.007
16. Harimoto N, Yoshizumi T, Sakata K, et al. Prognostic significance of preoperative Controlling Nutritional Status (CONUT) score in patients undergoing hepatic resection for hepatocellular carcinoma. World J Surg 2017;41:2805-2812. https://doi.org/10.1007/s00268-017-4097-1
17. Takagi K, Takahashi H, Miura T, et al. Prognostic value of the Controlling Nutritional Status (CONUT) score in patients at dialysis initiation. Nutrients 202231;14:2317(e1-11). https://doi.org/10.3390/nu14112317
18. Huo Q, He T, Xiong J, Zhao J. Controlling nutritional status score is associated with renal progression, cardiovascular events, and all-cause mortality in biopsy-proved diabetic kidney disease. Front Physiol 2023;14:1231448(e1-10). https://doi.org/10.3389/fphys.2023.1231448

19. 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 2020;39:2564-2570. https://doi.org/10.1016/j.clnu.2019.11.018

20. Zarifi SH, Shadnoush M, Pahlavani N, et al. Nutritional status in kidney transplant patients before and 6-month after transplantation: result of PNSI study. Clin Nutr ESPEN 2021;41:268-274. https://doi.org/10.1016/j.clnesp.2020.11.024

Ethics committee approval: Permission was obtained from Pamukkale University Non-Interventional Clinical Research Ethics Committee for the study (permission date: 16.01.2018, and number: 02).

Authors' contributions to the article

E.A., B.D., R.N. and S.D. constructed the main idea and hypothesis of the study. E.A. and R.N developed the theory and arranged/edited the material and method section. E.A., B.D., R.N. and S.D. have done the evaluation of the data in the Results section. Discussion section of the article was written by E.A., B.D., R.N. and S.D. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.