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Research Article

Correlation between Count Score and Cardiovascular Events in Maintenance Hemodialysis Patients

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Abstract

Purpose: Evaluating the nutritional status of patients with Maintenance Hemodialysis (MHD) based on CONUT score to explore its relationship with Cardiovascular Disease (CVD) in MHD patients.

Methods: Baseline data of new-coming MHD patients hospital hemodialysis center of our hospital undergoing hemodialysis treatment for the first time from January 1, 2014 to June 30, 2020 was collected. Cardiovascular events were used as the end point. Patients were divided into three groups according to CONUT score: normal nutrition group (CONUT score 0-1), mild malnutrition group (CONUT score 2-4) and moderate to severe malnutrition group (CONUT score ≥5), and the differences of clinical data and prognosis among the three groups were compared. The risk factors of cardiovascular events in MHD patients were determined by Logistic regression analysis, and the predictive ability of the risk factors was observed with Receiver Operating Characteristic (ROC) curve.

Results: A total of 424 MHD patients were included. According to the CONUT score, 31 (7.3%) patients were in the normal nutrition group, 160 (37.7%) patients in the mild malnutrition group, and 233 (55.0%) patients in the moderate to severe malnutrition group. A total of 159 patients had cardiovascular events, including 3 cases (9.7%) in the normal nutrition group, 38 cases (23.8%) in the mild malnutrition group, and 118 cases (50.6%) in the moderate to severe malnutrition group. The worse the nutritional status of patients is, the higher the incidence rate of cardiovascular events is ($P<0.05$). Logistic regression analysis showed that CONUT score and age were independently correlated with cardiovascular events in MHD patients ($P<0.05$). ROC curve analysis showed that CONUT score and age predicted cardiovascular events in MHD patients with areas under the curve were 0.683 (95% CI: 0.632-0.735, $P<0.001$) and 0.702 (95% CI: 0.702), respectively. 0.652 -- 0.753, $P<0.001$), the optimal cut-off points were 4.5 (≥5 in combination) and 68.5, the sensitivity were 74.2% and 49.1%, and the specificity was 56.6% and 81.1%, respectively.

Conclusion: There is a certain correlation between CONUT score the happening of cardiovascular events and MHD patients.

Keywords: Maintenance hemodialysis; Controlling nutritional status score; Cardiovascular events

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Introduction

Despite the significant improvement in overall survival for patients with Maintenance Hemodialysis (MHD) over the decades, it has remained critical to reduce MHD mortality. Cardiovascular Disease (CVD) is the main complication that affects the quality of life after hemodialysis in MHD patients, as well as the main cause of death [1]. Early identification of patients at high risk of CVD is critical to developing targeted preventive measures. It is reported that most CKD patients remain in a state of chronic Wasting, namely, Protein shortage and Energy reserve reduction, which is called "Protein-Energy Wasting (PEW)" [2]. Malnourished MHD patients are more prone to CVD and have a significantly increased risk of death [3,4]. A simple, objective and feasible immune nutrition assessment tool, Controlling Nutritional Status (CONUT) score, has been developed in 2005 [5]. Cardiovascular disease (CVD) is the main complication affecting the quality of life after hemodialysis in MHD patients, as well as the main cause of death[1]. CONUT score can comprehensively reflect the nutritional status of patients and has predictive value for the prognosis of patients with various diseases. Moreover, CVD in peritoneal dialysis patients is independently correlated with all-cause death events [6-8]. At present, the correlation between CONUT score and cardiovascular events in MHD patients is rarely reported. Therefore, the CONUT score was used to evaluate nutritional status in MHD patients and to investigate its predictive value for cardiovascular events.

Subjects and Methods

Subjects

Patients aged ≥18 years old newly admitted from January 1, 2014 to June 30, 2020 who needed long-term maintenance hemodialysis treatment were selected as subjects. Exclusion criteria: (1) acute kidney injury; (2) Previous renal transplantation history, peritoneal dialysis transfer or combined with peritoneal dialysis; (3) Complicated with blood, tumor or autoimmune systemic disease, severe abnormal liver function (such as cirrhosis); (4) recent severe infection, bleeding or cardiovascular disease; (5) Recent history of immunosuppressant and hormone use; (6) Changes in dialysis mode or renal transplantation during follow-up; (7) Lack of medical records and auxiliary examination data.

Data Collection and Grouping

General clinical data of patients were collected. Laboratory data included white blood cell count, lymphocyte count, hemoglobin, albumin, total cholesterol, etc., as well as the use of statins during hospitalization. CONUT score is to score the values of plasma albumin, total cholesterol and lymphocyte count, and calculate the total score of the three indicators. The detailed rules of CONUT scoring and malnutrition grading are shown in (Table 1). The nutritional status of patients was judged according to the sum of CONUT scores, and the higher the score is, the worse the nutritional status is. According to CONUT score, MHD patients were divided into three groups: normal nutrition group (CONUT score 0-1), mild malnutrition group (CONUT score 2-4) and moderate to severe malnutrition group (CONUT score ≥5).

Table 1: CONUT scoring rules and malnutrition classification.

	Eutrophy	Mild Malnutrition	Moderate malnutrition	Severe Malnutrition
Albumin (g/dl)	≥3.5	3.0-3.49	2.5-2.99	<2.5
Score	0	2	4	6
Lymphocyte Count (individual /ml)	≥1600	1200-1599	800-1199	<800
Score	0	1	2	3
Cholesterol (mg/dl)	>180	140-180	100-139	<100
Score	0	1	2	3
Total	0-1	2-4	5-8	9-12

End Point

End point event: The end point of this study was cardiovascular events, including heart failure, ischemic heart disease, malignant arrhythmia, cerebrovascular disease, sudden cardiac death and other related events.

Statistical Method

SPSS26.0 was used to complete data processing. The measurement data of normal distribution or approximate normal distribution are expressed as mean ± standard deviation, while those of non-normal distribution are expressed as median and quartile. With normal distribution and homogeneous variance, one-way ANOVA or independent sample t test was used for comparison between groups. Kruskal-Wallis test or Mann-Whitney U test was used for comparison between groups with abnormal distribution or uneven variance. The categorical variables were described by the number of cases (%), and the Chi-square test or Fisher's exact probability method was used for comparison between groups. The correlation between CONUT score and clinical indicators was analyzed by Spearman correlation, $\rho>0$ indicated positive correlation and $\rho<0$ indicated negative correlation. Logistic regression analysis identified independent risk factors for cardiovascular events in MHD patients, and MHD patients of different ages were analyzed. Meanwhile, the Receiver Operating Characteristic curve (ROC Curve) was plotted and the Area Under the ROC Curve (AUC) was calculated. The optimal diagnostic cut-off value was found and the corresponding sensitivity and specificity were calculated to evaluate the accuracy of CONUT score in predicting cardiovascular events in patients with MHD. $P<0.05$ indicates statistical significance.

Result

General conditions and nutritional distribution characteristics of MHD patients: As of June 30, 2021, a total of 424 MHD patients were included in this study, including 278 (65.6%) males and 146 (34.4%) females, with an average age of 59.78±15.07 years old, 224 (52.8%) ≥60 years old, and 173 (40.8%) patients complicated with diabetes mellitus. There were 347 patients (81.8 %) with hypertension and 46 patients (10.8%) with history of CVD. The mean of CONUT score was 4.81±2.28. According to the CONUT score, the nutritional status of 424 MHD patients included in this study was assessed, of which 31 were normal

(7.3%), 160 were mild (37.7%), and 233 were moderate to severe (55.0%).

Comparison of clinical data of normal nutrition group, mild malnutrition group and moderate and severe malnutrition group: The age of patients with moderate to severe malnutrition was higher than that of the other two groups, and the proportion of patients with diabetes was higher than that of the other two groups (P<0.05). The worse the nutritional status is, the lower the red blood cell count, hemoglobin, lymphocyte count, total protein, serum albumin, creatinine, triglyceride, total cholesterol, low density lipoprotein cholesterol and blood calcium levels (P<0.05) are, but the higher the red blood cell distribution width and CRP level (P<0.05) are. There was no significant difference in other indexes among the three groups. See (Table 2).

CONUT score and cardiovascular events in MHD patients: As of June 30, 2021, 269 among the 424 patients with MHD, There is no cardiovascular events and 159 cardiovascular events, including 63 patients with heart failure (39.6%), 15 patients with ischemic heart disease (9.4%), 11 patients with malignant arrhythmia (6.9%), 51 patients with cerebrovascular disease (32.1%) and 19 patients with sudden cardiac death (12.0%). Among MHD patients with cardiovascular events, 3 cases (1.9%) had normal nutrition, 38 cases (23.9%) had mild malnutrition, and 118 cases (74.2%) had moderate to severe malnutrition. The comparison of CONUT scores and nutritional status distribution based on CONUT scores between patients without cardiovascular events and those with cardiovascular events is shown in (Table 3).

Table 2: Comparison of clinical data among CONUT scores.

	Eutrophy n=31	Mild malnutrition n=160	Moderate to severe malnutrition n=233	*P*
Age	51.35±14.48	58.54±14.71*	61.74±14.97*#	<0.001
Male (%)	18 (41.9)	104 (65.0)	156 (67.0)	0.608
Previous history				
Diabetes (%)	7 (22.6)	55 (34.4)	113 (48.5)*	0.002
Hypertension (%)	26 (83.9)	130 (81.3)	191 (82.0)	0.939
CVDmedical history (%)	1 (3.2)	13 (8.1)	30 (12.9)	0.126
Smoking history (%)	9 (29.0)	42 (26.3)	60 (25.8)	0.926
RBC (10^12/L)	2.97±0.69	2.81±0.67	2.57±0.73*#	<0.001
Hb (g/L)	87.94±19.49	82.11±18.71	74.37±16.69*#	<0.001
RDW (%)	13.80(13.20, 14.40)	14.20(13.50, 15.38)*	14.80(14.00, 15.83)*	<0.001
WBC (10^9/L)	7.42(5.83, 8.79)	6.29(4.87, 7.84)	6.03(4.77, 8.10)	0.069
Lymphocyte count (10^9/L)	1.72±0.47	1.14±0.47*	0.91±0.39*#	<0.001
Neutrophil count (10^9/L)	5.00(3.50, 6.11)	4.58(3.39, 6.10)	4.50(3.45, 6.27)	0.900
PLT (10^9/L)	208.26±72.99	184.06±68.70	185.18±82.59	0.227
TP (g/L)	65.80±5.65	62.84±7.52*	55.48±7.28*#	<0.001
Albumin (g/L)	39.33±2.74	37.67±4.10*	30.09±5.10*#	<0.001
Cr (umol/L)	745.27±352.20	729.38±327.05	680.31±313.97#	0.009
BUN (mmol/L)	20.90 (17.00, 27.50)	22.50 (17.30, 31.05)	22.00 (14.90, 28.95)	0.174
UA (mmol/L)	405.74±145.52	428.89±133.83	418.26±151.50	0.637
Glu (mmol/L)	5.00 (4.46, 6.50)	4.82 (4.37, 5.84)	5.03 (4.36, 6.45)	0.227
TG (mmol/L)	1.83(1.44, 2.85)	1.44(0.99, 2.07)*	1.27(0.93, 2.00)*#	0.001
TCHO (mmol/L)	5.06±0.87	4.28±1.50*	4.03±1.50*#	<0.001
HDL-C (mmol/L)	1.11±0.37	1.12±0.38	1.09±0.39	0.812
LDL-C (mmol/L)	3.24±0.86	2.55±1.24*	2.50±1.24*	0.002
K^+(mmol/L)	4.27 (3.70, 4.94)	4.30 (3.83, 4.96)	4.30 (3.80, 4.90)	0.845
Na^+(mmol/L)	140.4 (138.0, 142.0)	140.0 (137.0, 141.4)	139.4 (136.3, 142.0)	0.380
Clinical medication				
EPO (%)	22 (71.0)	136 (85.0)	197 (84.5)	0.135
Fe^{2+} (%)	16 (51.6)	101 (63.1)	152 (65.2)	0.333
EPO+Fe^{2+} (%)	14 (45.2)	95 (59.4)	146 (62.7)	0.169
HMG-CoA (%)	4 (12.9)	27 (16.9)	53 (22.7)	0.216
Number of days in hospital for first hemodialysis (d)	12 (8, 17)	13 (9, 20)	15 (11, 22)*#	0.002
Clinical prognosis				
CVE (%)	3 (9.7)	38 (23.8)	118 (50.6)*#	<0.001

Note: *P<0.05 V.S. nutrition normal group; #P<0.05 V.S. mild malnutrition group

Table 3: Comparison of CONUT scores between the group without cardiovascular events and the group with cardiovascular events.

	No cardiovascular events n=265	cardiovascular event n=159	*P*
CONUT score	4.26 ± 2.22	5.72 ± 2.11	<0.001
CONUT score was used as a categorical variable			
CONUTscore classification			<0.001
Eutrophy (%)	28 (10.6)	3 (1.9)	
Mild malnutrition (%)	122 (46.0)	38 (23.9)	
Moderate to severe malnutrition (%)	115 (43.4)	118 (74.2)	

Factors influencing cardiovascular events in MHD patients: First, univariate Logistic regression was used to screen possible risk factors for cardiovascular events in MHD patients. The results showed that age, combined hypertension, diabetes, CVD history, length of stay for the first hemodialysis, total protein, creatinine, statins and CONUT score as continuous variables and categorical variables of normal nutrition group (P< 0.001) and moderate to severe malnutrition group (P< 0.001) had statistical differences in the model (P<0.05). Details can been seen in (Table 4). After the indexes with P < 0.05 were screened out in the univariate Logistic regression analysis, the independent risk factors for cardiovascular events in MHD patients were age and CONUT score after further excluding the indexes with high correlation with the COUNT score. The results showed that every one year increase in the age of patients, MHD patients had a 4.2% increased risk of cardiovascular events (P < 0.05), which was statistically significant. In addition, from the perspective of continuous variables, the risk of cardiovascular events in MHD patients increased by 33.1% for every 1-point increase in the COUNT score (P < 0.05), which was statistically significant. From the perspective of COUNT score as a categorical variable, the risk of cardiovascular events predicted by COUNT score of MHD patients in normal nutrition group and moderate to severe malnutrition group was statistically significant (P <0.05). The risk of cardiovascular events in MHD patients in the moderate to severe malnutrition group (CONUT≥5) was 9.364 times higher than that in the normal nutrition group (CONUT 0-1), as shown in (Table 5).

Table 4: Univariate Logistic regression analysis of cardiovascular events in MHD patients.

Variate	OR	95% CI	*P*
Age	1.055	(1.038, 1.071)	<0.001
HT	2.445	(1.370, 4.364)	0.002
Diabetes	2.430	(1.623, 3.639)	<0.001
CVD medical history	3.326	(1.737, 6.369)	<0.001
Number of days in hospital for initial hemodialysis	1.027	(1.012, 1.043)	0.001
TP	0.975	(0.952, 0.999)	0.044
Cr	0.998	(0.998, 0.999)	<0.001
HMG-CoA	2.432	(1.497, 3.951)	<0.001
CONUT score was used as continuous variable			
CONUT score	1.354	(1.228, 1.493)	<0.001
CONUT score was used as a categorical variable			
Eutrophy (0-1 point)	1		<0.001
Mild malnutrition (2-4 point)	2.907	(0.837, 10.097)	0.093
Moderate to severe malnutrition (≥5 point)	8.173	(2.833, 32.375)	<0.001

Table 5: Multivariate Logistic regression analysis of risk factors for cardiovascular events in MHD patients.

Variate	OR	95% CI	*P*
Age	1.042	(1.024, 1.061)	<0.001
CONUT score was used as continuous variable			
CONUT score	1.331	(1.171, 1.513)	<0.001
CONUT score was used as a categorical variable			
Eutrophy (0-1 point)	1		<0.001
Mild malnutrition (2-4 point)	2.862	(0.731, 11.215)	0.131
Moderate to severe malnutrition (≥5 point)	9.364	(2.337, 37.525)	0.002

ROC curve analysis the ability of CONUT score and age to predict CVD in MHD patients: The results of COUNT score and age predicting CVD in MHD patients analyzed by ROC curve can be seen in (Figure 1). The areas of COUNT score and age predicting cardiovascular events under the curve were 0.683 (95% CI:0.632-0.735, P<0.001) and 0.702 (95% CI: 0.652 -0.753, P<0.001), respectively, both of which were between 0.5 and 1, indicating that both of them had statistical significance in predicting CVD in MHD patients. Studies showed that age was an independent risk factor for predicting CVD in MHD patients.

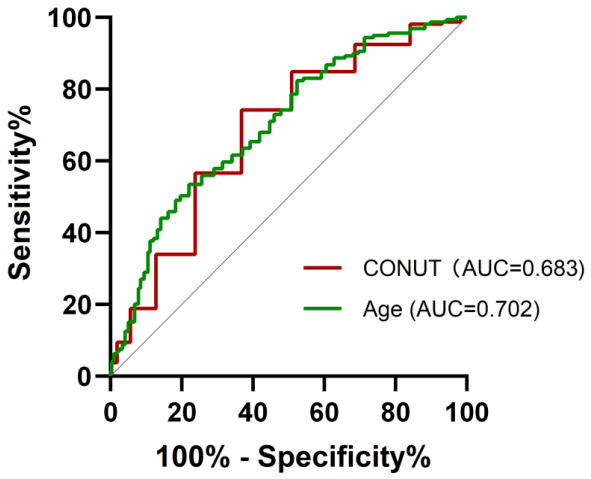

Figure 1: ROC curve of CONUT score and age predicting cardiovascular eventsin MHD patients.

Note: AUC: Area Under Curve; CONUT score: Control Nutritional Status score.

Discussion

The number of people with CKD increases year over year with lifestyle changes and eventually progresses to ESRD over time. Studies have found that the number of patients living with diabetic nephropathy has gradually surpassed that with chronic glomerulonephritis and diabetic nephropathy has been as the primary cause of ESRD patients in China [9]. Among the 424 MHD patients counted in this study, 152 were diabetic nephropathy patients occupying the first place in the composition of the primary disease, accounting for as high as 35.8%; while 138 patients with chronic glomerulonephritis ranking second accounting for 32.5%, which is consistent with the latest research. Currently, a large proportion of patients with ESRD use HD as the first choice for renal replacement therapy [10]. CVD is the most common and serious in the long-term hemodialysis treatment of patients with MHD, resulting in a non-negligible complication of declining quality of life and reduced survival rates [11]. In 2012, a study in China reported that about 56.3% of 1775 MHD patients developed CVD in the long-term hemodialysis process,

and the incidence of cardiac failure ranked first, accounting for 42.9%, which is the most common CVD complication in MHD patients [12]. In this study, 159 cases of cardiovascular events happened, with an incidence rate of 37.5%, which is slightly lower than that of previous studies, which is probably due to the sample size of this study, and with 63 cases (39.6%) of cardiac failure, occupying the first place, which is basically consistent with the statistical results of domestic research.

First of all, the prevalence of hypertension in patients with CKD is generally high, and the proportion of hypertension in this study is as high as 81.8%, and hypertension is the main risk factor for left ventricular hypertrophy and myocardial ischemia, and long-term increase in blood pressure keeps the cardiac afterload at a high level, prompts left ventricular remodeling, and eventually causes cardiac dysfunction. The risk of heart-related complications increases by 44 percent for every 10 mmHg increase in blood pressure which is as previously reported [13]. Secondly, some patients have intravenous fistula anastomosis for renal dialysis operation, and the venous blood flow of patient's increases after surgery, and the return of blood volume and cardiac output surges, which increases the burden on the heart. In addition, due to the patient's excretion disorders of certain toxins in the body, when dialysis is insufficient or the blood flow rate in the blood vessels is too fast and dehydration is too fast during hemodialysis, urea toxin and hemodynamic changes will damage the myocardium and affect the heart function. Finally, due to various factors such as serious renal endocrine dysfunction, insufficient intake and so on, MHD patients are prone to anemia and hypoproteinemia, which leads to insufficient blood and oxygen supply to cardiomyocytes for a long time, accelerated heart rate compensation, and increased cardiac output, which is easy to cause heart problems. Therefore, patients with MHD are prone to CVD under the long-term interaction of these factors.

The incidence of malnutrition in patients with MHD is higher than that in the general population, and some patients are already malnourished at the time of the first hemodialysis, and malnutrition is a recognized and non-traditional risk factor for CVD in patients with MHD, and accurate assessment of the patient's nutritional status at an early stage can effectively estimate the risk of CVD [14,15]. CONUT score is a score of serum albumin, total cholesterol and peripheral blood lymphocytes, the evaluation process is simple, inexpensive, non-invasive, and avoids subjective factors to make it reproducible, can comprehensively evaluate the patient's protein reserve, caloric loss and immune defense function, early screening of malnutrition in hospitalized patients, and has good sensitivity and specificity [5], and can still be used for regular self-nutrition risk monitoring in the follow-up. In recent years, the CONUT score has also been used to evaluate the nutritional status of patients with PD and explore its predictive value for cardiovascular adverse events and death. Zhou et al. used the CONUT score to evaluate the nutritional status of PD patients and found that the CONUT score was a good predictor of CVD and all-cause death in PD patients, while the CONUT score combined with age had higher predictive value [8]. In addition, a latest domestic study concluded that the CONUT score can be used as a nutritional assessment tool for predicting clinical prognosis in elderly patients with MHD, and the risk of death is significantly higher in patients with severe nutritional status than in other nutritional statuses, indicating a possible correlation [16].

The relationship between CONUT score and cardiovascular events in MHD patients has not been fully explored, but the correlation between the various components of CONUT score and cardiovascular events in MHD patients has been independently reported, but serum albumin, total cholesterol and peripheral blood lymphocyte count in vivo will be affected by many factors, and the use of any single index to evaluate the nutritional status of patients may not be comprehensive. Therefore, the CONUT score developed by combining the three is a more efficient tool to evaluate protein metabolism, lipid metabolism, inflammation and immune status of MHD patients at their first hemodialysis hospitalization, and is a reliable biomarker for identifying patients at high risk of CVD, which can improve the ability to predict poor clinical prognosis in MHD patients.

In this study, most patients were malnourished at the beginning of hemodialysis, of which 37.7 percent were mildly malnourished and 55 percent were moderately severe, which is basically consistent with the statistical results of malnutrition in patients with previous MHD [17]. Binary logistic regression analysis showed that CONUT score was independently correlated with cardiovascular events in MHD patients, and patients in the moderate to severe malnutrition group were more likely to develop CVD than patients in the normal nutrition group. After ROC curve analysis, it was found that COUNT score and age were significantly related to cardiovascular events in patients with MHD, which had certain diagnostic significance. After screening the risk factors for cardiovascular events in patients of different age groups, Logistic regression analysis showed that CONUT scores were independently associated with cardiovascular events in middle-aged and elderly patients with MHD.

Therefore, clinical nephrologists can use the CONUT score to conduct nutritional screening on MHD patients admitted to the hospital for the first time on hemodialysis, formulate individualized dietary plans for MHD patients with nutritional problems as soon as possible, try to meet the needs of patients for a variety of nutrients, maintain balanced nutrition, improve nutritional status, and reduce the incidence of adverse clinical prognosis such as cardiovascular events in MHD patients.

Limitations

This study is a single-center, small-sample study, and no significant difference was found when comparing cardiovascular events between the nutritionally normal group and the mildly malnourished group, which may be limited by the size of the sample size or region, and the study did not subdivide moderate malnutrition and severe malnutrition, so it is necessary to expand the total sample size in multi-center and multi-region to conduct in-depth study in the future.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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