Controlling Nutritional Status (CONUT) score as a good predictor of all-cause mortality in elderly hypertensive patients

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Title page

Controlling Nutritional Status (CONUT) score as a good predictor of all-cause mortality in elderly hypertensive patients

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Abstract

Objectives The aim of this study was to elucidate the impact of the nutritional status on survival by Controlling Nutritional Status(CONUT) score and geriatric nutritional risk index (GNRI) in patients with hypertension whose age over 80 y. **Design** Prospective follow-up study. **Participants** A total of 336 hypertensive patients over 80 y were included to this study. **Outcome measures** All-cause death were record Kaplan–Meier curves were plotted to evaluate the association between the CONUT and the all-cause mortality at follow-up. Using Cox regression models to investigate the prognostic value of CONUT and GNRI for all-cause mortality in 90 day after admission. **Results** Patients with higher CONUT score link to high mortality in hypertensive patients in 90 day after admission (1.49% ,6.74%,15.38% respectively, ｘ2 =30.92，P=0.000). Survival patients had a higher BMI (24.25±3.05 vs 24.25±3.05, p=0.012) ,Hemoglobin (123.78±17.05 vs 115.07±20.42 ， P=0.040), albumin level as well as lower FBS(6.90±2.48 vs 8.24±3.51,p=0.010). And also score higher in GRNI(99.42±6.55 vs 95.69±7.77,p=o.oo2) and lower for CONUT(3.13±1.98 vs 5.14±2.32), which both indicated better nutritional status. Kaplan–Meier curves show the survival rates were significantly worse in the high CONUT group compared to the low CONUT group(χ2 =13.372,p=0.001). Cox regression shown increasing hazard ratio (HR) was seen with increasing risk of CONUT (from normal to moderate to severe). HRs (95%CI) for three month mortality were 1.458(1.113-1.909). Both in RTI patients and other reason group, only CONUT was good predictor for all-cause mortality (HR=1.242, 95% confidence interval 1.062–1.452, P = 0.007) in hypertensive patients over 80 y. **Conclusion** Nutritional status assessed using the CONUT, not by other nutrition index ,is good predictors for all-cause mortality in 90 days after admission. Evaluation of nutritional status may provide additional prognostic information in patients with hypertension, and the management of nutritional status is of great significance.

Key word

Nutritional status; CONUT; Hypertension; All-cause mortality.

Strengths of this study

Nutritional status assessed using the CONUT in hypertensive patients aged over 80y can efficiently predict all-cause mortality within 90 d post-admission.

With an increase in CONUT score, the incidence of all-cause mortality exhibits an increasing trend in both RTI and other reasons admission.

Limitation of this study

(1) This study was a single center study that included a relatively small number of patients.

(2) Follow-up studies were performed for only 90 d

INTRODUCTION

The nutritional status of patients has drawn increased attention in the clinical setting. An increasing number of evidence have shown that nutritional and immunologic status upon admission closely is associated with the outcome of patients with cardiovascular disease[1-3]. For elderly patients, the role of nutritional status is more important. Studies indicate that elderly patients with high nutritional risks were more likely to stay longer in the hospital than those without such risks[4]. Nutritional risk was also identified as an independent predictor of functional status and mortality among institutionalized elderly patients[5].

Body mass index(BMI), serum albumin level, and pre albumin level are the most commonly indexes used for nutritional status evaluation in clinical settings. However, these single indexes exhibit limited clinical applications. Consequently, an improved nutritional index has been developed. An increasing number of complex nutritional indicators have emerged in recent years, providing substantial information.The Geriatric Nutritional Risk Index (GNRI) is one of the most commonly used nutritional indicators in the elderly[6].The Controlling Nutritional Status(CONUT) score, which is calculated based on the serum albumin concentration, total peripheral lymphocyte count, and total cholesterol concentration, was developed as a screening tool for early detection of poor nutritional status[7].Each of these two indexes, GNRI and CONUT score, provides good points for nutritional status evaluation, which are widely applied in the evaluation of patients with tumor[8]and undergoing dialysis[9].However, these tools exhibit limited application in cardiovascular disease.

Hypertension, the most commonly occurring disease in the elderly, usually includes comorbidities in the elderly group. When elderly patients are hospitalized because of infection or other reasons the effects of nutritional status on the prognosis of patients have to be evaluated. The more appropriate nutritional index, i.e., GNRI or CONUT score, to use in assessing such patients has to be properly selected. Studies on these issues are rarely reported. This study aimed to elucidate the effect of nutritional status on survival in patients with hypertension and aged over 80 y.

METHODS

Patients

This study included patients with hypertension who were diagnosed using the criteria listed in Chinese Hypertension Prevention Guidepublished in 2010[10],hospitalized from January 2011 to December 2013, and aged >80.The current study was conducted at the People’s Liberation Army General Hospital and sought the full ethical approval of Human Investigation Committee. Informed consent was obtained from each patient.

General information and medical history

General information, including age, sex, lifestyle (smoking and drinking) and basic medical history were collected. Patients were selected based on height, weight, resting heart rate, systolic blood pressure, and diastolic blood pressure.

Detection of nutritional metabolism and related biochemical indexes

Routine blood test upon admission was conducted for all enrolled patients in the Central Laboratory of our hospital. Detection indexes included white blood cells, lymphocytes, platelet, hemoglobin (Hgb), serum creatinine (sCr), albumin (Alb), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBS), blood urea nitrogen(BUN), uric acid(UA), pre albumin (PA), and electrolyte index.

The nutritional status of each patient was also evaluated using two composite indexes: CONUT score and GNRI. The CONUT score was determined in accordance with the tool described in Table 1, which was first used by Ulibarri[7]. The GNRI combining two nutritional indicators, albumin and actual weight compared with ideal body weight, was developed by modifying thenutritional risk index for elderly patients. The GNRI formula is as follows: GNRI=[1.487* serum albumin (g/L)] t[41.7 *present/usual weight (kg)][6].

Follow□up

A follow-up on all selected subjects was conducted after admission for 90 don the average. Follow-up times were set to occur 7, 14, 30,and 90 dafter admission. Follow-ups were conducted by interviewing each patient via telephone and reviewing the medical record of the patient. All-cause mortality was determined at the end of the follow-up period. Death was ascertained from the death record, i.e., a legal document including time, site, and other information.

Statistical analysis

All calculations were performed using SPSS ver. 22.0. For continuous quantitative data, the K–S normality test was first conducted to analyze whether the normal distribution and the normal distribution of quantitative data were analyzed by the independent-samples t-test. Data that were not normally distributed were analyzed by the Mann–Whitney U test. Pearson'schi-squared (χ^2) test was used to analyze categorical variables. Survival curves were generated using the Kaplan–Meier method. Multivariate analysis using a Cox proportional hazards model was used for independent tests of significance. Two-tailed P values <0.05 were considered to indicate significance.

RESULTS

Clinical characteristics

A total of 336 hypertensive patients were enrolled, including 323 males and 13 females, with an average age of 87.39± 5.23 years. All patients were diagnosed as hypertension ranging from 5-27years and received antihypertensive drug treatment.All patients had a history of CAD, 83 patients had a history of myocardial infarction, 29 patients had received stent therapy, 67 cases suffered from chronic heart failure,167 cases had T2DM, and 124 had anemia. Of these cases, 192 were admitted for respiratory tract infection(RTI), and the remaining 144 patients were admitted for non-infective factors, such as angina pectoris and uncontrolled blood pressure, among others.

The CONUT scores of the selected patients were determined, and analysis was conducted by the group. The results are presented in Table 2.Only 5 patients scored over 9, which indicated severe malnutrition. Thus, we combined the data with those of moderate malnutrition for analysis. Heart rate and blood glucose level were higher in people with high CONUT scores than in those with low CONUT scores. The proportion of patients with poor nutritional status due to admission caused by RTI was significantly high(χ^2 =70.835,p=0.000).

Table 3 compares the nutritional index of patients with different reasons for admission. Patients with RTI typically have low nutritional status, which shows low BMI, albumin level, GNRI score, high FBS, and CONUT score upon admission.

Follow-up results

A total of 27 deaths were recorded in the 90-day follow-up, and most of these deaths occurred during the period 30 to 90 d (n=17, 62.97%) post-admission. The parameters and characteristics of different outcomes for the patients are presented in Table 4. No differences in age, sex, and combination of diseases were indicated between different outcomes. Likewise, no differences in systolic blood pressure were found. However, the surviving patients showed increased BMI (24.25±3.05 vs.24.25±3.05, p=0.012), hemoglobin (123.78±17.05 vs. 115.07±20.42, P=0.040),and albumin level, as well as reduced DBP(62.48±9.60 vs. 68.31±12.02, p=0.016) and

FBS(6.90±2.48 vs. 8.24±3.51,p=0.010).No significant difference in plasma pre albumin level between different outcomes was indicated (19.21±8.70 vs.16.25±11.68,p=0.200).

Surviving patients obtained improved scores in GRNI(99.42±6.55 vs. 95.69±7.77,p=0.002)and reduced scores in CONUT(3.13±1.98 vs. 5.14±2.32), both of which indicated improved nutritional status. We found that along with the increase in CONUT score, which suggests worse malnutrition, the incidence of all-cause mortality increased. The same tendency was not observed in the GRNI group, as illustrated in Figure 1.

Survival analysis according to CONUT and GNRI

Survival curves based on different nutritional evaluations were plotted. The survival rates were significantly lower in the high-CONUT group than in the low-CONUT group(χ^2=13.372,p=0.001), as shown in Figure 2.The survival curves based on the GNRI is shown in Figure 3. Differences among groups could not be determined (χ^2=7.694,p=0.053).

Prognostic values of CONUT and GNRI

Multivariate Cox regression analyses were conducted to investigate the possible predictors of all-cause mortality in the study population (Table 5).By regression, both RTI and CONUT were independent predictors of three-month all-cause mortality. Increasing hazard ratios (HR) were observed with increasing risks of CONUT (from normal to moderate to severe). The HRs (95%CI) for the three-month mortality were 1.458(1.113–1.909).No significant correlation was indicated between the Alb level and all-cause mortality in such patients (HR=1.019, 95% confidence interval 0.774–1.810, P = 0.436); the same was found for the GNRI(HR=0.950, 95% confidence interval 0.780–1.256, P = 0.717).

Given that RTI is an independent risk factor for all-cause mortality, we further conducted Cox regression according to different reasons of admission, as shown in Table 6.In the non-infection group, Alb, Hgb, GNRI, and CONUT could independently predict all-cause mortality in hypertensive patients aged >80 y. However, in RTI patients, only CONUT was identified as a good predictor of all-cause mortality(HR=1.242, 95% confidence interval 1.062–1.452, P = 0.007).

DISCUSSION

The findings in this study indicated that nutritional status was associated with 90-day all-cause mortality in patients with hypertension and aged > 80 y. Moreover, a CONUT score that was higher on admission was an independent predictor for all-cause mortality(HR=1.458, 95% confidence interval 1.113–1.909, P = 0.006). With increasing CONUT score, the incidence of all-cause mortality exhibits an increasing trend in both RTI(HR=1.242, 95% confidence interval1.062–1.452, P = 0.007) and in other reasons (HR=2.440, 95% confidence interval1.140–5.220, P = 0.021).

The relationship between nutritional status, particularly malnutrition, and prognosis of patients with cardiovascular disease has drawn increasing interest[11]. In a study including 2,251 patients with a mean age of 65.0±12.8 y, multiple logistic regression analysis indicated that malnutrition was an independent factor influencing post-MI complications[12].A study of Chinese population confirmed that nutritional status was independently associated with the risk of all-cause mortality in geriatric patients with CAD. Whether nutritional support in appropriate patients improves clinical outcomes deserves further investigation[13]. A study involving subjects with heart failure indicated that a poor nutritional status, as assessed using the CONUT score, and atherosclerosis, as indicated by CIMT, was significantly associated with inflammation and predicted poor outcomes in patients with CHF[14]. A relationship between nutritional status and prognosis in patients with hypertension is rarely observed; for elderly patients, such a relationship occurs even more rarely. CONUT is calculated using laboratory data, including albumin concentration, lymphocyte count, and cholesterol level of the patients. This index can more accurately reflect the nutritional status and immune function of the body. Previous reports regarding prognosis evaluation mostly focused on tumor orliver diseases. Yoshida[15]found that a moderate or severe CONUT score was an independent risk factor for any morbidity and severe morbidities for esophageal cancer. The study also concluded that CONUT was a convenient and useful tool for nutritional status assessment prior to esophagectomy. In patients with nasopharyngeal carcinoma, the same conclusion was drawn[16].Studies on cardiovascular disease are rarely reported. A study on STEMI patients showed that the CONUT score was associated with an increased risk of all-cause mortality for both the unadjusted as well as the age- and sex-adjusted models; in a full-adjusted model, the best predictors were age and BNP[17].In patients with chronic heart failure, a mean follow-up period of 28.4 months revealed that patients experiencing cardiovascular events had impaired nutritional status, higher CONUT scores, lower PNI scores, and lower GNRI scores, compared with patients who did not experience cardiovascular events[18].The current study found that for patients with hypertension, only CONUT, not GNRI, is a good predictor for all-cause mortality 3 month after admission.

A study involving patients admitted to an acute geriatric unit showed that both albumin and CONUT are identified as good predictors of short-and medium-term mortality; however, the study adds little to the information provided by albumin alone[19], which differs from our conclusion. Our finding shows that for hypertensive patients admitted for other reasons, albumin and CONUT are independent predictors of all-cause mortality; however, for hypertensive patients suffering from RTI, only CONUT can provide prognostic information. We therefore conclude that for admitted patients with hypertension, CONUT is a preferable nutritional status index.

GNRI, which is determined based on the albumin level and weight of the patient, has also recently been used as a new index of nutritional assessment for elderly patients [5 20].Past studies found that a higher risk GNRI was positively correlated with length of hospital stay; meanwhile, the association between a higher risk GNRI an in-hospital mortality was not significant[21].GNRI is the most widely used tool in chronic kidney disease with or without dialysis[9 22 23]. Multivariate Cox proportional hazards analysis demonstrated that GNRI <100, serum ferritin >/= 500 mu g/L, and age ≥65 y were significant predictors for mortality in hemodialysis patients[24].Increased GNRI was associated with increased CRP levels and low lymphocyte counts after multivariable adjustment. Some studies have also reported on

GNRI as a prognostic factor in cardiovascular diseases[25 26]; however, in our study, we found that GNRI is not an independent predictor for all-cause mortality in patients with hypertension.

The present study includes certain limitations. (1) This study was a single center study that included a relatively small number of patients. (2) Follow-up studies were performed for only 90 d;a further study is being conducted.

CONCLUSION

We found that nutritional status assessed using the CONUT and not by other nutritional index in patients with hypertension admitted to the hospital can efficiently predict all-cause mortality within 90 d post-admission. With an increase in CONUT score, which indicates malnutrition, the incidence of all-cause mortality exhibits an increasing trend in both RTI(HR=1.242, 95% confidence interval1.062–1.452, P = 0.007) and other reasons (HR=2.440, 95% confidence interval1.140–5.220, P = 0.021). Evaluation of nutritional status may provide additional prognostic information for patients with hypertension, and management of nutritional status is highly significant. Regardless, a study involving more patients has to be conducted for confirm these findings.

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Contributors

SXN, LLM and YP contributed to the design of the review. SXN, ZXQ acquired the data. SXN, LLM, and contributed to analysis. SXN wrote the draft. SXN, LLM, ZXQ and YP critically revised the intellectual content of this work.

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Competing interests

The authors declare no conflict of interest.

Data sharing statement

No additional data are available.

Conflict of Interest

Table 1.Screening Tool for Controlling Nutritional Status or CONUT

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Parameter	Requirements	Score
Albumin(g/l)	≥35	0
	30-34	2
	25-29	4
	＜25	6
Total lymphocyto count(/ml)	≥1600	0
	1200-1599	1
	800-1199	2
	＜800	3
Total cholesterol(mmol/l)	≥4.65	0
	3.62-4.64	1
	2.58-3.61	2
	＜2.58	3

Dysnutritional states: Normal 0-1;Mild 2-4;Moderate 5-8;Severe 9-12

Table 2 Characteristics of the study population and nutritional parameters based on nutritional status

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	Normal (CONUT=0–1,n=67)	Mild malnutrition (CONUT 2–4,n=178)	Moderate–severe malnutrition (CONUT ≥5,n=91)	P
Age(year, $\bar{x}$ ±s)	87.24±4.75	87.18±4.95	87.75±5.56	0.638
Male(n,%)	64 (95.52)	169 (94.54)	90(98.90)	0.270
Smoking history(n,%)	19(28.36)	60(33.71)	44(48.35)	0.018
Anemia(n,%)	20(29.85)	63(35.39)	41(45.05)	0.129
DM(n,%)	37(55.22)	93(52.24)	34(37.36)	0.035
Admission for RTI(n,%)	18(26.86)	91 (51.12)	83(91.21)	0.000
SBP (mmHg, $\bar{x}$ ±s)	129.49±15.11	133.96±18.88	134.04±19.92	0.236
DBP (mmHg, $\bar{x}$ ±s)	67.85±9.40	67.71±13.03	68.50±11.03	0.953
HR (beat/min， $\bar{x}$ ±s)	70.97±12.94	73.22±14.61	82.20±17.46	0.000
BMI (kg/m^2, $\bar{x}$ ±s)	25.08±3.10	24.15±3.09	23.03±2.73	0.010
Hgb(g/l, $\bar{x}$ ±s)	125.06±17.23	123.01±16.81	122.64±18.76	0.475
TC(mmol/l, $\bar{x}$ ±s）	4.53±0.08	2.77±1.60	0.93±1.51	0.000
TG(mmol/l, $\bar{x}$ ±s）	1.85±1.28	1.15±1.02	0.54±0.27	0.000
LDL-C(mmol/l, $\bar{x}$ ±s）	2.63±0.61	1.76±0.72	1.53±0.71	0.000
HDL-C(mmol/l, $\bar{x}$ ±s）	1.16±0.36	1.03±0.46	1.03±0.48	0.104
Scr(mmol/l, $\bar{x}$ ±s）	106.66±44.72	109.24±53.41	110.03±59.36	0.941
BUN(mmol/l, $\bar{x}$ ±s）	8.18±3.95	9.20±4.61	10.21±4.76	0.016
UA(umol/l， $\bar{x}$ ±s）	335.51±101.25	347.15±97.37	321.76±109.13	0.081
TP(g/l, $\bar{x}$ ±s)	69.40±5.25	68.75±6.36	65.90±7.56	0.000
Albumin(g/l, $\bar{x}$ ±s)	40.13±3.31	39.49±3.50	35.83±4.73	0.000
FBS(mmol/l, $\bar{x}$ ±s）	6.26±2.41	7.11±2.64	7.39±2.60	0.021
Prealbumin(mg/dl, $\bar{x}$ ±s)	10.76±12.88	17.02±12.05	19.15±7.25	0.000

Table 3 Characteristics of the study population and nutritional parameters by different admission reasons

Table 3 Characteristics of the study population and nutritional parameters by different admission reasons

	RTI (n=192)	Other causes (n=144)	Statistical value	P
Age(year)	87.56±5.29	87.25±5.11	0.292	0.589
Male(n,%)	185(96.35%)	143(95.97%)	0.033	0.855
Smoking history(n,%)	77(40.1%)	46(30.87%)	3.101	0.078
DM(n,%)	88(45.83%)	79(53.02%)	1.734	0.188
Hyperlipidemia(n,%)	98(51.04%)	79(53.02%)	0.132	0.717
BMI(kg/m^2)	23.68±3.16	24.53±3.00	4.991	0.026
TP(g/l)	67.79±7.65	68.08±5.67	0.150	0.699
Alb(g/l)	37.43±4.62	40.00±5.25	33.01	0.000
Hemoglobin(g/l)	122.69±19.10	123.61±15.14	0.235	0.628
Creatinine (umol/l)	109.40±56.54	108.73±48.46	0.013	0.909
BUN(mmol/l)	9.92±5.10	8.53±3.84	7.670	0.006
FBS(mmol/l)	7.63±2.75	6.19±2.14	27.98	0.000
UA(mmol/l)	328.74±102.06	350.96±104.49	3.875	0.050
Pre albumin(mg/dl)	18.73±8.89	13.58±13.65	17.645	0.000
GRNI score	97.72±7.68	100.49±5.35	11.822	0.001
CONUT score	4.19±2.08	2.09±1.34	112.593	0.000

Table 4 Comparison of the characteristics of the study population and laboratory parameters by different outcomes

Table 4 Comparison of the characteristics of the study population and laboratory parameters by different outcomes

	Death for all cause (n=27)	Survival (n=314)	P
Age(year)	89.29±4.57	87.26±5.25	0.052
Male (n, %)	27(100)	308(98.08)	0.281
DM (n,%)	15 (55.56)	152 (48.41)	0.304
Hyperlipidemia (n,%)	12 (44.44)	165 (52.55)	0.431
CKD (n,%)	9(33.33)	88(28.02)	0.667
Anemia (n,%)	13(48.15)	112(35.67)	0.206
SBP (mmHg)	133.29±18.43	126.85±20.16	0.085
DBP (mmHg)	68.31±12.02	62.48±9.60	0.016
BMI (kg/m^2）	22.31±3.31	24.25±3.05	0.012
TP(g/l)	67.85±9.59	67.92±6.58	0.962
Alb(g/l)	36.37±5.00	38.74±4.16	0.005
Hemoglobin (g/l)	115.07±20.42	123.78±17.05	0.040
Creatinine (umol/l)	110.74±61.19	108.97±52.44	0.868
BUN(mmol/l)	10.86±4.64	9.18±4.62	0.071
FBS(mmol/l)	8.24±3.51	(6.90±2.48	0.010
UA(mmol/l)	312.00±82.94	340.72±105.31	0.169
Prealbumin(mg/dl)	19.21±8.70	16.25±11.68	0.200
COUNT score	5.14±2.32	3.13±1.98	0.000
GNRI	95.69±7.77	99.42±6.55	0.026

DM: diabetes mellitus; SBP:systolic blood pressure; DBP: diastolic blood pressure; BMI:body mass index; TP:total protein; Alb: albumin; BUN:blood urea nitrogen; UA:uric acid

Table 5 Multivariate Cox regression for all-cause mortality

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	B	Wald	Sig	HR	95%CI
RTI	0.971	4.808	0.028	2.641	1.109–6.29
Age	0.093	2.92	0.087	1.097	0.980–1.220
BMI	-0.121	0.642	0.423	1.184	0.660–1.191
Alb	0.109	0.606	0.436	1.019	0.774–1.810
Prealbumin	-2.352	0.607	0.436	0.095	0.00–35.271
GNRI	-0.520	0.132	0.717	0.950	0.780–1.256
CONUT	0.377	7.511	0.006	1.458	1.113–1.909

Table 6. Cox regression analysis of common nutritional evaluation index for possible

Table 6. Cox regression analysis of common nutritional evaluation index for possible predictors of all-cause mortality by reason of admission

	Adjusted HR with 95% CI for RTI			Adjusted HR with 95% CI for other reasons		
	HR	95%CI	P	HR	95%CI	P
BMI	0.980	0.958–1.003	.084	0.629	0.354–1.107	.114
Alb	0.989	0.904–1.082	.810	0.649	0.439–0.958	.030
Hgb	0.982	0.962–1.003	.092	0.891	0.800–0.992	.035
Prealbumin	1.013	0.969–1.060	.092	1.034	0.941–1.137	.448
GNRI	0.995	0.929–1.066	.897	0.692	0.500–0.957	.026
CONUT	1.242	1.062–1.452	.007	2.440	1.14–5.22	.021

predictors of all-cause mortality by reason of admission

Figure 1. All-cause mortality in different nutritional status.

Figure 2.Kaplan–Meier survival curves for the CONUT

Figure 3 Kaplan–Meier survival curves for the GNRI

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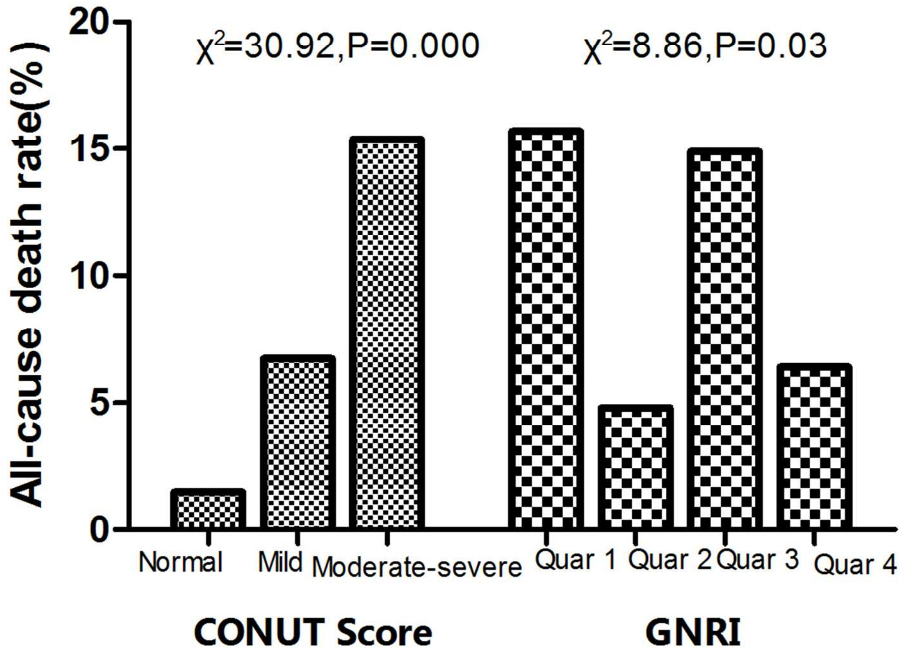

All-cause mortality in different nutritional status.

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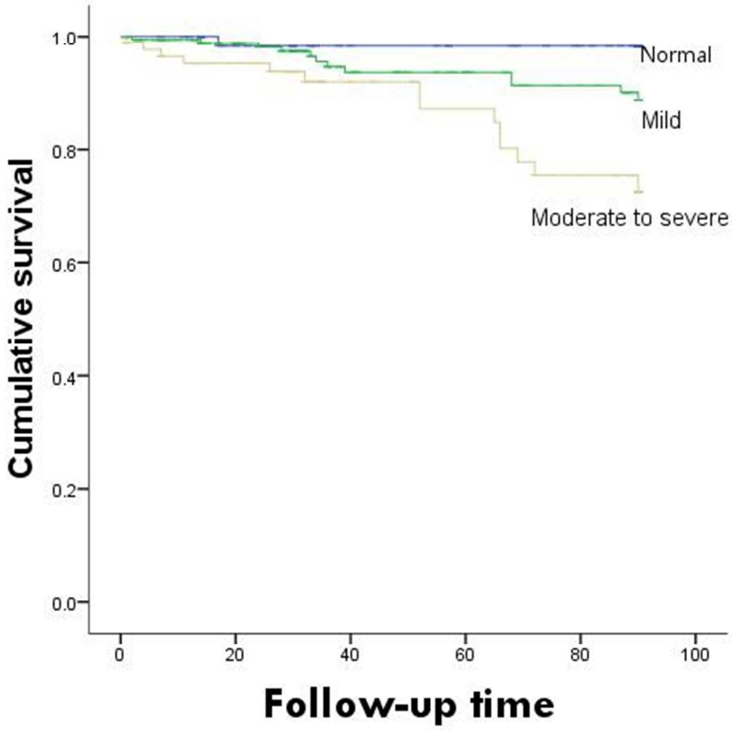
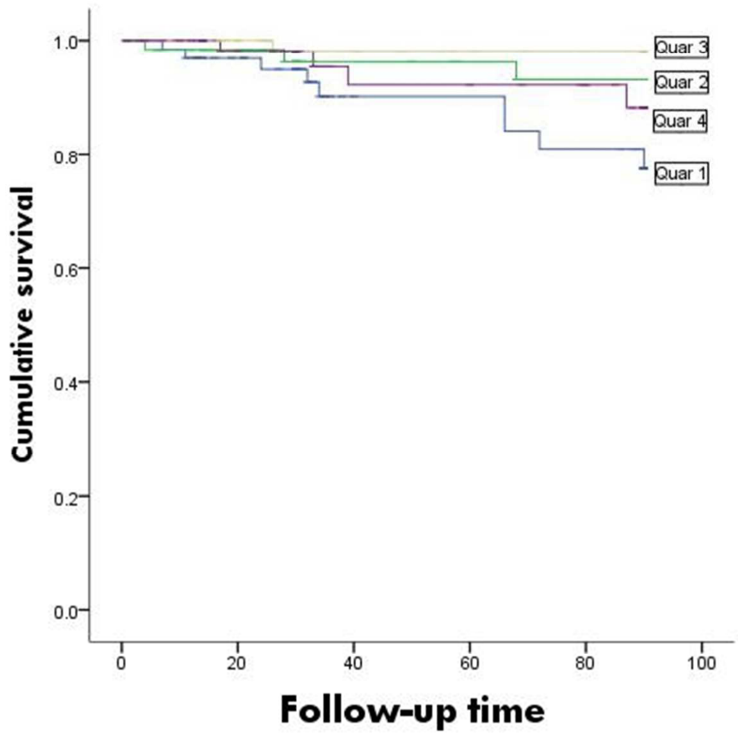


Kaplan–Meier survival curves for the CONUT

220x176mm (72 x 72 DPI)



Kaplan–Meier survival curves for the GNRI

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Controlling Nutritional Status (CONUT) score as an effective predictor of all-cause mortality in elderly hypertensive patients

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Title page

Controlling Nutritional Status (CONUT) score as an effective predictor of all-cause mortality in elderly hypertensive patients

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Running title: CONUT is good predictor of all-cause mortality in hypertension

Conflict of Interest: The authors declare no conflict of interest.

Abstract

Objectives: The aim of this study was to elucidate the impact of nutritional status on survival per Controlling Nutritional Status (CONUT) score and geriatric nutritional risk index (GNRI) in hypertension patients over 80 years of age.

Design: Prospective follow-up study.

Participants: A total of 336 hypertensive patients over 80 years old (80 y) were included to this study.

Outcome measures: All-cause death were recorded as Kaplan-Meier curves to evaluate the association between CONUT and all-cause mortality at follow-up. Cox regression models were used to investigate the prognostic value of CONUT and GNRI for all-cause mortality in the 90 day period after admission.

Results: Hypertensive patients with higher CONUT scores exhibited higher mortality within 90 days after admission (1.49%, 6.74%, 15.38% respectively, $\chi 2$ =30.92, P=0.000). Surviving patients had higher BMI (24.25±3.05 vs 24.25±3.05, p=0.012), Hemoglobin (123.78±17.05 vs 115.07±20.42, P=0.040), and albumin levels, as well as lower FBS (6.90±2.48 vs 8.24±3.51, p=0.010). Higher GRNI score (99.42±6.55 vs 95.69±7.77, p=o.oo2) and lower CONUT (3.13±1.98 vs 5.14±2.32) both indicated better nutritional status. Kaplan-Meier curves indicated that survival rates were significantly worse in the high CONUT group compared to the low CONUT group ($\chi 2$ =13.372, p=0.001). Cox regression indicated an increase in hazard ratio (HR) with increasing CONUT risk (from normal to moderate to severe). HRs (95%CI) for three-month mortality were 1.458 (1.113-1.909). In both RTI patients and the “other reason” group, only CONUT was a sufficiently accurate predictor for all-cause mortality (HR=1.242, 95% confidence interval 1.062–1.452, P = 0.007) in hypertensive patients over 80 y.

Conclusion: Nutritional status assessed via CONUT, as opposed to other nutrition indexes, is an accurate predictor of all-cause mortality 90 days post-admission. Evaluation of nutritional status may provide additional prognostic information in patients with hypertension, and the management of nutritional status is of great significance in reducing patient mortality.

Key words

Nutritional status; CONUT; Hypertension; All-cause mortality

Strengths of this study

Nutritional status assessed using the CONUT in hypertensive patients aged over 80 y efficiently predict all-cause mortality within 90 d post-admission.

Increased CONUT score relates to increase in all-cause mortality in patients admitted for RTI and other reasons.

Study limitations

1) This study was a single-center study that included a relatively small number of patients.

2) Follow-up studies were performed for only 90 d.

Funding

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INTRODUCTION

The nutritional status of patients has drawn increased attention in a variety of clinical settings. There is a wealth of evidence to suggest that nutritional and immunologic status upon admission is closely associated with the outcome of patients with cardiovascular disease[1-3]. For elderly patients, the role of nutritional status is all the more important. Studies have shown that elderly patients with high nutritional risks are more likely to stay longer in the hospital than those without such risks[4]. Nutritional risk has also been identified as an independent predictor of functional status and mortality among institutionalized elderly patients[5].

Body mass index (BMI), serum albumin level, and pre albumin levels are the most commonly indexes used for evaluating nutritional status clinically. However, these single indexes exhibit limited clinical applications. Researchers have established improved nutritional indexes with an increasing number of complex nutritional indicators. The Geriatric Nutritional Risk Index (GNRI) is one of the most commonly used nutritional indicators in the elderly patient population[6]. The Controlling Nutritional Status (CONUT) score, which is calculated based on the serum albumin concentration, total peripheral lymphocyte count, and total cholesterol concentration, was developed as a screening tool for early detection of poor nutritional status[7]. Both indexes provide useful information for evaluating nutritional status comprehensively, and are currently widely applied in the evaluation of patients with tumors[8] that are undergoing dialysis[9]. These tools exhibit limited application in cardiovascular disease, however.

Hypertension, the most commonly occurring diseases in the elderly population, is associated with a number of comorbidities. When elderly patients are hospitalized due to infection or other reasons, the effects of nutritional status on their prognosis of merits further evaluation. The applicability of indexes such as GNRI or CONUT scores in assessing such patients has yet to be fully validated. The primary goal of this study was to elucidate the effect of nutritional status on survival in patients with hypertension and aged over 80 y.

METHODS

Patients

This study included patients with hypertension who were diagnosed using the criteria listed in Chinese Hypertension Prevention Guide (2010)[10], hospitalized from January 2011 to December 2013, and aged >80 y. The study was conducted at the People's Liberation Army General Hospital under the full ethical approval of the Human Investigation Committee. Informed consent was obtained from each patient prior to their participation.

General information and medical history

General information, including age, sex, lifestyle (smoking and drinking) and basic medical history were collected. Patients were selected based on height, weight, resting heart rate, systolic blood pressure, and diastolic blood pressure.

Nutritional metabolism and related biochemical indexes

Upon admission routine blood tests was conducted for all enrolled patients in the Central Laboratory of our hospital. Detection indexes included white blood cells, lymphocytes, platelets, hemoglobin (Hgb), serum creatinine (sCr), albumin (Alb), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBS), blood urea nitrogen (BUN), uric acid (UA), pre albumin (PA), and electrolyte index.

The nutritional status of each patient was also evaluated using two composite indexes: CONUT score and GNRI. The CONUT score was determined in accordance with the tool described in Table 1, which was first used by Ulibarri[7]. The GNRI, which includes two nutritional indicators (albumin and actual weight compared to ideal body weight), was developed by modifying the nutritional risk index for elderly patients. GNRI=[1.487* serum albumin (g/L)] t[41.7 *present/usual weight (kg)][6].

Follow-up

A follow-up on all selected subjects was conducted throughout a 90-d post-admission period. Follow-up times were set to occur 7, 14, 30, and 90 d after admission and were conducted by interviewing each patient via telephone and by reviewing his or her medical records. All-cause mortality was determined at the end of the follow-up period. Death was ascertained from the death record, i.e., a legal document including time, site, and other necessary information.

Statistical analysis

All calculations were performed in SPSS ver. 22.0. For continuous quantitative data, the K-S normality test was first applied to analyze whether the normal distribution of quantitative data could be analyzed by an independent-sample t-test. Data that were not normally distributed were analyzed via Mann-Whitney U test. A Pearson's chi-squared (χ^2) test was run to analyze the categorical variables. Survival curves were generated via Kaplan-Meier method, and multivariate analysis using a Cox proportional hazards model was used for independent tests of significance. Two-tailed P values <0.05 were considered significant.

RESULTS

Clinical characteristics

A total of 336 hypertensive patients were enrolled, including 323 males and 13 females, with an average age of 87.39± 5.23 years. All patients were diagnosed with hypertension ranging from 5-27 years and had received antihypertensive drug treatment. All patients had a history of CAD; 83 patients had a history of myocardial infarction, 29 patients had received stent therapy, 67 suffered from chronic heart failure, 167 had T2DM, and 124 had anemia. Of these cases, 192 were admitted for respiratory tract infection (RTI) and the remaining 144 patients were admitted for non-infective factors, such as angina pectoris or uncontrolled blood pressure, among others.

The CONUT scores of the selected patients were determined and analysis was conducted as presented in Table 2. Only five patients scored over 9, which indicates severe malnutrition. We combined their data with those exhibiting moderate malnutrition for analysis. Heart rate and blood glucose levels were higher in patients with high CONUT scores than in those with low CONUT scores. The proportion of patients with poor nutritional status due to admission caused by RTI was significantly high, as well (χ^2 =70.835, p=0.000).

Table 3 compares the nutritional index of patients with different reasons for admission. Patients with RTI showed generally low nutritional status, including low BMI, albumin level, GNRI score, high FBS, and CONUT score upon admission.

Follow-up results

A total of 27 deaths were recorded in the 90-d follow-up; most of these deaths occurred between 30 to 90 d (n=17, 62.97%) post-admission. The parameters and characteristics of different outcomes for the patients are presented in Table 4. No differences in age, sex, or combination of diseases were found between different outcomes. Likewise, no differences in systolic blood pressure were found. The surviving patients, however, showed increased BMI (24.25±3.05 vs.24.25±3.05, p=0.012), hemoglobin (123.78±17.05 vs. 115.07±20.42, P=0.040), and albumin level, as well as reduced DBP (62.48±9.60 vs. 68.31±12.02, p=0.016) and FBS (6.90±2.48 vs. 8.24±3.51, p=0.010). No significant difference in plasma pre albumin level between different outcomes was indicated (19.21±8.70 vs.16.25±11.68, p=0.200).

Surviving patients had improved GRNI scores (99.42±6.55 vs. 95.69±7.77, p=0.002) and reduced CONUT scores (3.13±1.98 vs. 5.14±2.32) in the follow-up period, both of which indicated improved nutritional status. We found that along with increase in CONUT score, which suggests worse malnutrition, the incidence of all-cause mortality increased. This tendency was not observed in the GRNI group, however, as illustrated in Fig. 1.

Survival analysis according to CONUT and GNRI

Survival curves based on different nutritional evaluations were plotted as shown in Fig. 2. The survival rates were significantly lower in the high-CONUT group than in the low-CONUT group (χ^2 =13.372, p=0.001). The survival curves based on the GNRI are shown in Fig. 3. Differences among groups could not be determined (χ^2 =7.694, p=0.053).

Prognostic values of CONUT and GNRI

Multivariate Cox regression analyses were conducted to investigate the possible predictors of all-cause mortality in the study population (Table 5). By regression, both RTI and CONUT were independent predictors of three-month all-cause mortality. Increasing hazard ratios (HR) were observed with increasing CONUT risk (from normal to moderate to severe). The HRs (95% CI) for the 90-d mortality were 1.458

(1.113–1.909). No significant correlation was indicated between the Alb level and all-cause mortality in these patients (HR=1.019, 95% confidence interval 0.774-1.810, P = 0.436); similar phenomena were observed in GNRI participants (HR=0.950, 95% confidence interval 0.780-1.256, P = 0.717).

Given that RTI is an independent risk factor for all-cause mortality, we further conducted Cox regression according to different reasons for admission as shown in Table 6. In the non-infection group, Alb, Hgb, GNRI, and CONUT independently predicted all-cause mortality in the patients. However, in the RTI group, only CONUT was identified as an accurate predictor of all-cause mortality (HR=1.242, 95% confidence interval 1.062-1.452, P = 0.007).

DISCUSSION

The findings in this study indicated that nutritional status is associated with 90-d all-cause mortality in hypertension patients aged > 80 y. A CONUT score that was higher on admission was an independent predictor for all-cause mortality (HR=1.458, 95% confidence interval 1.113–1.909, P = 0.006). As CONUT score increased, the incidence of all-cause mortality likewise increased in patients admitted for both RTI (HR=1.242, 95% confidence interval1.062–1.452, P = 0.007) and other reasons (HR=2.440, 95% confidence interval1.140–5.220, P = 0.021).

The relationship between nutritional status, particularly malnutrition, and prognosis of patients with cardiovascular disease has garnered increasing research interest[11]. In a study including 2,251 patients with a mean age of 65.0±12.8 y, multiple logistic regression analysis indicated that malnutrition is an independent factor influencing post-MI complications[12]. Another Chinese study confirmed that nutritional status is independently associated with the risk of all-cause mortality in geriatric patients with CAD. Whether nutritional support in these types of patients improves clinical outcomes merits further investigation[13]. A study involving subjects with heart failure indicated that poor nutritional status, as assessed via CONUT score, and atherosclerosis, as indicated via CIMT, is significantly associated with inflammation and predicts poor outcomes in CHF patients[14]. A relationship between nutritional status and prognosis in patients with hypertension is rarely observed; for elderly patients, such a relationship occurs even more rarely.

CONUT is calculated using laboratory data including albumin concentration, lymphocyte count, and cholesterol level. This index can accurately reflect the nutritional status and immune function of the body. Previous reports on prognosis evaluation and CONUT have mostly focused on tumor or liver diseases. Yoshida[15], for example, found that a moderate or severe CONUT score is an independent risk factor for any morbidity and severe morbidities for esophageal cancer. The same research team also concluded that CONUT is a convenient and useful tool for nutritional status assessment prior to esophagectomy. Similar conclusions were drawn for patients with nasopharyngeal carcinoma[16]. Studies on cardiovascular disease have been rare in this regard, however.

A study on STEMI patients showed that the CONUT score is associated with an increased risk of all-cause mortality for both unadjusted as well as age- and sex-adjusted models; in a full-adjusted model, the best predictors were age and

BNP[17]. In patients with chronic heart failure, a mean follow-up period of 28.4 months revealed that patients experiencing cardiovascular events had impaired nutritional status, higher CONUT scores, lower PNI scores, and lower GNRI scores compared to patients who did not experience cardiovascular events[18]. In this study, we found that only CONUT, not GNRI, is an accurate predictor for all-cause mortality in hypertension patients up to three months after admission.

A study involving patients admitted to an acute geriatric unit showed that both albumin and CONUT are accurate predictors of short- and medium-term mortality; however, the study added little to the information provided by albumin alone[19]. Our results indicate that for hypertensive patients admitted for other reasons, albumin and CONUT are independent predictors of all-cause mortality; for hypertensive patients suffering from RTI, however, only CONUT provided useful prognostic information. We therefore conclude that for patients admitted with hypertension, CONUT is a valuable nutritional status index.

GNRI, which is determined based on the albumin level and weight of the patient, is a relatively new index for the nutritional assessment for elderly patients [5 20]. Past studies have shown that a higher-risk GNRI is positively correlated with length of hospital stay though the association between higher-risk GNRI and in-hospital mortality is not significant[21]. GNRI is the most widely used tool in chronic kidney disease with or without dialysis[9 22 23]. Multivariate Cox proportional hazards analysis demonstrated that GNRI <100, serum ferritin >/= 500 mu g/L, and age ≥65 y are significant predictors for mortality in hemodialysis patients[24]. Increased GNRI is also associated with increased CRP levels and low lymphocyte counts after multivariable adjustment. Some studies have also reported on GNRI as a prognostic factor in cardiovascular diseases[25 26]. In this study, however, we found that GNRI is not an independent predictor for all-cause mortality in patients with hypertension.

The present study was not without limitations. First, it was a single-center study that included a relatively small number of patients. Follow-up studies were only performed for only 90 d; a lengthier follow-up study is currently being conducted to further explore the results reported here.

CONCLUSION

We found that nutritional status assessed using CONUT and not by other nutritional index in patients with hypertension admitted to the hospital can efficiently predict all-cause mortality within 90 d post-admission. Increase in CONUT score, which indicates malnutrition, was related to an increase in the incidence of all-cause mortality in patients admitted for RTI (HR=1.242, 95% confidence interval1.062-1.452, P = 0.007) and other reasons (HR=2.440, 95% confidence interval1.140-5.220, P = 0.021). An accurate evaluation of nutritional status may provide additional prognostic information for patients with hypertension, and management of nutritional status may significantly improve treatment outcomes. In the future, longer-term studies on larger numbers of patients are warranted to further verify the results presented here.

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Contributors

SXN, LLM, and YP contributed to the design of the review. SXN and ZXQ acquired the data. SXN and LLM contributed to the analysis. SXN wrote the draft. SXN, LLM, ZXQ, and YP critically revised the intellectual content of this work.

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Conflicts of interest

The authors declare no conflict of interest.

Data sharing statement

No additional data are available.

Table 1. Screening Tool for Controlling Nutritional Status or CONUT

Table 1.Screening Tool for Controlling Nutritional Status or CONUT

Parameter	Requirements	Score
Albumin(g/l)	≥35	0
	30-34	2
	25-29	4
	＜25	6
Total lymphocyto count(/ml)	≥1600	0
	1200-1599	1
	800-1199	2
	＜800	3
Total cholesterol(mmol/l)	≥4.65	0
	3.62-4.64	1
	2.58-3.61	2
	＜2.58	3

Dysnutritional states: Normal 0-1;Mild 2-4;Moderate 5-8;Severe 9-12

Table 2. Characteristics of study population and nutritional parameters based on nutritional status

Table 2 Characteristics of the study population and nutritional parameters based on nutritional status

	Normal (CONUT=0–1,n=67)	Mild malnutrition (CONUT 2–4,n=178)	Moderate–severe malnutrition (CONUT ≥5,n=91)	P
Age(year, $\bar{x}$ ±s）	87.24±4.75	87.18±4.95	87.75±5.56	0.638
Male(n,%)	64 (95.52)	169 (94.54)	90(98.90)	0.270
Smoking history(n,%)	19(28.36)	60(33.71)	44(48.35)	0.018
Anemia(n,%)	20(29.85)	63(35.39)	41(45.05)	0.129
DM(n,%)	37(55.22)	93(52.24)	34(37.36)	0.035
Admission for RTI(n,%)	18(26.86)	91 (51.12)	83(91.21)	0.000
SBP (mmHg, $\bar{x}$ ±s)	129.49±15.11	133.96±18.88	134.04±19.92	0.236
DBP (mmHg, $\bar{x}$ ±s)	67.85±9.40	67.71±13.03	68.50±11.03	0.953
HR (beat/min， $\bar{x}$ ±s)	70.97±12.94	73.22±14.61	82.20±17.46	0.000
BMI (kg/m^2, $\bar{x}$ ±s)	25.08±3.10	24.15±3.09	23.03±2.73	0.010
Hgb(g/l, $\bar{x}$ ±s)	125.06±17.23	123.01±16.81	122.64±18.76	0.475
TC(mmol/l, $\bar{x}$ ±s）	4.53±0.08	2.77±1.60	0.93±1.51	0.000
TG(mmol/l, $\bar{x}$ ±s）	1.85±1.28	1.15±1.02	0.54±0.27	0.000
LDL-C(mmol/l, $\bar{x}$ ±s）	2.63±0.61	1.76±0.72	1.53±0.71	0.000
HDL-C(mmol/l, $\bar{x}$ ±s）	1.16±0.36	1.03±0.46	1.03±0.48	0.104
Scr(mmol/l, $\bar{x}$ ±s）	106.66±44.72	109.24±53.41	110.03±59.36	0.941
BUN(mmol/l, $\bar{x}$ ±s）	8.18±3.95	9.20±4.61	10.21±4.76	0.016
UA(umol/l， $\bar{x}$ ±s）	335.51±101.25	347.15±97.37	321.76±109.13	0.081
TP(g/l, $\bar{x}$ ±s)	69.40±5.25	68.75±6.36	65.90±7.56	0.000
Albumin(g/l, $\bar{x}$ ±s)	40.13±3.31	39.49±3.50	35.83±4.73	0.000
FBS(mmol/l, $\bar{x}$ ±s）	6.26±2.41	7.11±2.64	7.39±2.60	0.021
Prealbumin(mg/dl, $\bar{x}$ ±s)	10.76±12.88	17.02±12.05	19.15±7.25	0.000

Table 3. Characteristics of study population and nutritional parameters by different admission reasons

Table 3 Characteristics of the study population and nutritional parameters by different admission reasons

	RTI (n=192)	Other causes (n=144)	Statistical value	P
Age(year)	87.56±5.29	87.25±5.11	0.292	0.589
Male(n,%)	185(96.35%)	143(95.97%)	0.033	0.855
Smoking history(n,%)	77(40.1%)	46(30.87%)	3.101	0.078
DM(n,%)	88(45.83%)	79(53.02%)	1.734	0.188
Hyperlipidemia(n,%)	98(51.04%)	79(53.02%)	0.132	0.717
BMI(kg/m^2)	23.68±3.16	24.53±3.00	4.991	0.026
TP(g/l)	67.79±7.65	68.08±5.67	0.150	0.699
Alb(g/l)	37.43±4.62	40.00±5.25	33.01	0.000
Hemoglobin(g/l)	122.69±19.10	123.61±15.14	0.235	0.628
Creatinine (umol/l)	109.40±56.54	108.73±48.46	0.013	0.909
BUN(mmol/l)	9.92±5.10	8.53±3.84	7.670	0.006
FBS(mmol/l)	7.63±2.75	6.19±2.14	27.98	0.000
UA(mmol/l)	328.74±102.06	350.96±104.49	3.875	0.050
Pre albumin(mg/dl)	18.73±8.89	13.58±13.65	17.645	0.000
GRNI score	97.72±7.68	100.49±5.35	11.822	0.001
CONUT score	4.19±2.08	2.09±1.34	112.593	0.000

Table 4. Comparison of characteristics of study population and laboratory parameters by different outcomes

Table 4 Comparison of the characteristics of the study population and laboratory parameters by different outcomes

	Death for all cause (n=27)	Survival (n=314)	P
Age(year)	89.29±4.57	87.26±5.25	0.052
Male (n, %)	27(100)	308(98.08)	0.281
DM (n,%)	15 (55.56)	152 (48.41)	0.304
Hyperlipidemia (n,%)	12 (44.44)	165 (52.55)	0.431
CKD (n,%)	9(33.33)	88(28.02)	0.667
Anemia (n,%)	13(48.15)	112(35.67)	0.206
SBP (mmHg)	133.29±18.43	126.85±20.16	0.085
DBP (mmHg)	68.31±12.02	62.48±9.60	0.016
BMI (kg/m^2)	22.31±3.31	24.25±3.05	0.012
TP(g/l)	67.85±9.59	67.92±6.58	0.962
Alb(g/l)	36.37±5.00	38.74±4.16	0.005
Hemoglobin (g/l)	115.07±20.42	123.78±17.05	0.040
Creatinine (umol/l)	110.74±61.19	108.97±52.44	0.868
BUN(mmol/l)	10.86±4.64	9.18±4.62	0.071
FBS(mmol/l)	8.24±3.51	(6.90±2.48	0.010
UA(mmol/l)	312.00±82.94	340.72±105.31	0.169
Prealbumin(mg/dl)	19.21±8.70	16.25±11.68	0.200
COUNT score	5.14±2.32	3.13±1.98	0.000
GNRI	95.69±7.77	99.42±6.55	0.026

DM: diabetes mellitus; SBP:systolic blood pressure; DBP: diastolic blood pressure; BMI:body mass index; TP:total protein; Alb: albumin; BUN:blood urea nitrogen; UA:uric acid

Table 5. Multivariate Cox regression for all-cause mortality

Table 5 Multivariate Cox regression for all-cause mortality

	B	Wald	Sig	HR	95%CI
RTI	0.971	4.808	0.028	2.641	1.109–6.29
Age	0.093	2.92	0.087	1.097	0.980–1.220
BMI	-0.121	0.642	0.423	1.184	0.660–1.191
Alb	0.109	0.606	0.436	1.019	0.774–1.810
Prealbumin	-2.352	0.607	0.436	0.095	0.00–35.271
GNRI	-0.520	0.132	0.717	0.950	0.780–1.256
CONUT	0.377	7.511	0.006	1.458	1.113–1.909

Table 6. Cox regression analysis of common nutritional evaluation index for possible predictors of all-cause mortality by reason of admission

Table 6. Cox regression analysis of common nutritional evaluation index for possible predictors of all-cause mortality by reason of admission

	Adjusted HR with 95% CI for RTI			Adjusted HR with 95% CI for other reasons		
	HR	95%CI	P	HR	95%CI	P
BMI	0.980	0.958–1.003	.084	0.629	0.354–1.107	.114
Alb	0.989	0.904–1.082	.810	0.649	0.439–0.958	.030
Hgb	0.982	0.962–1.003	.092	0.891	0.800–0.992	.035
Prealbumin	1.013	0.969–1.060	.092	1.034	0.941–1.137	.448
GNRI	0.995	0.929–1.066	.897	0.692	0.500–0.957	.026
CONUT	1.242	1.062–1.452	.007	2.440	1.14–5.22	.021

Figure 1. All-cause mortality among different nutritional statuses

Figure 2. Kaplan-Meier survival curves for CONUT

Figure 3. Kaplan-Meier survival curves for GNRI

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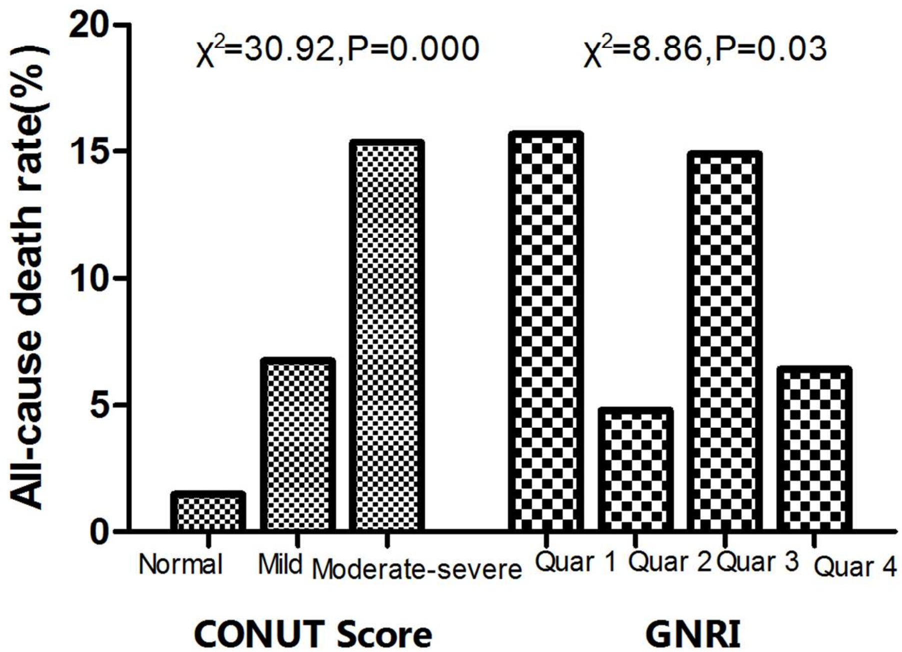
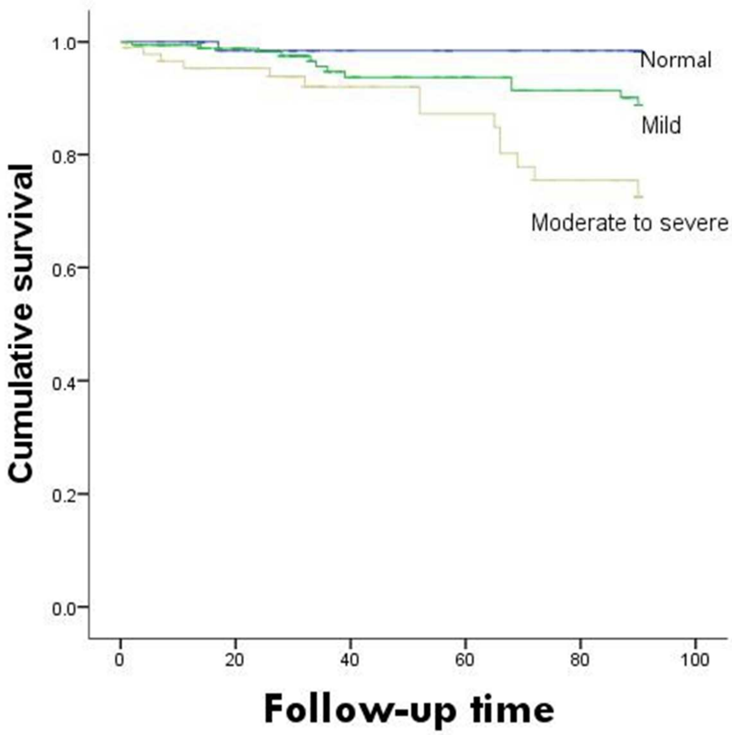


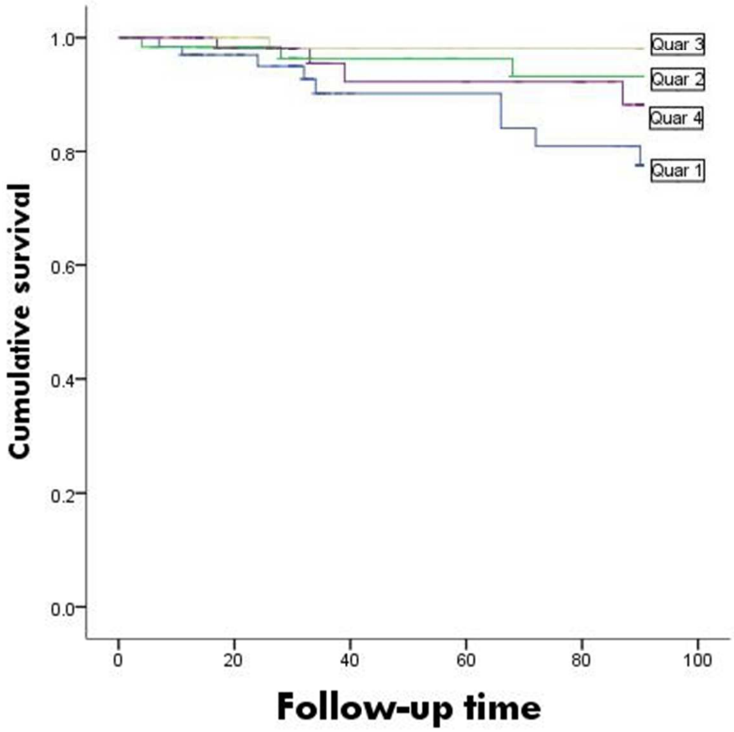
All-cause mortality in different nutritional status.

99x75mm (300 x 300 DPI)



Kaplan–Meier survival curves for the CONUT

220x176mm (72 x 72 DPI)



Kaplan–Meier survival curves for the GNRI

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Controlling Nutritional Status (CONUT) score as a predictor of all-cause mortality in elderly hypertensive patients: a prospective follow-up study

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Title page

Controlling Nutritional Status (CONUT) score as a predictor of all-cause mortality in elderly hypertensive patients: a prospective follow-up study

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Running title: CONUT is good predictor of all-cause mortality in hypertension

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Abstract

Objectives: The aim of this study was to elucidate the impact of nutritional status on survival per Controlling Nutritional Status (CONUT) score and geriatric nutritional risk index (GNRI) in hypertension patients over 80 years of age.

Design: Prospective follow-up study.

Participants: A total of 336 hypertensive patients over 80 years old (80 y) were included to this study.

Outcome measures: All-cause death were recorded as Kaplan-Meier curves to evaluate the association between CONUT and all-cause mortality at follow-up. Cox regression models were used to investigate the prognostic value of CONUT and GNRI for all-cause mortality in the 90 day period after admission.

Results: Hypertensive patients with higher CONUT scores exhibited higher mortality within 90 days after admission (1.49%, 6.74%, 15.38% respectively, χ^2 =30.92, P=0.000). Surviving patients had higher BMI (24.25±3.05 VS 24.25±3.05, p=0.012), Hemoglobin (123.78±17.05 VS 115.07±20.42, P=0.040) and albumin levels, as well as lower FBS (6.90±2.48 VS 8.24±3.51, p=0.010). Higher GRNI score (99.42±6.55 VS 95.69±7.77, p=o.oo2) and lower CONUT (3.13±1.98 VS 5.14±2.32) both indicated better nutritional status. Kaplan-Meier curves indicated that survival rates were significantly worse in the high CONUT group compared to the low CONUT group (χ^2 =13.372, p=0.001). Cox regression indicated an increase in hazard ratio (HR) with increasing CONUT risk (from normal to moderate to severe). HRs (95%CI) for three-month mortality was 1.458 (1.102-1.911). In both RTI and "other reason" group, only CONUT was a sufficiently predictor for all-cause mortality (HR=1.284,95%CI 1.013–1.740, P = 0.020 & HR=1.841, 95% CI1.117–4.518, P = 0.011). ROC showed CONUT higher than 3.0 was found to predict all-cause mortality with a sensitivity of 77.8% and a specificity of 64.7% (AUC = 0.778, P<0.001).

Conclusion: Nutritional status assessed via CONUT, is an accurate predictor of all-cause mortality 90 days post-admission. Evaluation of nutritional status may provide additional prognostic information in hypertensive patients.

Key words

Nutritional status; CONUT; Hypertension; All-cause mortality

Strengths of this study

- This was a study including 336 hypertensive patients over 80 years combined with diagnosed cardiovascular (CVD) disease.
- It is the first study to explore the relationship between the nutritional status based on CONUT or GNRI on admission and all-cause death in such very elderly hypertensive patients.

Study limitations

1) This study was a single-center study that included a relatively small number of patients.

2) Follow-up studies were performed for only 90 day.

Funding

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INTRODUCTION

The nutritional status of patients has drawn increased attention in a variety of clinical settings. There is a wealth of evidence to suggest that nutritional and immunologic status upon admission is closely associated with the outcome of patients with cardiovascular disease[1-3]. For elderly patients, the role of nutritional status is all the more important. Studies have shown that elderly patients with high nutritional risks are more likely to stay longer in the hospital than those without such risks[4]. Nutritional risk has also been identified as an independent predictor of functional status and mortality among institutionalized elderly patients[5].

Body mass index (BMI), serum albumin level, and pre albumin levels are the most commonly indexes used for evaluating nutritional status clinically. However, these single indexes exhibit limited clinical applications. Researchers have established improved nutritional indexes with an increasing number of complex nutritional indicators. The Geriatric Nutritional Risk Index (GNRI) is one of the most commonly used nutritional indicators in the elderly patient population[6]. The Controlling Nutritional Status (CONUT) score, which is calculated based on the serum albumin concentration, total peripheral lymphocyte count, and total cholesterol concentration, was developed as a screening tool for early detection of poor nutritional status[7]. Both indexes provide useful information for evaluating nutritional status comprehensively, and are currently widely applied in the evaluation of patients with tumors[8] that are undergoing dialysis[9]. These tools exhibit limited application in cardiovascular disease, however.

Hypertension, the most commonly occurring diseases in the elderly population, is associated with a number of comorbidities. When elderly patients are hospitalized due to infection or other reasons, the effects of nutritional status on their prognosis of merits further evaluation. The applicability of indexes such as GNRI or CONUT scores in assessing such patients has yet to be fully validated. The primary goal of this study was to elucidate the effect of nutritional status on survival in patients with hypertension and aged over 80 years.

METHODS

Study Design

This is a single center, prospective, randomized, control and observational trial. We design to consecutively enrolled hypertensive patients hospitalized in prescribed time and followed up to 90 days. The relationship between nutritional status and prognosis was analyzed.

Patients

This study included patients with hypertension who were diagnosed using the criteria listed in Chinese Hypertension Prevention Guide (2010)[10], hospitalized from January 2011 to December 2013, and aged >80 years. The study cohort comprised 336 Chinese hypertensive patients aged≥80 years who were enrolled consecutively at the Department of Geriatric Cardiology. All the patients are veterns. The study was conducted at the People's Liberation Army General Hospital under the full ethical approval of the Human Investigation Committee. Informed consent was obtained from each patient prior to their participation. The Chinese People's Liberation Army General Hospital was their designated hospital and held their integrated long-term medical and final death records, which made it easier for us to follow them up effectively and judge endpoints accurately.

Follow-up

A follow-up on all selected subjects was conducted throughout a 90-day post-admission period. Follow-up times were set to occur 7, 14, 30, and 90 day after admission and were conducted by interviewing each patient via telephone and by reviewing his or her medical records. All-cause mortality was determined at the end of the follow-up period. No patient dropped out during the study period. Follow-up data was tracked directly and telephoned to interviews. Death was ascertained from the death record, i.e., a legal document including time, site, and other necessary information.

General information and medical history

General information, including age, sex, lifestyle (smoking and drinking) and basic medical history were collected. Patients were selected based on height, weight, resting heart rate, systolic blood pressure, and diastolic blood pressure.

Nutritional metabolism and related biochemical indexes

Upon admission routine blood tests was conducted for all enrolled patients in the Central Laboratory of our hospital. Detection indexes included white blood cells, lymphocytes, platelets, hemoglobin (Hgb), serum creatinine (sCr), albumin (Alb), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBS), blood urea nitrogen (BUN), uric acid (UA), pre albumin (PA), and electrolyte index.

The nutritional status of each patient was also evaluated using two composite indexes: CONUT score and GNRI. The CONUT score was determined in accordance with the tool described in Table 1, which was first used by Ulibarri[7]. The GNRI, which includes two nutritional indicators (albumin and actual weight compared to ideal body weight), was developed by modifying the nutritional risk index for elderly patients. GNRI=[1.487* serum albumin (g/L)] t[41.7 *present/usual weight (kg)][6].

Statistical analysis

All calculations were performed in SPSS ver. 22.0. For continuous quantitative data, the K-S normality test was first applied to analyze whether the normal distribution of quantitative data could be analyzed by an independent-sample t-test. Data that were not normally distributed were analyzed via Mann-Whitney U test. A Pearson's chi-squared (χ^2) test was run to analyze the categorical variables. Survival curves were generated via Kaplan-Meier method, and multivariate analysis using a Cox proportional hazards model was used for independent tests of significance. Two-tailed P values <0.05 were considered significant.

RESULTS

Clinical characteristics

A total of 336 hypertensive patients were enrolled, including 323 males and 13 females, with an average age of 87.39± 5.23 years. All patients were diagnosed with hypertension ranging from 5-27 years and had received antihypertensive drug treatment. All patients had a history of CAD; 83 patients had a history of myocardial infarction, 29 patients had received stent therapy, 67 suffered from chronic heart failure, 167 had T2DM, and 124 had anemia. Of these cases, 192 were admitted for respiratory tract infection (RTI) and the remaining 144 patients were admitted for non-infective factors, such as angina pectoris or uncontrolled blood pressure, among others.

The CONUT scores of the selected patients were determined and analysis was conducted as presented in Table 2. Only five patients scored over 9, which indicates severe malnutrition. We combined their data with those exhibiting moderate malnutrition for analysis. Heart rate and blood glucose levels were higher in patients with high CONUT scores than in those with low CONUT scores. The proportion of patients with poor nutritional status due to admission caused by RTI was significantly high, as well (χ^2 =70.835, p=0.000).

Table 3 compares the nutritional index of patients with different reasons for admission. Patients with RTI showed generally low nutritional status, including low BMI, albumin level, GNRI score, high FBS, and CONUT score upon admission.

Follow-up results

A total of 27 deaths were recorded in the 90-day follow-up; most of these deaths occurred between 30 to 90 day (n=17, 62.97%) post-admission. The parameters and characteristics of different outcomes for the patients are presented in Table 4. No differences in age, sex, or combination of diseases were found between different outcomes. Likewise, no differences in systolic blood pressure were found. The surviving patients, however, showed increased BMI (24.25±3.05 vs.24.25±3.05, p=0.012), hemoglobin (123.78±17.05 vs. 115.07±20.42, P=0.040), and albumin level, as well as reduced DBP (62.48±9.60 vs. 68.31±12.02, p=0.016) and FBS (6.90±2.48 vs. 8.24±3.51, p=0.010). No significant difference in plasma pre albumin level between different outcomes was indicated (19.21±8.70 vs.16.25±11.68, p=0.200).

Surviving patients had improved GRNI scores (99.42±6.55 vs. 95.69±7.77, p=0.002) and reduced CONUT scores (3.13±1.98 vs. 5.14±2.32) in the follow-up period, both of which indicated improved nutritional status. We found that along with increase in CONUT score, which suggests worse malnutrition, the incidence of all-cause mortality increased. This tendency was not observed in the GRNI group, however, as illustrated in Fig. 1.

Survival analysis according to CONUT and GNRI

Survival curves based on different nutritional evaluations were plotted as shown in Fig. 2. The survival rates were significantly lower in the high-CONUT group than in the low-CONUT group (χ^2 =13.372, p=0.001). The survival curves based on the GNRI are shown in Fig. 3. Differences among groups could not be determined (χ^2 =7.694, p=0.053).

Prognostic values of CONUT and GNRI

Multivariate Cox regression analyses were conducted to investigate the possible predictors of all-cause mortality in the study population (Table 5). By regression, both RTI and CONUT were independent predictors of three-month all-cause mortality. Increasing hazard ratios (HR) were observed with increasing CONUT risk (from normal to moderate to severe). The HRs (95% CI) for the 90-d mortality were 1.458 (95% confidence interval 1.102–1.911, P=0.015). No significant correlation was indicated between the GNRI participants (HR=1.038, 95% confidence interval 0.960-1.115, P = 0.313).

Given that RTI is an independent risk factor for all-cause mortality, we further conducted Cox regression according to different reasons for admission as shown in Table 6. In the non-infection group, CONUT independently predicted all-cause mortality in the patients. However, in the RTI group, except CONUT was identified as an accurate predictor of all-cause mortality (HR=1.284, 95% confidence interval 1.013-1.740, P = 0.020), age also was link to all-cause mortality(HR=1.139, 95%

confidence interval 1.007-1.287, P=0.038).

Regarding the ROC analysis, an admission CONUT higher than 3.0 was found to predict all-cause mortality with a sensitivity of 77.8% and a specificity of 64.7% (AUC = 0.778, P<0.001).

DISCUSSION

The findings in this study indicated that nutritional status is associated with 90-d all-cause mortality in hypertension patients aged > 80 years. A CONUT score that was higher on admission was an independent predictor for all-cause mortality 1.458 (95% confidence interval 1.102–1.911, P=0.015). As CONUT score increased, the incidence of all-cause mortality likewise increased in patients admitted for both RTI (HR=1.284, 95% confidence interval 1.013-1.740, P = 0.020) and other reasons (HR=1.841, 95% confidence interval1.117–4.518, P = 0.011).

The relationship between nutritional status, particularly malnutrition, and prognosis of patients with cardiovascular disease has garnered increasing research interest[11]. In a study including 2,251 patients with a mean age of 65.0±12.8 years, multiple logistic regression analysis indicated that malnutrition is an independent factor influencing post-MI complications[12]. Another Chinese study confirmed that nutritional status is independently associated with the risk of all-cause mortality in geriatric patients with CAD. Whether nutritional support in these types of patients improves clinical outcomes merits further investigation[13]. A study involving subjects with heart failure indicated that poor nutritional status, as assessed via CONUT score, and atherosclerosis, as indicated via CIMT, is significantly associated with inflammation and predicts poor outcomes in CHF patients[14]. A relationship between nutritional status and prognosis in patients with hypertension is rarely observed; for elderly patients, such a relationship occurs even more rarely.

CONUT is calculated using laboratory data including albumin concentration, lymphocyte count, and cholesterol level. This index can accurately reflect the nutritional status and immune function of the body. Previous reports on prognosis evaluation and CONUT have mostly focused on tumor or liver diseases. Yoshida[15], for example, found that a moderate or severe CONUT score is an independent risk factor for any morbidity and severe morbidities for esophageal cancer. The same research team also concluded that CONUT is a convenient and useful tool for nutritional status assessment prior to esophagectomy. Similar conclusions were drawn for patients with nasopharyngeal carcinoma[16]. Studies on cardiovascular disease have been rare in this regard, however.

A study on STEMI patients showed that the CONUT score is associated with an increased risk of all-cause mortality for both unadjusted as well as age- and sex-adjusted models; in a full-adjusted model, the best predictors were age and BNP[17]. In patients with chronic heart failure, a mean follow-up period of 28.4 months revealed that patients experiencing cardiovascular events had impaired nutritional status, higher CONUT scores, lower PNI scores, and lower GNRI scores compared to patients who did not experience cardiovascular events[18]. In this study, we found that only CONUT, not GNRI, is an accurate predictor for all-cause mortality in hypertension patients up to three months after admission.

A study involving patients admitted to an acute geriatric unit showed that both albumin and CONUT are accurate predictors of short- and medium-term mortality; however, the study added little to the information provided by albumin alone[19]. Our results indicate that for hypertensive patients admitted for other reasons, albumin and CONUT are independent predictors of all-cause mortality; for hypertensive patients suffering from RTI, however, only CONUT provided useful prognostic information. We therefore conclude that for patients admitted with hypertension, CONUT is a valuable nutritional status index.

GNRI, which is determined based on the albumin level and weight of the patient, is a relatively new index for the nutritional assessment for elderly patients [5 20]. Past studies have shown that a higher-risk GNRI is positively correlated with length of hospital stay though the association between higher-risk GNRI and in-hospital mortality is not significant[21]. GNRI is the most widely used tool in chronic kidney disease with or without dialysis[9 22 23]. Multivariate Cox proportional hazards analysis demonstrated that GNRI <100, serum ferritin >/= 500 mu g/L, and age ≥65 y are significant predictors for mortality in hemodialysis patients [24]. Increased GNRI is also associated with increased CRP levels and low lymphocyte counts after multivariable adjustment. Some studies have also reported on GNRI as a prognostic factor in cardiovascular diseases [25 26]. In this study, however, we found that GNRI is not an independent predictor for all-cause mortality in patients with hypertension.

The present study was not without limitations. First, it was a single-center study that included a relatively small number of patients. Follow-up studies were only performed for only 90-day; a lengthier follow-up study is currently being conducted to further explore the results reported here.

CONCLUSION

We found that nutritional status assessed using CONUT and not by other nutritional index in hypertensive patients over 80-year can efficiently predict all-cause mortality within 90 day post-admission. Increased CONUT score was related to an increase in the incidence of all-cause mortality in patients admitted for RTI and other reasons. An accurate evaluation of nutritional status may provide additional prognostic information for such patients and management of nutritional status may significantly improve treatment outcomes.

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Contributors

Guarantor of overall study integrity: LLM.The design of the study:SXN, LLM, and YP. Data collection and interpretation:SXN and ZXQ. Statistical analysis:SXN and LLM. Manuscript preparation:SXN and LLM. Final approval of manuscript:SXN, LLM, ZXQ, and YP.

Data sharing statement

All data generated or analyzed during this study are included in this article and no additional data are available.

Ethics approval

Human Investigation Committee of the People's Liberation Army general hospital.

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Conflicts of interest

The authors declare no conflict of interest.

Table 1. Screening Tool for Controlling Nutritional Status or CONUT

Table 1.Screening Tool for Controlling Nutritional Status or CONUT

Parameter	**Requirements**	**Score**
Albumin(g/l)	≥35	0
	30-34	2
	25-29	4
	＜25	6
Total lymphocyto count(/ml)	≥1600	0
	1200-1599	1
	800-1199	2
	＜800	3
Total cholesterol(mmol/l)	≥4.65	0
	3.62-4.64	1
	2.58-3.61	2
	＜2.58	3

Dysnutritional states: Normal 0-1;Mild 2-4;Moderate 5-8;Severe 9-12

Table 2. Characteristics of study population and nutritional parameters based on nutritional status

Table 2 Characteristics of the study population and nutritional parameters based on nutritional status

	Normal (CONUT=0–1,n=67)	Mild malnutrition (CONUT 2–4,n=178)	Moderate–severe malnutrition (CONUT ≥5,n=91)	P

Age(year, $\bar{x}\pm s$）	87.24±4.75	87.18±4.95	87.75±5.56	0.638
Male(n,%)	64 (95.52)	169 (94.54)	90(98.90)	0.270
Smoking history(n,%)	19(28.36)	60(33.71)	44(48.35)	0.018
Anemia(n,%)	20(29.85)	63(35.39)	41(45.05)	0.129
DM(n,%)	37(55.22)	93(52.24)	34(37.36)	0.035
Admission for RTI(n,%)	18(26.86)	91 (51.12)	83(91.21)	0.000
SBP (mmHg, $\bar{x}\pm s$)	129.49±15.11	133.96±18.88	134.04±19.92	0.236
DBP (mmHg, $\bar{x}\pm s$)	67.85±9.40	67.71±13.03	68.50±11.03	0.953
HR (beat/min， $\bar{x}\pm s$)	70.97±12.94	73.22±14.61	82.20±17.46	0.000
BMI (kg/m^2, $\bar{x}\pm s$)	25.08±3.10	24.15±3.09	23.03±2.73	0.010
Hgb(g/l, $\bar{x}\pm s$)	125.06±17.23	123.01±16.81	122.64±18.76	0.475
TC(mmol/l, $\bar{x}\pm s$）	4.53±0.08	2.77±1.60	0.93±1.51	0.000
TG(mmol/l, $\bar{x}\pm s$）	1.85±1.28	1.15±1.02	0.54±0.27	0.000
LDL-C(mmol/l, $\bar{x}\pm s$）	2.63±0.61	1.76±0.72	1.53±0.71	0.000
HDL-C(mmol/l, $\bar{x}\pm s$）	1.16±0.36	1.03±0.46	1.03±0.48	0.104
Scr(mmol/l, $\bar{x}\pm s$）	106.66±44.72	109.24±53.41	110.03±59.36	0.941
BUN(mmol/l, $\bar{x}\pm s$）	8.18±3.95	9.20±4.61	10.21±4.76	0.016
UA(umol/l， $\bar{x}\pm s$）	335.51±101.25	347.15±97.37	321.76±109.13	0.081
TP(g/l, $\bar{x}\pm s$)	69.40±5.25	68.75±6.36	65.90±7.56	0.000
Albumin(g/l, $\bar{x}\pm s$)	40.13±3.31	39.49±3.50	35.83±4.73	0.000
FBS(mmol/l, $\bar{x}\pm s$）	6.26±2.41	7.11±2.64	7.39±2.60	0.021
Prealbumin(mg/dl, $\bar{x}\pm s$)	10.76±12.88	17.02±12.05	19.15±7.25	0.000

Table 3. Characteristics of study population and nutritional parameters by different admission reasons

Table 3 Characteristics of the study population and nutritional parameters by different admission reasons

	RTI （n=192）	Other causes （n=144）	Statistical value	P
Age(year)	87.56±5.29	87.25±5.11	0.292	0.589
Male(n,%)	185(96.35%)	143(95.97%)	0.033	0.855
Smoking history(n,%)	77(40.1%)	46(30.87%)	3.101	0.078
DM(n,%)	88(45.83%)	79(53.02%)	1.734	0.188
Hyperlipidemia(n,%)	98(51.04%)	79(53.02%)	0.132	0.717
BMI(kg/m^2)	23.68±3.16	24.53±3.00	4.991	0.026
TP(g/l)	67.79±7.65	68.08±5.67	0.150	0.699
Alb(g/l)	37.43±4.62	40.00±5.25	33.01	0.000
Hemoglobin(g/l)	122.69±19.10	123.61±15.14	0.235	0.628
	109.40±56.54	108.73±48.46	0.013	0.909

Creatinine (umol/l)				
BUN(mmol/l)	9.92±5.10	8.53±3.84	7.670	0.006
FBS(mmol/l)	7.63±2.75	6.19±2.14	27.98	0.000
UA(mmol/l)	328.74±102.06	350.96±104.49	3.875	0.050
Pre albumin(mg/dl)	18.73±8.89	13.58±13.65	17.645	0.000
GRNI score	97.72±7.68	100.49±5.35	11.822	0.001
CONUT score	4.19±2.08	2.09±1.34	112.593	0.000

Table 4. Comparison of characteristics of study population and laboratory parameters by different outcomes

Table 4 Comparison of the characteristics of the study population and laboratory parameters by different outcomes

	Death for all cause (n=27)	Survival (n=314)	P
Age(year)	89.29±4.57	87.26±5.25	0.052
Male (n, %)	27(100)	308(98.08)	0.281
DM (n,%)	15 (55.56)	152 (48.41)	0.304
Hyperlipidemia (n,%)	12 (44.44)	165 (52.55)	0.431
CKD (n,%)	9(33.33)	88(28.02)	0.667
Anemia (n,%)	13(48.15)	112(35.67)	0.206
SBP (mmHg)	133.29±18.43	126.85±20.16	0.085
DBP (mmHg)	68.31±12.02	62.48±9.60	0.016
BMI (kg/m^2)	22.31±3.31	24.25±3.05	0.012
TP(g/l)	67.85±9.59	67.92±6.58	0.962
Alb(g/l)	36.37±5.00	38.74±4.16	0.005
Hemoglobin (g/l)	115.07±20.42	123.78±17.05	0.040
Creatinine (umol/l)	110.74±61.19	108.97±52.44	0.868
BUN(mmol/l)	10.86±4.64	9.18±4.62	0.071
FBS(mmol/l)	8.24±3.51	(6.90±2.48	0.010
UA(mmol/l)	312.00±82.94	340.72±105.31	0.169
Prealbumin(mg/dl)	19.21±8.70	16.25±11.68	0.200

COUNT score	5.14±2.32	3.13±1.98	0.000
GNRI	95.69±7.77	99.42±6.55	0.026

DM: diabetes mellitus; SBP:systolic blood pressure; DBP: diastolic blood pressure; BMI:body mass index; TP:total protein; Alb: albumin; BUN:blood urea nitrogen; UA:uric acid

Table 5. Multivariate Cox regression for all-cause mortality

	B	Wald	Sig	HR	95%CI
RTI	0.436	4.915	0.018	1.461	1.109–2.791
Chronic heart failure	0.037	1.829	0.052	1.008	0.873–1.059
Age	1.691	1.016	0.098	1.023	0.731–1.078
BMI	-0.148	2.180	0.140	1.102	0.831-1.213
Prealbumin	0.025	0.675	0.411	1.026	0.965–1.090
GNRI	0.037	1.019	0.313	1.038	0.916–1.115
CONUT	0.359	5.926	0.015	1.458	1.012–1.911

Table 6. Cox regression analysis of common nutritional evaluation index for possible predictors of all-cause mortality by reason of admission

Table 6. Cox regression analysis of common nutritional evaluation index for possible predictors of all-cause mortality by reason of admission

	Adjusted HR with 95% CI for RTI			Adjusted HR with 95% CI for other reasons		
	HR	95%CI	P	HR	95%CI	P
Age	1.139	1.007–1.287	0.038	1.254	0.873–2.497	0.986
BMI	0.837	0.676–1.035	0.101	0.817	0.364–1.007	0.748
Prealbumin	1.022	0.948–1.102	0.573	2.418	0.014–42.28	0.633
GNRI	1.057	0.978–1.143	0.159	1.231	0.816–4.941	0.747
CONUT	1.284	1.013–1.740	0.020	1.841	1.117–4.518	0.011

Figure 1. All-cause mortality among different nutritional statuses

Figure 2. Kaplan-Meier survival curves for CONUT

Figure 3. Kaplan-Meier survival curves for GNRI

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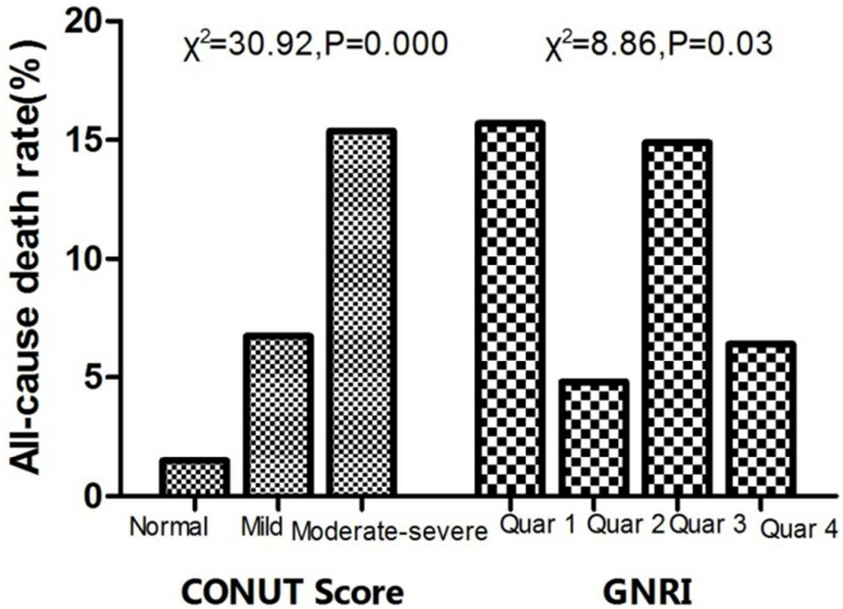

Figure 1. All-cause mortality among different nutritional statuses

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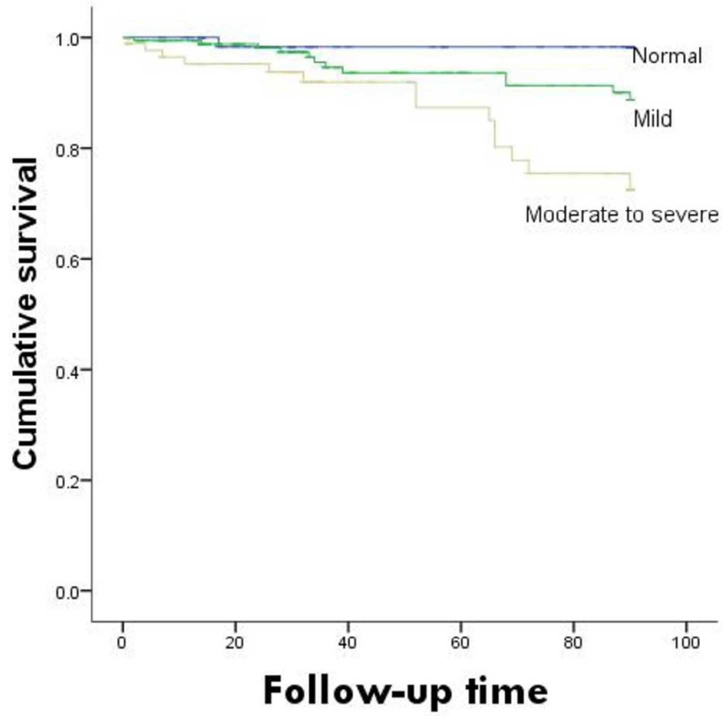

Figure 2. Kaplan-Meier survival curves for CONUT

79x59mm (300 x 300 DPI)

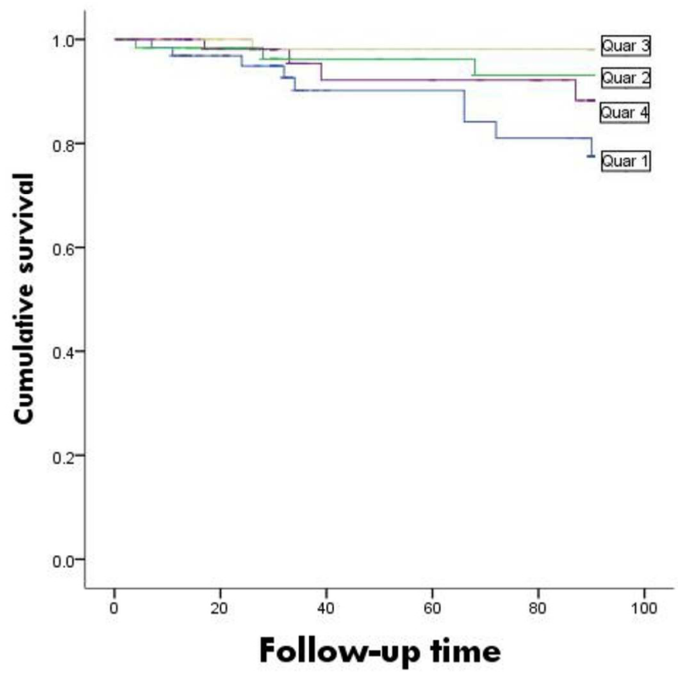

Figure 3. Kaplan-Meier survival curves for GNRI

82x60mm (300 x 300 DPI)