

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Controlling Nutritional Status (CONUT) score as a predictor of all-cause mortality in elderly hypertensive patients: a prospective follow-up study
AUTHORS	Sun, Xiaonan ; Luo, Leiming; Zhao, Xiaoqian; Ye, Ping

VERSION 1 - REVIEW

REVIEWER	Giuseppina Basta CNR, Institute of Clinical Physiology, Pisa, Italy
REVIEW RETURNED	13-Jan-2017

GENERAL COMMENTS	<p>The authors elucidated the effect of nutritional status on survival in patients with hypertension and aged over 80 y, through the nutritional indexes such as CONUT and GNRI. The survival rates were significantly lower in the high-CONUT group than in the low-CONUT group.</p> <p>1)The description of the main drugs used from the patients (which are CAD patients) should be indicated.</p> <p>2)The English is to be reviewed and errors are to correct (see: COUNT instead CONUT).</p>
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REVIEWER	Ian Ball Western University, London, Ontario, Canada
REVIEW RETURNED	21-Feb-2017

GENERAL COMMENTS	It is difficult to provide a fair assessment of this manuscript due to its very poor English grammar. I suggest that the authors hire a professional writer to help them with the grammar, then resubmit.
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VERSION 1 – AUTHOR RESPONSE

1. Based on the reviewers' comments, we added to the general drug treatment of patients with CAD.
2. The article has been polished by professional company, modified grammar errors, and made the article more fluency.

VERSION 2 – REVIEW

REVIEWER	Kotaro Nochioka Tohoku University Hospital, Japan
REVIEW RETURNED	29-Apr-2017

GENERAL COMMENTS	<p>This observational study “Controlling Nutritional Status (CONUT) score as an effective predictor of all-cause mortality in elderly hypertensive patients” evaluates the association between nutritional status assessed by CONUT score and 90-day all-cause mortality in elderly people with hypertension admitted for respiratory tract infection (RTI) and non-infective reasons. The authors concluded that nutritional status is an independent predictor for short term mortality in this population. Topic is clinically importance and good clinical data are urgently needed.</p> <p>This reviewer has the following points for the authors to address:</p> <p>1. Sample selection: The authors enrolled 336 hospitalized patients with hypertension and age>80 years. Of these, 192 were admitted for RTI and the remaining 144 patients were for non-infective reasons. As results, 323 (89%) are male and 336 (100%) had a history of coronary artery disease; 83 patients had a history of myocardial infarction, 29 patients had received stent therapy, 67 suffered from chronic heart failure. Therefore, I am not sure the authors can say “patients with hypertension” to this population. I also have a concern about selection bias. How they enrolled this sample? Consecutively? Why the number of women is so small (11%) and all patients had a history of coronary artery disease?</p> <p>2. Variable selections in Cox models: During 90 days, 27 patients died. For evaluating the association between CONUT score and all-cause death, the authors adjusted for RTI, age, BMI, Alb, pre-albumin, GNRI in Table 5, and BMI, Alb, Hemoglobin, pre-albumin and GNRI in Table 6. I have a concern about overfitting in the models. In addition, how they chose covariates for adjustment? For example, chronic heart failure would be also one of potential confounders. Furthermore, calculations for CONUT score and for GNRI need albumin level. Did the author check collinearity among CONUT score, GNRI and albumin before putting together in the models?</p> <p>3. Predictive performance of CONUT score: For comparison with GNRI, applying AUC or NRI would be better to justify the authors 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..”.</p>
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REVIEWER	Takanori Arimoto From the Department of Cardiology, Pulmonology, and Nephrology, Yamagata University School of Medicine, Yamagata, Japan
REVIEW RETURNED	09-May-2017

GENERAL COMMENTS	Sun et al. describe the prognostic importance of objective nutritional index, CONUT score, in elderly patients with hypertension. Please
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summarize the Conclusion section. The conclusion is too long.

VERSION 2 – AUTHOR RESPONSE

1. Please edit your title to make sure that it is not declarative and that it contains the study design. We suggest: 'Controlling Nutritional Status (CONUT) score as a predictor of all-cause mortality in elderly hypertensive patients: a prospective follow-up study'.

Thank you for your suggestion on the title. We considered that your proposal includes the study design and purpose, and it is an excellent title, so we revised the title according to your suggestion.

2. Please complete and include a STROBE checklist, ensuring that all points are included and state the page numbers where each item can be found. The checklist can be downloaded from here:

<http://www.strobe-statement.org/?id=available-checklists>

We completed the contents according to STROBE checklist requirements, and modify and upload.

3. Please put years instead of just y and days instead of just d

As suggested, we modified the relevant abbreviated contents of “y” and “d” in the article.

4. In the Strengths and Limitations section, the strengths need to just be strengths, this should not be an article summary. Please include sample size information.

According to the suggestions, we modified Strengths and Limitations sections.

Reviewer 3

1. Sample selection: The authors enrolled 336 hospitalized patients with hypertension and age > 80 years. Of these, 192 were admitted for RTI and the remaining 144 patients were for non-infective reasons. As results, 323 (89%) are male and 336 (100%) had a history of coronary artery disease; 83 patients had a history of myocardial infarction, 29 patients had received stent therapy, 67 suffered from chronic heart failure. Therefore, I am not sure the authors can say “patients with hypertension” to this population.

I also have a concern about selection bias. How they enrolled this sample? Consecutively? Why the number of women is so small (11%) and all patients had a history of coronary artery disease?

The hypertensive patients admitted in our hospital in the stipulated period were successively selected as the study objects. The author team work in a military hospital and undertakes the medical work of the retired army cadre group. The selected patients of this age period were all retired military officers. Subject to the conditions, there are few female subjects finally selected. There was the detailed medical record for this part of people in our hospital. From the medical record, cardiovascular initial diagnosis of such patients was hypertension and accepting antihypertensive therapy. With the increase of age and extension of course of disease, there were diseases of other categories for such hypertensive patients, as mentioned in the article. Therefore we still defined such patients as hypertensive patients. In our clinical practice, there was a higher proportion for patients who were aged above 80 having multiple diseases.

2. Variable selections in Cox models: During 90 days, 27 patients died. For evaluating the association between CONUT score and all-cause death, the authors adjusted for RTI, age, BMI, Alb, pre-albumin, GNRI in Table 5, and BMI, Alb, Hemoglobin, pre-albumin and GNRI in Table 6. I have a concern about overfitting in the models.

In addition, how they chose covariates for adjustment? For example, chronic heart failure would be also one of potential confounders. Furthermore, calculations for CONUT score and for GNRI need albumin level. Did the author check collinearity among CONUT score, GNRI and albumin before putting together in the models?

Thanks for the reviewer's statistical suggestions proposed on COX model. We just list parameters which univariate analysis be incorporate meaningful in multivariate table and we modified the correction parameters and relevant statistics in the article after asking for professional statisticians'

suggestions. See details on new table 5 and table 6. 67 enrolled patients combined with chronic heart failure but most of them were well controlled, so the Cox regression showed no significance difference.

3. Predictive performance of CONUT score: For comparison with GNRI, applying AUC or NRI would be better to justify the authors 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."

Thanks for the suggestions proposed. By our new Cox regression analysis results, only CONUT score was linked to all-cause mortality. And we also conducted the ROC of CONUT. We found that CONUT higher than 3.0 on admission 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).

Reviewer 4

Sun et al. describe the prognostic importance of objective nutritional index, CONUT score, in elderly patients with hypertension. Please summarize the Conclusion section. The conclusion is too long. According to the suggestions, the modification was conducted, and simplifying the conclusion. Thank the reviewers for the pertinent advice of the manuscript. If any question, please do not hesitate to contact me.

VERSION 3 - REVIEW

REVIEWER	Takanori Arimoto Department of Cardiology, Pulmonology, and Nephrology, Yamagata University School of Medicine, Yamagata, Japan
REVIEW RETURNED	03-Jun-2017

GENERAL COMMENTS	This article seems to be corrected properly.
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