

Association between the modified Nutrition Risk in Critically Ill (mNUTRIC) score and clinical outcomes in the intensive care unit: A secondary analysis of a large prospective observational study

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1 **Association between the modified Nutrition Risk in Critically Ill (mNUTRIC) score**
2 **and clinical outcomes in the intensive care unit: A secondary analysis of a large**
3 **prospective observational study**

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18 **Abstract**

19 **Background**

20 Malnutrition in intensive care unit (ICU) patients is associated with adverse clinical outcomes.

21 The nutrition risk in the critically ill score (NUTRIC) was proposed as an appropriate nutritional

22 assessment tool in critically ill patients. This score uses interleukin-6 (IL-6), a biomarker that

23 is not always available. This prospective observational study was conducted to identify the
24 nutritional risk in ICU patients using the modified NUTRIC (mNUTRIC) score (which does
25 not include IL-6) and to explore the relationship between 28-day mortality and high mNUTRIC
26 scores.

27 **Methods**

28 The data were extracted from The Beijing Acute Kidney Injury Trial (BAKIT). This trial was
29 a prospective, observational, multi-centre study conducted in 30 ICUs at 28 tertiary hospitals
30 in Beijing, China, from March 1 to August 31, 2012. In total, 9049 patients were admitted
31 consecutively, and 3107 patients with complete clinical data were included in this study. The
32 predictive capacity of the mNUTRIC score was studied by receiver operating characteristic
33 (ROC) curve analysis. The significance level was set at 5%.

34 **Results**

35 Among the 3107 patients, the 28-day mortality rate was 17.4% (540 patients died). High
36 nutritional risk patients were older ($P < 0.001$), with higher illness severity scores than low
37 nutritional risk patients. Multivariate analysis revealed that the mNUTRIC score was an
38 independent risk factor for 28-day mortality and mortality increased with increasing scores (p
39 = 0.000). The calculated area under curve (AUC) for the mNUTRIC score was 0.763 (CI 0.740
40 - 0.786).

41 **Conclusions**

42 Nearly 28.2% of patients admitted to the ICU were at risk of malnutrition, and a high
43 mNUTRIC score was associated with increased ICU length of stay and higher mortality.

44 **Trial Registration**

45 This study was registered at www.chictr.org.cn (registration number Chi CTR-ONC-11001875).

46 Registered on 14 December 2011.

47 **Key words**

48 The modified nutrition risk in critically ill score, Intensive care unit, Mortality

49 **Background**

50 Malnutrition is common in intensive care unit (ICU) patients, it is associated with a variety of

51 adverse outcomes, including higher complication rates, prolonged mechanical ventilation,

52 prolonged hospitalization, and higher mortality[1, 2]. For critically ill patients, we need to

53 assess their nutritional status and provide adequate nutritional support[3], so effective tools are

54 needed to determine which ICU patients need nutritional support and the benefits of nutritional

55 support. However, traditional methods of nutrition assessment are limited in the hospital setting.

56 Recently, Heyland et al[4] published the first nutritional risk assessment tool specifically

57 designed for critically ill patients: the NUTRIC score.

58 The NUTRIC score includes age, the Acute Physiology and Chronic Health Evaluation II

59 (APACHE II) score[5], the Sequential Organ Failure Assessment (SOFA) score[6],

60 comorbidities, days from hospitalization to ICU admission, and the interleukin-6 (IL-6) level,

61 which was developed to link starvation, inflammation, and clinical outcomes[4]. Patients are

62 scored from 0 to 10, a score of 6 or greater indicates a high nutritional risk.

63 The NUTRIC score can predict 28-day mortality in a medical-surgical ICU population, high-

64 risk patients who stayed in the ICU for more than 3 days benefited more from nutritional support

65 than low-risk patients[4]. But the use of original NUTRIC score is limited by the availability of
66 IL-6, which is not readily available in many institutions. Another study evaluated a modified
67 NUTRIC score excluding IL-6 and found that a score of 5 or higher still indicated a high risk
68 of malnutrition[7]. Moreover, Heyland et al.[4] stated that IL-6 only increased the C-index by
69 0.007 (from 0.776 to 0.783), with no statistical difference. Therefore, they suggested that in
70 settings in which IL-6 is not available, it could be omitted from the NUTRIC score. This
71 adjusted score is called the modified NUTRIC score (mNUTRIC). Rahman et al[8] evaluated
72 this modified NUTRIC score and found that mortality increased by 1.4 % (95% CI, 1.3-1.5) for
73 every point increase in the mNUTRIC score.

74 Using appropriate nutrition screening and assessment tools will help identify effective strategies
75 that reduce the negative impact of malnutrition. Our study was conducted to identify the
76 prevalence of nutritional risk in general ICU patients based on mNUTRIC scores.

77 **Methods**

78 **Study design and data collection**

79 This study used a database from a prospective, multi-centre, observational study that
80 investigated the epidemiology of acute kidney injury (AKI) in critically ill patients in 30 ICUs
81 at 28 tertiary hospitals in Beijing, China, from March 1 to August 31, 2012 (the Beijing Acute
82 Kidney Injury Trial (BAKIT)[9]. (for a complete list of these hospitals and the persons
83 responsible for the data acquisition, see Additional file 1). Study subjects included all adult
84 patients (age \geq 18 years) admitted consecutively to the ICU. Only the initial ICU admission was
85 considered in this study. The following patients were excluded: patients with preexisting end-
86 stage chronic kidney disease, patients already receiving renal replacement therapy (RRT)

87 before admission to the ICU, and patients who had received kidney transplantation in the
88 previous 3 months[10]. Pre-existing comorbidities were diagnosed based on the International
89 Classification of Diseases (ICD-10) codes. Patients were followed up until death, until hospital
90 discharge, or for 28 days. Among the 9079 patients who were admitted consecutively, 3107
91 patients were included in our study (Figure 1).

92 Thorough follow-up of all patients included in the study was conducted in the first 10 days after
93 ICU admission. The collected data included demographics, anthropometrics, admission
94 diagnosis, comorbidities, daily vital signs and laboratory data, which were used to automatically
95 calculate the APACHE II score, the Simplified Acute Physiology Score II (SAPS II) score[11]
96 and the SOFA score, days from hospital to ICU admission, ICU length of stay (LOS), hospital
97 LOS, use of vasoactive drugs, and length of mechanical ventilation. RRT data were also
98 reported.

99 The patients were followed up until death, hospital discharge, or for 28 days.

100 **Nutritional support**

101 Nutritional support methods were based on the guidelines for enteral and parenteral nutrition
102 issued by the European and American Society of Enteroprotective Nutrition[12], combined
103 with our accumulated clinical experience, individualized nutritional support was given to all
104 patients. The patients began enteral nutrition (EN) 20-25 kcal/(kg.d) within 24-48 hours of
105 admission to the ICU (on average). If the patient was intolerant of EN or had contraindications
106 to EN, parenteral nutrition (PN) support was given within 24 - 48 hours. If EN could not fully
107 meet the nutritional needs of patients, appropriate intravenous supplementation with glucose,
108 amino acids, or fat emulsion was given, that is, the combination of EN and PN.

109 **Definitions**

110 We used the modified 9-point scale of the NUTRIC score, the mNUTRIC score. We defined
111 the scores from 0 to 4 as “low scores”, which indicated a low level of risk of malnutrition, and
112 the scores from 5 to 9 as “high scores”, which were associated with worse clinical outcomes.

113 **Statistical analysis**

114 Non-normally distributed continuous variables were expressed as the medians with interquartile
115 ranges (IQRs) and were compared using the Mann-Whitney U test or Kruskal-Wallis analysis
116 of variance with Bonferroni correction. Categorical variables were expressed as the number of
117 cases and proportions and were compared using the Mantel-Haenszel Chi-square test.

118 A multivariate Cox regression analysis was performed using a backward stepwise selection
119 method, with P value < 0.05 as the entry criterion, and P value \geq 0.10 as the removal criterion.

120 The assumption of proportional hazards was checked graphically using log (-log (survival
121 probability)) plots and was found to be appropriate. Variables considered for multivariable
122 analysis included age, sex, body mass index (BMI), illness severity scores, use of vasoactive
123 drugs, mechanical ventilation and underlying diseases. We tested for collinearity among all
124 variables using a Cox regression analysis to generate hazard ratios (HR) and 95% confidence
125 intervals (CIs).

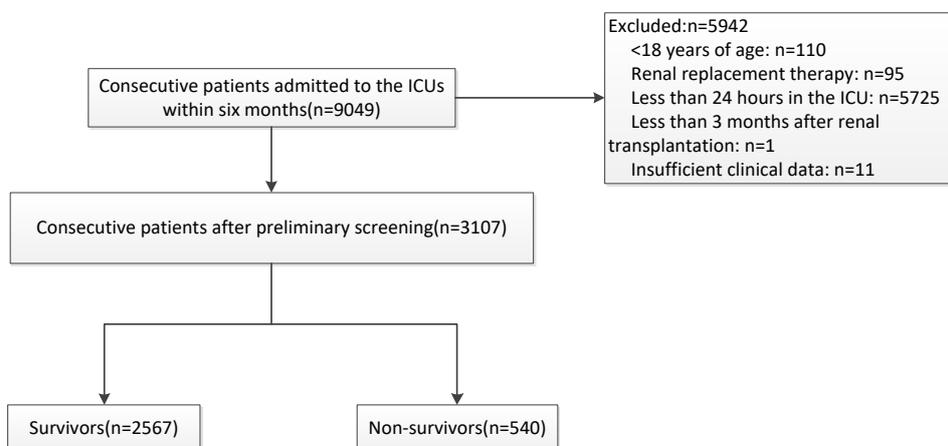
126 Receiver operator characteristic curve analysis was used to calculate the sensitivity and
127 specificity for comparisons of outcomes and mNUTRIC scores. The 28-day survival stratified
128 by low and high mNUTRIC scores was additionally evaluated graphically using the Kaplan-
129 Meier product limit survival plot.

130 All statistical analyses were performed using SPSS software (IBM Corp., Statistics for
131 Windows, version 22.0, Armonk, NY, USA), with a two-sided P value < 0.05 considered
132 statistically significant.

133 **Results**

134 **Study population**

135 Among the 9049 patients enrolled in the BAKIT study, 5942 were excluded for the reasons
136 shown in Figure 1, leaving 3107 patients for analysis. The characteristics of the entire cohort
137 are shown in Table 1. The median age was 64.0 (IQR: 51.0 - 77.0) years, and 61.5% were men.
138 The all-cause 28-day mortality rate was 17.4% and the median ICU LOS was 4.0 (IQR: 2.0 -
139 9.0) days. Among the included patients, the median BMI was 24.0 (IQR: 21.0 - 26.0) kg/m²,
140 the median APACHE II score was 14.0 (IQR:10.0 - 20.0), the median SOFA score was 6.0
141 (IQR: 3.0 - 8.0), and the median number of comorbidities was 1 (IQR: 0 - 2). Mechanical
142 ventilation was used in 2021 (65.0%) patients, 1307 patients (42.1%) received vasopressors,
143 and 281 patients (9.0%) underwent RRT. A total of 876 patients (28.2%) had high mNUTRIC
144 scores.



145
146 Figure.1 Flowchart of validation cohort
147

Table 1 Patient characteristics by mNUTRIC score

Characteristic	All patients (n=3107) Median(IQR) Number (%)	Low nutrition risk(n=2231) Median(IQR) Number (%)	High nutrition risk(n=876) Median(IQR) Number (%)	P value
Age(years)	64(51 -77)	60(47 -72)	76(66-82)	<0.001
Male sex	1912(61.5)	1378(61.8)	534(61.0)	0.919
BMI	24(21-26)	24(22-26)	23(21- 26)	0.003
Vasoactive therapy	1307(42.1)	954(42.8)	353(40.3)	0.457
Mechanical ventilation	2021(65.0)	1354(60.7)	667(76.1)	<0.001
Sepsis	896(28.8)	419(18.8)	477(54.5)	<0.001
Severity of illness				
APACHEII	14(10-20)	12(8-15)	23(19- 28)	<0.001
SAPSII	34(26-45)	30(23-38)	50(39- 64)	<0.001
SOFA	6(3-8)	4(3-7)	9(6-11)	<0.001
NUTRIC score	3(2-5)	3(2-3)	6(5-7)	<0.001
Admission category				
medical	1480(47.6)	878(39.4)	602(68.7)	<0.001
surgical	1627(52.4)	1353(60.6)	274(31.3)	
Comorbid diseases				
Cancer	486(15.6)	297(13.3)	189(21.6)	
Hypertension	1222(39.3)	739(33.1)	483(55.1)	
Coronary disease	615(19.8)	293(13.1)	322(36.8)	
Chronic kidney disease	170(5.5)	63(2.8)	107(12.2)	
Diabetes	532(17.1)	277(12.4)	255(29.1)	
COPD	166(5.3)	89(4.0)	77(8.8)	
Category of ICU admission diagnosis				
Cardiovascular	848(27.3)	681(30.5)	167(19.1)	
Respiratory	548(17.6)	316(14.2)	232(26.5)	

Neurologic	462(14.9)	321(14.4)	141(16.1)	
Trauma	238(7.7)	191(8.6)	47(5.4)	
Gastrointestinal	607(19.4)	413(18.5)	194(22.1)	
Metabolic	77(2.5)	43(1.9)	34(3.9)	
Outcome data				
ICU LOS(days)	4(2-9)	4(2-7)	6(3-13)	<0.001
Hospital LOS(days)	19(12-29)	19(12-28)	21(11-34)	0.002
28-day mortality	540(17.4)	208(9.3)	332(37.9)	<0.001
In-hospital mortality	521(16.8)	173(7.8)	348(39.7)	<0.001
AKI	1334(42.9)	752(33.7)	582(66.4)	<0.001
RRT	281(9.0)	108(4.8)	173(19.7)	<0.001
Hospitalization expense (thousand yuan)	40(19-96)	34(17-87)	55(27-113)	<0.001

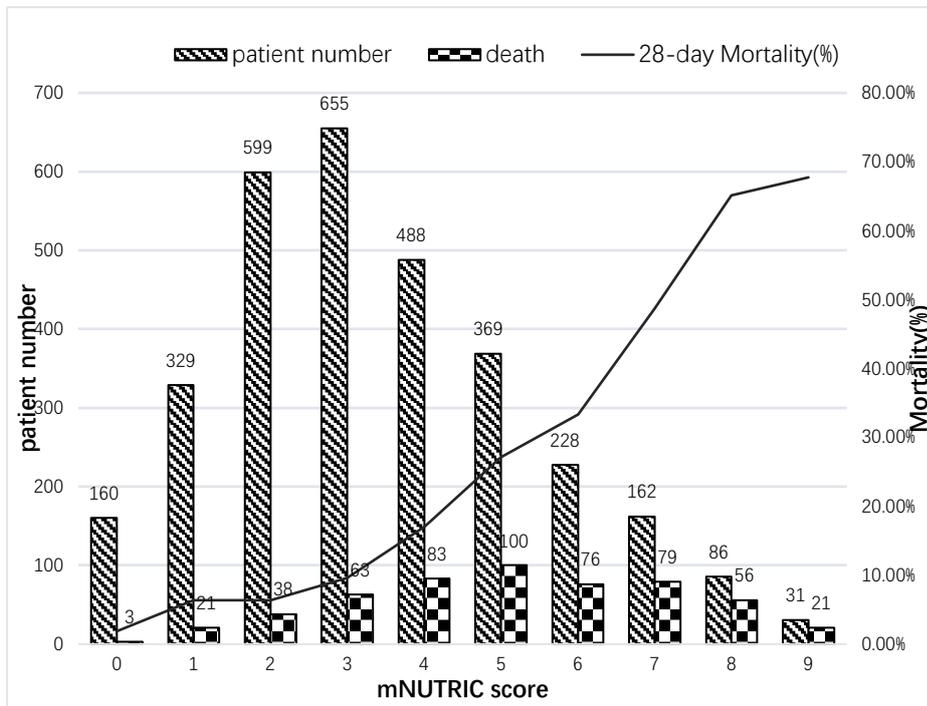
148 Data are expressed as the median (interquartile range),and number (percentage). BMI,body mass index;SAPS II,
149 Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; APACHE II, Acute
150 Physiology and Chronic Health Evaluation II; NUTRIC score, the nutrition risk in the critically ill
151 score;COPD,chronic obstructive pulmonary disease;LOS, length of stay;AKI, acute kidney injury; RRT, renal
152 replacement therapy.
153

154 **Characteristics of high nutritional risk patients**

155 From Table 1, we can see high nutritional risk patients were older ($P < 0.001$), with higher illness
156 severity scores than low nutritional risk patients. High nutritional risk patients were more likely
157 to present with sepsis on ICU admission and had longer durations of ICU and hospital stays
158 when compared to the low nutritional risk group. Furthermore, mechanical ventilation was
159 more commonly used in high nutritional risk patients (76.1% vs 60.7%; $P < 0.001$). The 28-day
160 mortality and in-hospital mortality rates were higher among high nutritional risk patients than
161 low nutritional risk patients ($P < 0.001$).

162 **28-Day mortality according to score**

163 Our analysis showed that the 28-day mortality increased with higher mNUTRIC scores (Figure
 164 2), and the 28-day mortality for the maximum mNUTRIC score was 67.4%.



165
 166 Figure 2. The 28-day mortality according to modified NUTRIC score.

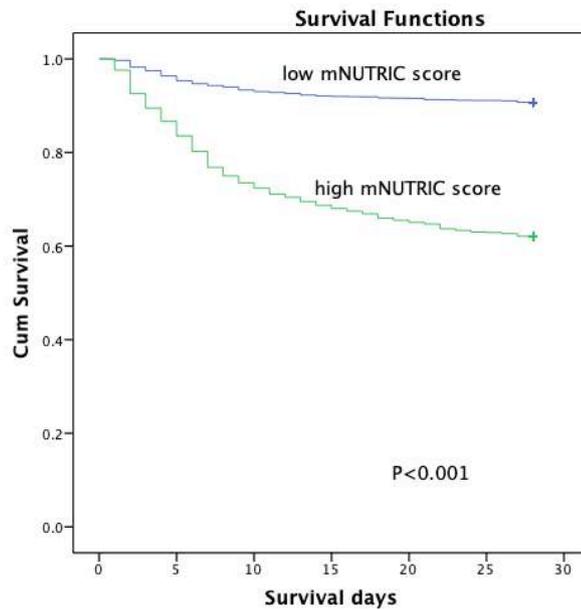
167
 168 **High mNUTRIC score and the 28-day mortality**

169 In multivariate Cox regression analysis (Table 2), after adjusting for age, sex, BMI, illness
 170 severity scores, use of vasoactive drugs, mechanical ventilation and underlying diseases, the
 171 mNUTRIC score, sepsis and AKI were independent predictors of 28-day mortality. The
 172 presence of high mNUTRIC scores was associated with a higher risk of mortality (Figure 3).

Table 2 Multivariate Cox regression analysis of 28-day mortality in all patients

Characteristic	Hazard ratio	95%CI	P
mNUTRIC score	1.430	1.351–1.514	0.000
Sepsis	2.832	2.272-3.529	0.000
AKI	2.171	1.732-2.720	<0.001

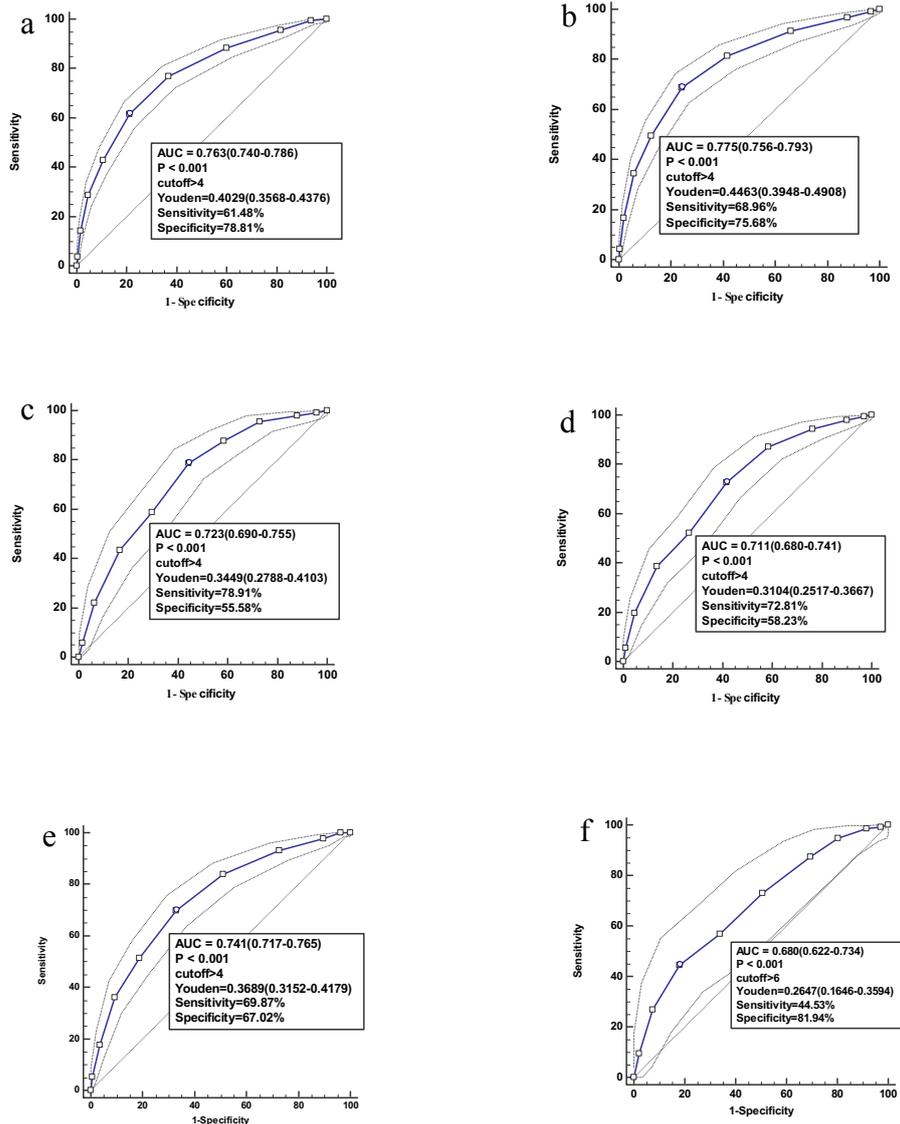
173 mNUTRIC score, the modified nutrition risk in the critically ill score; AKI, acute kidney
174 injury; CI, confidence interval



175 Figure 3 Survival curve of 28-day mortality stratified by mNUTRIC scores.

176 **Area under the curve of scores for predicting 28-day mortality**

177 We can see that in this cohort and each subgroup, the areas under the curve (AUCs) of the
178 mNUTRIC score for predicting 28-day mortality indicated good predictive performance of the
179 score (Figure 4). In the ROC curve for the mNUTRIC score, the best cut-off value was at 4
180 (sensitivity 61.48% and specificity 78.81%) in this cohort, and the Youden index was 0.4029.



181
 182 Figure 4 Performance of mNUTRIC scores in predicting 28-day mortality. a. All patients (n=3107); b. All
 183 mechanical ventilation patients (n=2021); c. Medical mechanical ventilation patients (n=751); d. Sepsis
 184 patients (n=896); e. AKI patients (n=1334); f. CRRT patients (n=281)

185
 186 **Discussion**

187 This study was a secondary analysis of a prospective observational study in surgical-medical
 188 ICUs. We used a validated nutrition assessment tool in an attempt to demonstrate an association
 189 between malnutrition and 28-day mortality. We found a high incidence of malnutrition in ICU
 190 patients, and malnutrition was associated with a poor prognosis.

191 In the present study, 28.2% of the critically ill patients admitted to the ICU were at high
192 nutritional risk and had mNUTRIC scores ≥ 5 . These findings were similar to the results of a
193 study conducted in Turkey[13], in which 22.4% patients were evaluated as having high scores
194 (between 5 and 9). Lew et al[14] also demonstrated that the prevalence of malnutrition in the
195 ICU was 28% using the 7-point Subjective Global Assessment (7-point SGA) to determine
196 patients' nutritional status. Recently, a study[15] reported that 45% of mechanically ventilated
197 patients admitted to the ICU were at high nutritional risk. Similarly, Kalaiselvan et al.[16]
198 reported that 42.5% of mechanically ventilated patients had NUTRIC scores ≥ 5 . Our study is
199 more generalizable because of the inclusion of both medical and surgical patients. The
200 aforementioned studies included only patients on mechanical ventilation, and patients on
201 mechanical ventilation were more seriously ill than those not on mechanical ventilation. The
202 differences among studies are mainly the result of different populations and nutrition screening
203 tools.

204 In our study, the 28-day mortality associated with the maximum mNUTRIC score was 67.7%,
205 which is similar to the finding in the study by Jeong[17], in which this rate was 62.5%.
206 Compared with patients with a low NUTRIC score, patients with high NUTRIC score had a
207 higher mortality rate and longer ICU LOS. Similar results were reported by Mendes et al[1], in
208 which the NUTRIC score was used in an ICU population, and the findings are consistent with
209 those in the study by Heyland[4].

210 The mortality rate in our study was 17.4%, which was lower than the rate reported in the second
211 validation study of the NUTRIC score (29%) by Rahman et al[8]. This difference may be

212 because our study included many postoperative care patients. In this study, we found that the
213 mNUTRIC score was a good prognostic predictor in critically ill patients and that high
214 mNUTRIC scores were associated with an elevated risk of death at 28 days (HR=1.430, 95%
215 CI=1.351 to 1.514, P=0.000). This finding is consistent with those of prior studies [1, 18, 19].
216 Several studies have shown that the beneficial effects of adequate nutritional support are more
217 evident in high-risk patients than in low-risk patients[20, 21]. The mNUTRIC score may be
218 helpful in guiding clinicians in providing adequate nutritional support to ICU patients.

219 The mNUTRIC score was found to have a fair predictive performance for 28-day mortality in
220 this cohort (AUC 0.763; 95% CI 0.740 - 0.786) and each subgroup. These results are in line
221 with those of the initial validation study by Heyland et al. (AUC: 0.783)[4] and a recently
222 published validation study of the mNUTRIC score by Mukhopadhyay et al. (AUC 0.71)[22].
223 Recently, a study[17] showed that the AUC of the NUTRIC score for the prediction of 28-day
224 mortality was 0.762 (95% CI: 0.718-0.806), while that of the mNUTRIC score was 0.757 (95%
225 CI: 0.713-0.801). There was no significant difference between the two scores ($p = 0.45$). The
226 mNUTRIC score is a good nutritional risk assessment tool for critically ill patients.

227 We found that the best cut-off value for the mNUTRIC score was > 4 (sensitivity 61.48% and
228 specificity 78.81%) in this cohort, and the Youden index was 0.4029, which is consistent with
229 previous work by de Vries et al[23]. However, in another study, the best cut-off value was at 6
230 (sensitivity 75% and specificity 65%), and the Youden index was 0.401[17]. Jung et al reported
231 that patients were considered to be at high risk of malnutrition and to benefit from aggressive
232 nutritional support when their mNUTRIC score was ≥ 5 [24]. Our study included patients with

233 various diseases, while Jung's study population was limited to patients with sepsis. Further
234 investigation is needed to find the best cut-off value of the mNUTRIC score to define the high-
235 risk group.

236 The limitations of our study stem mainly from the fact that it is a secondary analysis of an
237 original database that lacked data on inflammation indicators such as IL-6. Therefore, we could
238 not calculate the NUTRIC score to verify the differences between the two scores. Second,
239 nutrition history and feeding parameters were not available in our cohort, so the associations
240 among nutritional adequacy, mNUTRIC score and mortality could not be confirmed by our
241 results.

242 **Conclusion**

243 Patients were considered to be at high risk of malnutrition when their mNUTRIC score was >
244 4. The mNUTRIC score is a practical, easy-to-use tool based on variables that are easy to obtain
245 in the critical care setting.

246 **Abbreviations**

247 ICU: intensive care unit;NUTRIC: the nutrition risk in the critically ill score;IL-6: interleukin-
248 6;mNUTRIC: the modified nutrition risk in the critically ill score;ROC: receiver operating
249 characteristic;AUC: area under curve;AKI: acute kidney injury;BAKIT: the Beijing Acute
250 Kidney Injury Trial;BMI: body mass index;RRT: renal replacement therapy;APACHE II: acute
251 physiology and chronic health evaluation II;SAPS II: the simplified acute physiology score
252 II;SOFA: sequential organ failure assessment;LOS: length of stay;EN: enteral nutrition; PN:

253 parenteral nutrition; IQR: interquartile range;HR: hazard ratio; CI: confidence interval;COPD:
254 chronic obstructive pulmonary disease

255 **Acknowledgments**

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257 (see Additional file 1) for participating in database management.

258 **Authors' contributions**

259 NW and MPW designed and carried out the study, NW performed the statistical analysis, and
260 drafted the manuscript. LJ and BD were involved in design and in acquisition of data and helped
261 to revise the manuscript critically for important content. BZ was involved in the design and the
262 statistical analysis. The Beijing Acute Kidney Injury Trial (BAKIT) Workgroup participated in
263 acquisition and interpretation of data. XX conceived of the study, participated in its design, and
264 helped to revise manuscript. All authors read and approved the final manuscript.

265 **Conflict of interest**

266 The authors declare that they have no conflict of interest.

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269 Commission, a government fund used to improve health-care quality (No. D101100050010058).
270 It offered financial support for data collection.

271 **Availability of data and materials**

272 The datasets used and analyzed during the current study are available from the corresponding
273 author on reasonable request.

274 **Ethics approval and consent to participate**

275 This study was approved by the Institutional Review Boards of the Ethics Committees of the
276 lead study centre (Fu Xing Hospital, Capital Medical University, China) and all other
277 participating hospitals (Additional file 2). We confirm that all methods were carried out in
278 accordance with relevant guidelines and regulations.

279 Being an observational study, written informed consent from participants to partake into the
280 study was not necessary. Hence, we obtained an informed consent waiver from the above
281 ethical committees.

282 **Consent for publication**

283 Not applicable.

284 **Competing interests**

285 The authors declare that they have no competing interests.

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356 Table 1 Patient characteristics by mNUTRIC score

357 Table 2 Multivariate Cox regression analysis of 28-day mortality in all patients

358 Figure.1 Flowchart of validation cohort

359 Figure 2. The 28-day mortality according to modified NUTRIC score.

360 Figure 3 Performance of mNUTRIC scores in predicting 28-day mortality. a. All patients

361 (n=3107); b. All mechanical ventilation patients (n=2021); c. Medical mechanical ventilation

362 patients (n=751); d. Sepsis patients (n=896); e. AKI patients (n=1334); f. CRRT patients

363 (n=281)

364 Figure 4 Survival curve of 28-day mortality stratified by mNUTRIC scores.

Figures

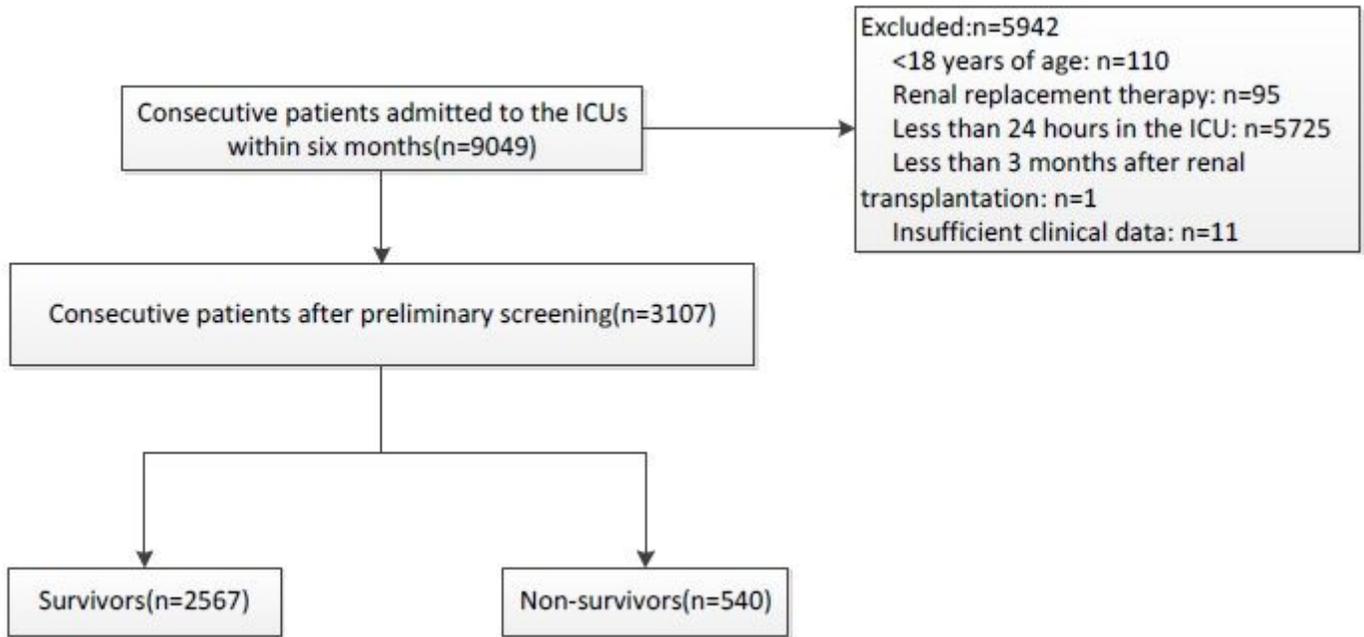


Figure 1

Flowchart of validation cohort

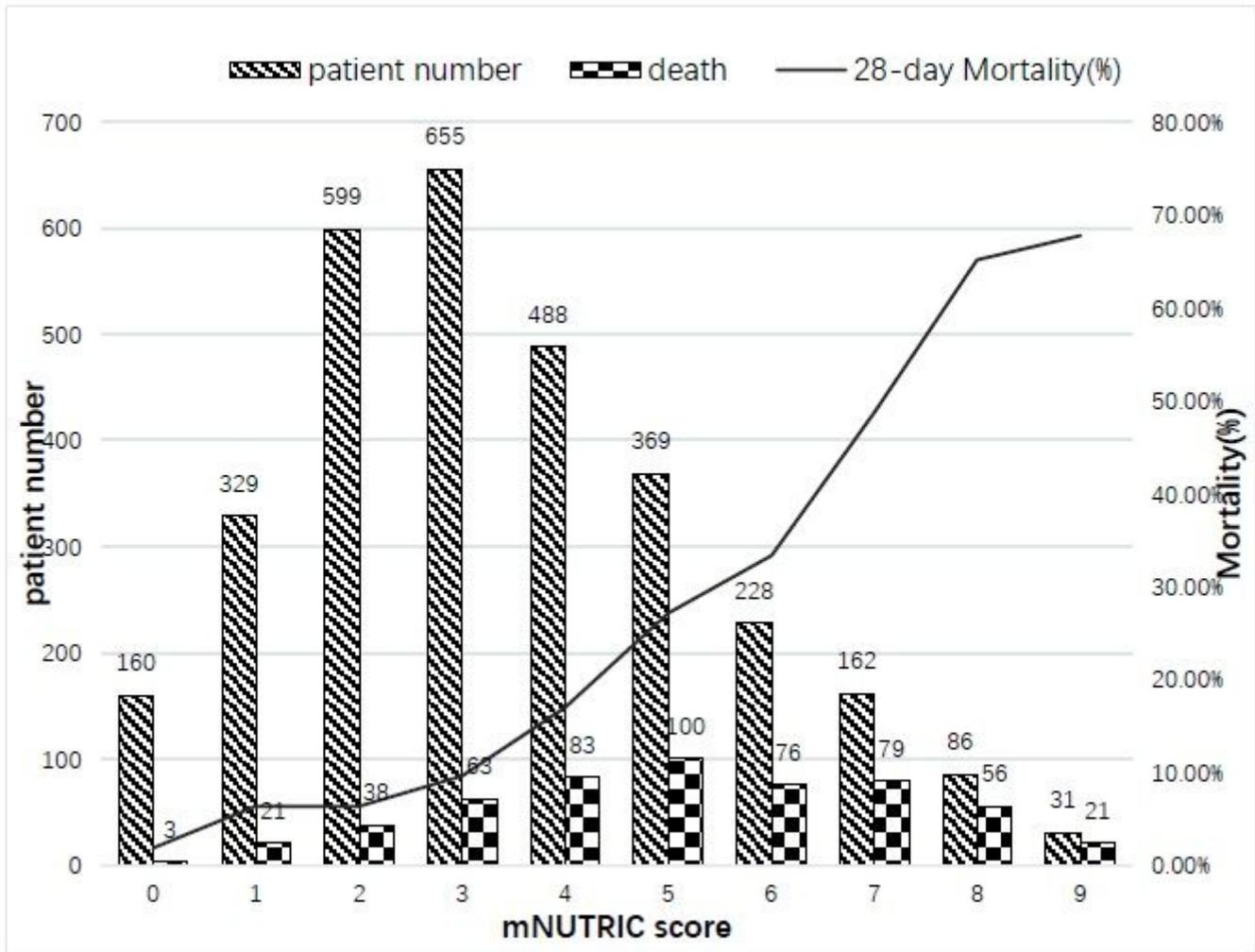


Figure 2

The 28-day mortality according to modified NUTRIC score.

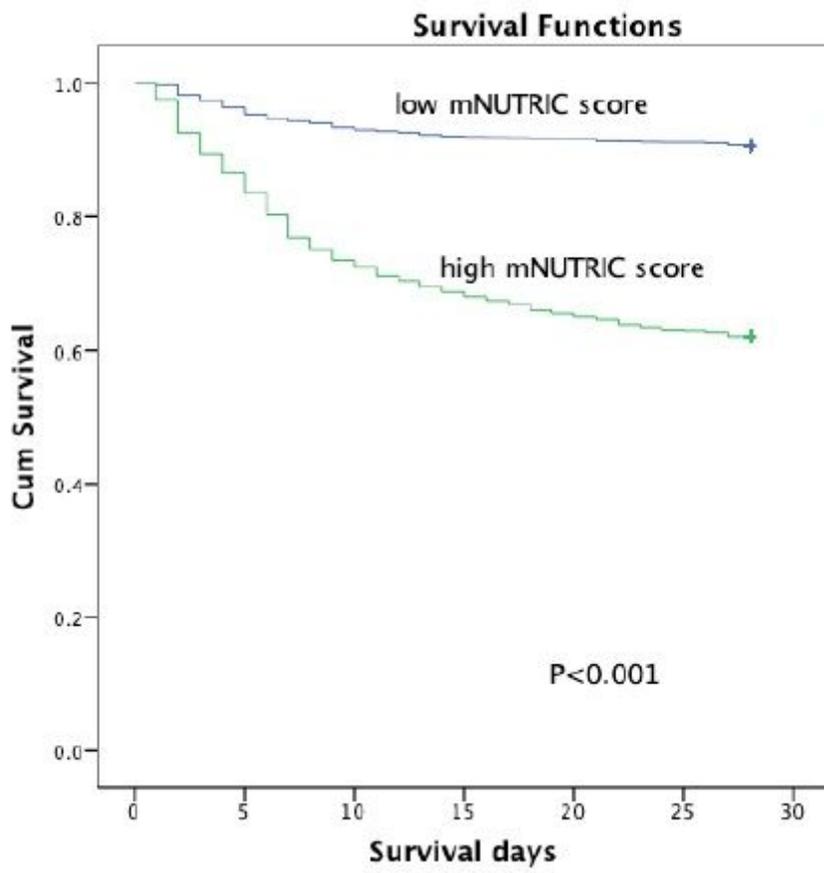


Figure 3

Survival curve of 28-day mortality stratified by mNUTRIC scores.

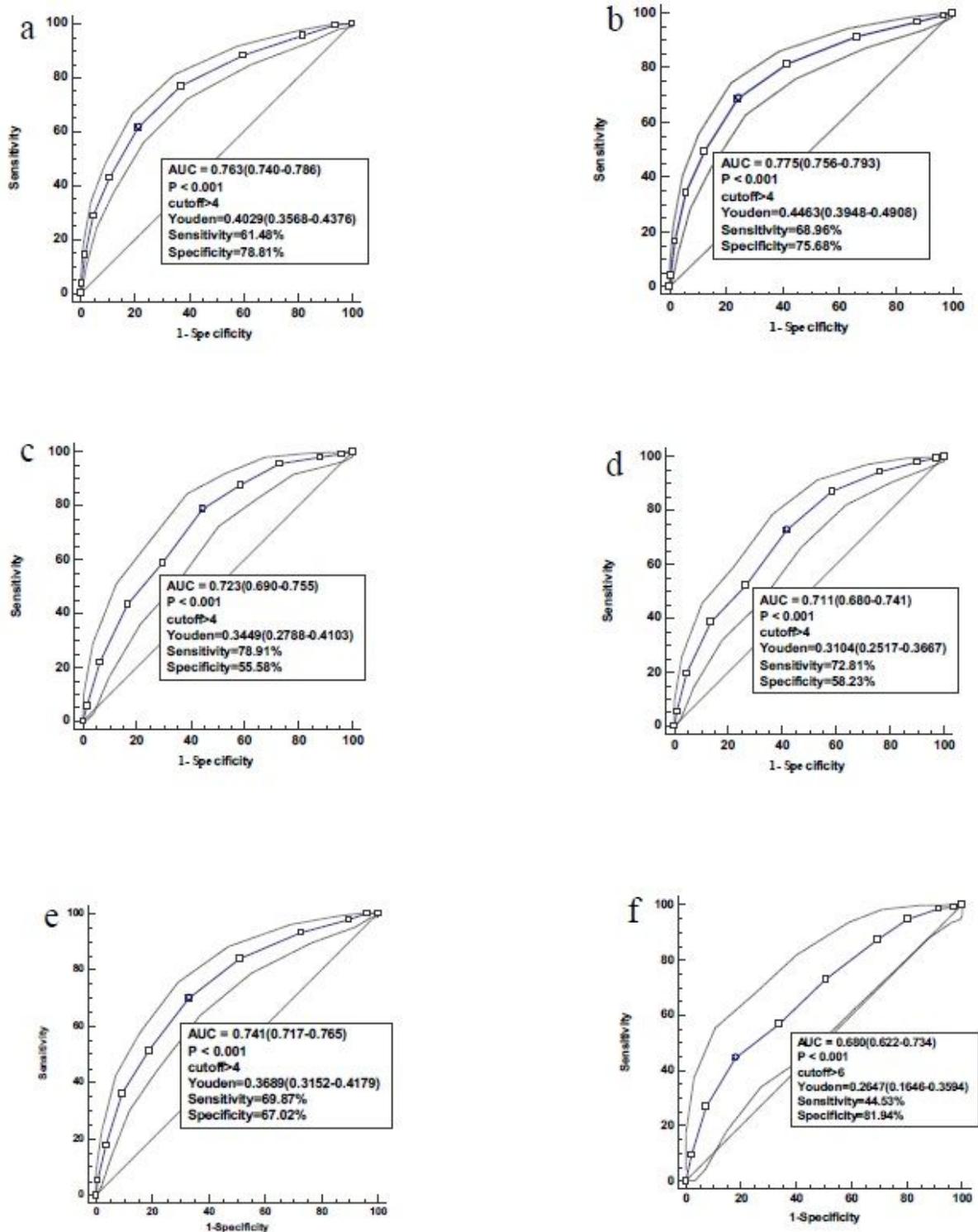


Figure 4

Performance of mNUTRIC scores in predicting 28-day mortality. a. All patients (n=3107); b. All mechanical ventilation patients (n=2021); c. Medical mechanical ventilation patients (n=751); d. Sepsis patients (n=896); e. AKI patients (n=1334); f. CRRT patients (n=281)

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