

# Lower geriatric nutritional risk index is associated with a higher risk of all-cause mortality in patients with chronic obstructive pulmonary disease: a cohort study from the National Health and Nutrition Examination Survey 2013–2018

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## ABSTRACT

**Object** Malnutrition negatively affects patients with chronic obstructive pulmonary disease (COPD). This study aimed to explore the potential association between malnutrition, as defined by the Geriatric Nutritional Risk Index (GNRI), and all-cause mortality in patients with COPD using the National Health and Nutrition Examination Survey (NHANES).

**Method** The data of 579 adults with COPD during NHANES 2013–2018 were analysed. Each patient was assigned to one of the two groups according to GNRI values: normal nutritional status (GNRI>98) and malnutrition status (GNRI≤98). Survival curves and Cox regressions were applied to evaluate the association between nutritional status and mortality.

**Results** Overall, the mean age was 63.4±0.5 years, and 53.9% of the patients were women. The prevalence of malnutrition was 6.6%, and the Kaplan-Meier curves for all-cause mortality according to nutritional status showed that malnutrition was associated with a higher incidence of all-cause mortality. The Cox regression analysis found that in the unadjusted model, the HR was 2.30 (95% CI 1.24 to 4.27, p=0.01). In the fully adjusted model, the adjusted HR was 2.47 (95% CI 1.36 to 4.5, p=0.003). Furthermore, subgroup analysis revealed that the risk of death due to malnutrition increased more than threefold in the low education and cancer subgroups.

**Conclusion** A low GNRI was an independent risk factor for all-cause mortality in patients with COPD.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of death worldwide, and many people die prematurely from COPD or its complications. Despite years of efforts, the mortality rate remains high. In 2016, there were 3 million deaths due to COPD, accounting for 6% of all deaths globally.<sup>1</sup>

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Malnutrition is prevalent in chronic obstructive pulmonary disease (COPD). Several tools were used to assess nutritional risk and have been proven to be related to the prognosis of COPD, but those tools have limitations.

### WHAT THIS STUDY ADDS

⇒ We developed a simple but accurate tool, the geriatric nutritional risk index (GNRI), to detect nutritional risk in patients with COPD. We proved that a low GNRI is associated with a higher risk of all-cause mortality in patients with COPD from the National Health and Nutrition Examination Survey.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ A low GNRI value might identify a group of patients at high risk of all-cause mortality, and this group of patients with COPD should be managed carefully to avoid poor prognosis caused by malnutrition.

In 2019, COPD was the third-leading cause of death worldwide, after ischaemic heart disease and stroke.<sup>2</sup> COPD is characterised by symptoms, such as cough, sputum production and particularly dyspnoea, which result in airflow obstruction. In addition, it is associated with multiple systemic manifestations leading to high treatment costs and poor prognosis. Abnormal nutritional status is the most prevalent comorbidity in patients with COPD. Data from previous studies<sup>3–5</sup> indicate that 30%–60% of the patients hospitalised with COPD are malnourished, depending on the different diagnostic methods and criteria used, and malnutrition has a negative impact



on prognosis, including a higher risk of hospitalisation, poor exercise tolerance, severe airflow obstruction or mortality.<sup>6–8</sup> Although a wide range of effective therapeutic approaches can be used, malnutrition remains underdiagnosed and undermanaged in patients with COPD.<sup>9</sup>

The Geriatric Nutritional Risk Index (GNRI) is a nutritional assessment tool that has recently become popular because of its simplicity and strong prognostic value in populations with different diseases.<sup>10–12</sup> Several medical indices, such as present body weight and serum albumin, were combined using a simple formula instead of many complicated indicators, which may overcome the shortcomings of limited indicators and subjective assessment. Therefore, the primary purpose of this study was to assess the relationship between malnutrition according to GNRI score and all-cause mortality using data from the National Health and Nutrition Examination Survey (NHANES).

## METHODS

### Data source and study design

The NHANES provides a representative sample of the entire USA population. A total of 5000 individuals are sampled every 2 years in this nationally representative cross-sectional survey conducted by the National Center for Health Statistics. Data collection includes three stages for all participants. First, highly trained field investigators conduct in-person household interviews. In the second stage, all participants are asked to complete a comprehensive health examination consisting of clinical tests, laboratory studies and additional interviews. These investigations are performed by experienced scientific personnel in specially designed and equipped mobile centres that travel to locations throughout the country. Postexamination interviews and questionnaires are administered via telephone or mail during the final stage. The NHANES website (<https://www.cdc.gov/nchs/nhanes/index.htm>) provides detailed information about the survey.

In the present analysis, publicly available data without personally identifiable information were used, and all methods were performed in accordance with relevant regulations and guidelines. A total of 29 400 people participated in 2013–2014 through the 2017–2018 NHANES surveys. Of these, 679 were initially included based on the following inclusion criteria: (1) participants  $\geq 18$  years of age and (2) participants who self-reported 'yes' to the questionnaire item 'Has a doctor or other health professional ever told you that you had COPD?', which was defined as having self-reported COPD. The exclusion criteria were as follows: (1) insufficient body information or laboratory data to calculate the GNRI score (99 participants were excluded) or (2) ineligible survival status data (1 participant was excluded). Finally, a total of 579 patients were included in this study.

### Definitions and outcomes

The GNRI is a simply nutritional assessment score but it has strong prognostic value for different medical populations, especially surgical patients. The GNRI was calculated based on serum albumin levels (g/L), present body weight (PBW, kg) and ideal body weight (IBW= $\text{height}^2 (\text{m}^2) \times 22$ ) according to the following formula:  $\text{GNRI} = 1.489 \times \text{albumin} + 41.7 \times \text{PBW} / \text{IBW}$ .<sup>10</sup> When the PBW exceeded the IBW, it was considered 1. Participants with COPD were categorised into two groups: malnutrition (GNRI $\leq 98$ ) and normal nutrition groups (GNRI $> 98$ ). The primary outcome was mortality rate. Determination of mortality status and causes of death using the NHANES National Death Index Public Access files on 31 December 2018.

### Covariates

Several predefined covariates associated with mortality were selected as possible confounders, based on previous NHANES studies. Sociodemographic characteristics included age, sex, ethnicity (including Mexican American, non-Hispanic black, non-Hispanic white, other Hispanic and other race—including multiracial), educational attainment (less than 9th grade, 9th–12th grade and above 12th grade),<sup>13</sup> marital status (married or living with partner and unmarried, including widowed, divorced, separated and never married), the ratio of family income to poverty (RIP) (low income: RIP $< 1$ , middle income:  $1 \leq \text{RIP} \leq 3$  and high income: RIP $> 3.0$ ) and health insurance (yes/no). Health-related lifestyle behaviours included smoking status, categorised as never smoking (defined as smoking less than 100 cigarettes in life), former smoking (defined as smoking more than 100 cigarettes in life and not at all now) and smoking (defined as smoking more than 100 cigarettes in life on some days or every day), according to a previous study.<sup>14</sup> The medical comorbidities included (1) dysglycaemia, defined as: diabetes mellitus diagnosed through random blood glucose  $\geq 11.1$  mmol/L, 2-hour glucose  $\geq 11.1$  mmol/L in an oral glucose tolerance test, measured glycosylated haemoglobin  $\geq 6.5\%$  or self-reported current users of insulin or oral hypoglycaemic agents or impaired fasting glucose, defined as fast glucose  $\geq 6.1$  mmol/L but  $< 7.0$  mmol/L or impaired glucose tolerance, defined as 2-hour glucose  $\geq 7.8$  mmol/L but  $< 11.1$  mmol/L; (2) hypertension, defined as a measured average systolic blood pressure  $\geq 140$  mm Hg or a measured average diastolic blood pressure  $\geq 90$  mm Hg; (3) cancer, defined as self-reported physician's diagnosis of cancer or malignancy and (4) congestive heart failure (CHF), defined as self-reported physician's diagnosis of CHF.

### Patient and public involvement

The patients did not participate in the design, conduct, report or dissemination of this study.

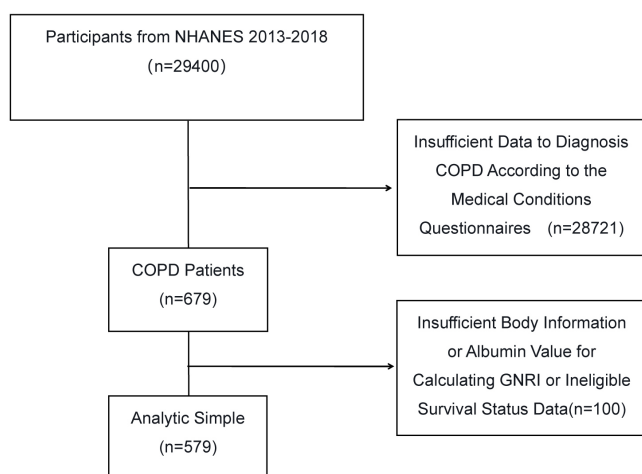
## Statistical analysis

Recommended weights were used to account for the planned oversampling of specific groups. The continuous variables were expressed as the mean±SD, and the categorical variables were presented as counts (percentages). A t-test was used for continuous variables and a  $\chi^2$  test for categorical variables to compare baseline characteristics between the two groups. The cumulative survival probabilities for all causes of death were calculated with the Kaplan-Meier survival analysis. Univariate and multivariate Cox proportional hazard regressions were used to estimate HRs and 95% CIs for the associations between nutritional status and mortality. Three models were constructed to obtain statistical inferences. Model 1 included only nutritional status. In model 2, age and smoking status were adjusted for statistically significant demographic variables, as determined through the univariate Cox analysis. Finally, model 3 was fully adjusted for all statistically significant variables determined using the univariate Cox analysis. Statistical significance was set at  $p < 0.05$ . Data were processed using R V.4.2.0 and GraphPad Prism V.20.0. In all analyses, differences were considered statistically significant at  $p < 0.05$ .

## RESULTS

### Baseline characteristics

Overall, 679 (4.1%) eligible patients with COPD were obtained from the publicly available NHANES according to the ‘medical conditions’ questionnaire. Of those with COPD, 100 participants lacked body information or albumin values for calculating the GNRI or survival status data eligible for the study. Therefore, this study included 579 participants (figure 1). The demographics and characteristics of the participants are presented in table 1. Their mean age was  $63.4 \pm 0.5$  years, and there was a higher proportion of women than that of men (53.9% vs 46.1%). Most patients were non-Hispanic



**Figure 1** Flow diagram of the study participants. COPD, chronic pulmonary obstructive disease; GNRI, Geriatric Nutritional Risk Index; NHANES, National Health and Nutrition Examination Survey.

Caucasian (80.9%). There were 403 (67.3%) patients with COPD with hypertension, 280 (46.9%) with dyslipidaemia, 132 (18.9%) with CHF and 143 (28.6%) with cancer. In accordance with GNRI scoring criteria, the 579 patients were divided into two categories: normal nutritional status and malnutrition groups. The incidence of malnutrition as defined by the GNRI was 6.6%, whereas 541 patients had no nutritional risk according to their GNRI score as shown in table 1. The prevalence of hypertension, dyslipidaemia, CHF and cancer did not differ between the two groups with respect to the nutritional risk indicated by the GNRI score. An overview of the data on the baseline characteristics of the study population is presented in table 1.

### Primary outcomes

By the census day of 31 December 2018, 109 (16.5%) participants had died. The median follow-up duration of the participants in this study was 37 months (range 1–85 months). The median follow-up time was 29 months (range 6–82 months) in the group with the lower GNRI index, while it was 38 months (range 1–85 months) in the group with the higher GNRI index. Online supplemental table 1 shows the reported causes of death. The participants who died were older, former smokers and more frequently non-Hispanic whites, with a higher proportion of hypertension and CHF, as shown in online supplemental table 2. The Kaplan-Meier curves of nutritional status for all-cause mortality indicated that malnutrition had a higher all-cause cumulative mortality (figure 2). Further, the Cox proportional risk regression analysis showed that malnutrition was correlated with a significantly elevated risk of long-term all-cause mortality when compared with normal nutritional status. Univariate Cox regression analysis identified nutritional status, age, smoking status, hypertension and CHF as significant variables. There were no significant differences in sex, ethnicity, education level, marital status, the RIP or health insurance coverage between the two groups. The details are presented in online supplemental table 3. Malnutrition was related to significantly increased risk of all-cause mortality in the unadjusted model 1 and adjusted model 2, (HR for malnutrition, respectively: 2.30 (95% CI 1.24 to 4.27) for unadjusted model 1 and 2.28 (95% CI 1.19 to 4.40) for adjusted model 2;  $p < 0.05$ ). In the whole significant variables adjusted model 3, the adjusted HR was slightly higher than that in model 1, and in model 2, and the HR was 2.47 (95% CI 1.36 to 4.5,  $p = 0.003$ ) (table 2). The details of the multivariate Cox hazard analyses are shown in online supplemental table 4.

### Subgroup analyses

In most subgroups, the Cox regression analysis revealed that malnutrition was associated with a higher mortality risk (figure 3). In the low education and COPD with cancer subgroups, malnutrition significantly increased the mortality risk. Analysis of the subgroup with low

**Table 1** Baseline characteristics of the study population (weighted)

Characteristics	Total (n=579)	No malnutrition (n=541 930.4%)	Malnutrition (n=3860.6%)	P value
Age, mean±SD	63.4±0.5	63.4±0.5	62.9±2.8	0.85
<65	281 (55.6)	265 (55.3)	16 (60.2)	0.61
≥65	298 (44.4)	276 (44.7)	22 (39.8)	
Gender, N (%)				0.46
Male	304 (46.1)	277 (45.7)	27 (53.2)	
Female	275 (53.9)	264 (54.3)	11 (46.9)	
Race/ethnicity, N (%)				0.78
Mexican American	26 (1.9)	6 (2.0)	0 (0.0)	
Non-Hispanic black	92 (6.7)	85 (6.6)	7 (8.3)	
Non-Hispanic white	383 (80.9)	356 (80.8)	27 (84.4)	
Other Hispanic	27 (2.3)	26 (2.3)	1 (0.9)	
Other race—including multiracial	51 (8.3)	48 (8.4)	3 (6.5)	
Educational attainment, N (%)				0.05
>12th grade	240 (44.2)	226 (45.3)	14 (25.3)	
9–12th grade	286 (50.3)	263 (49.1)	23 (71.5)	
<9th grade	52 (5.4)	51 (5.6)	1 (3.2)	
Marital status, N (%)				0.72
Married or living with partner	275 (56.6)	258 (56.3)	17 (61.3)	
Unmarried	303 (43.4)	282 (43.6)	21 (38.7)	
Smoking status, N (%)				0.09
Never	81 (12.5)	81 (13.2)	0(0.0)	
Former	243 (40.8)	231 (41.4)	12 (30.9)	
Present	254 (46.6)	228 (45.4)	26 (69.1)	
RIP, mean±SD	2.2±0.1	2.2±0.2	1.9±0.3	0.29
<1	167 (24.9)	155 (26.6)	12 (28.8)	0.59
1–3	265 (38.7)	244 (40.9)	21 (50.2)	
3	100 (29.8)	96 (32.5)	4 (21.1)	
Covered by health insurance, N (%)	542 (93.5)	506 (94.2)	36 (82.5)	0.06
Dysglycaemia, N (%)	280 (46.9)	269 (47.1)	11 (44.2)	0.83
Hypertension, N (%)	403 (67.3)	378 (68.0)	25 (54.6)	0.32
CHF, N (%)	132 (18.8)	123 (19.2)	9 (15.0)	0.55
Cancer, N (%)	143 (28.6)	132 (28.5)	11 (36.3)	0.35

CHF, congestive heart failure; RIP, the ratio of family income to poverty.

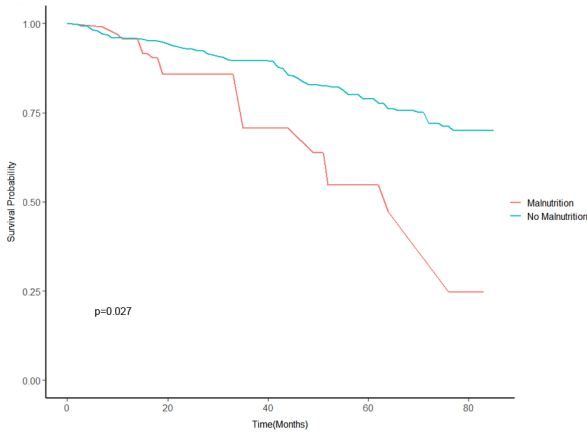
educational levels revealed that the HR for malnutrition was 4.85-fold higher ( $p<0.0001$ ). In patients with COPD-related cancers, malnutrition increased the risk of mortality by 328% ( $p=0.01$ ). In addition, malnutrition raised the risk of mortality, particularly in the male subgroup (HR for malnutrition was 3.51 (95% CI 1.72 to 7.15)), married or living with partner subgroup (HR for malnutrition was 3.88 (95% CI 1.22 to 12.32)), hypertension subgroup (HR for malnutrition was 3.10 (95% CI 1.67 to 5.74)), present smoking subgroup (HR for malnutrition was 3.71 (95% CI 1.52 to 9.01)), low income subgroup (HR for malnutrition, respectively: 2.55 (95% CI 1.36 to 4.75) for  $RIP<1$ , 2.88 (95% CI 1.12 to 7.36) for  $RIP 1<3$ ), and covered by health insurance subgroup

(HR for malnutrition was 2.58 (95% CI 1.43 to 4.67)). Furthermore, malnutrition raised the risk of death in both age subgroups (HR 2.42 for ages  $<65$  years old vs HR 2.71 for ages  $\geq 65$  years old). However, there were inadequate numbers of malnutrition cases in the Mexican-American subgroup to permit ethnicity-specific analyses.

## DISCUSSION

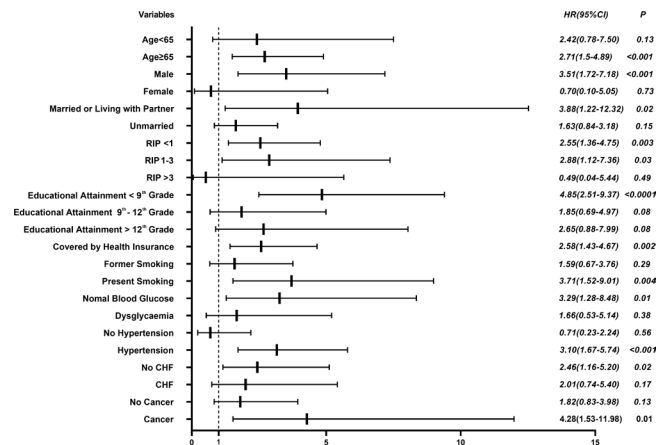
This study demonstrated that a low GNRI ( $\leq 98$ ) was correlated with increased mortality and was an independent risk factor for mortality.

COPD involves not only the airways, but also extrapulmonary organs, and malnutrition is a serious



**Figure 2** Kaplan-Meier survival estimates for long-term all-cause mortality (weighted).

extrapulmonary manifestation. Previous studies<sup>8</sup> and guidelines<sup>9</sup> have indicated that malnutrition develops as illness severity progresses, indicating a poor prognosis in patients with COPD. A low GNRI score was correlated with a high risk of malnutrition. The incidence of malnutrition, defined as a low GNRI, was close to the incidence reported by Jerng *et al.*<sup>15</sup> However, our incidence rate was lower than the average incidence reported in previous studies, possibly because all participants in this study were in a stable phase, and the severity of the disease was less than that of hospitalised patients. Malnutrition is defined as a nutrient deficiency that negatively affects the body's structural and/or functional capacity, including a decrease in calories and proteins. Malnutrition in patients with COPD may be associated with a lack of appetite caused by diminished general physical activity or depressive tendencies.<sup>16</sup> Second, increased energy expenditure due to respiratory effort may cause malnutrition in patients with COPD. Third, humoral factors, such as inflammatory cytokines, adipokines and hormones, are considered possible causes for malnutrition in patients with COPD.<sup>17 18</sup> Collectively, the imbalance between decreased oral intake and increased energy expenditure leads to a negative nitrogen balance and decreased skeletal muscle mass and function. In addition, this imbalance can reduce the diaphragm muscle mass and thickness, resulting in respiratory failure. Moreover,



**Figure 3** Forest plot of overall survival in subgroups (weighted). The reference group was no malnutrition group. CHF, congestive heart failure; RIP, the ratio of family income to poverty.

malnutrition can weaken immune defences in patients with COPD. Decreased immune defences are essential for the development and progression of COPD. Moreover, the risks of respiratory failure and pulmonary infection are significantly increased in patients with COPD and malnutrition.<sup>19 20</sup> Therefore, timely action should be taken to manage nutrition and avoid a poor prognosis due to malnutrition.

Malnutrition affects the prognosis of patients with COPD.<sup>21 22</sup> Malnutrition, as defined by a low GNRI, indicates a high risk of death, as demonstrated in this study. This association was stronger in the low education (less than ninth grade), COPD and cancer, hypertension, present smoking, low-income (RIP<3) and male subgroups. Thus, clinicians should be aware of this population's high risk of death and develop timely nutritional supplementation plans.

Currently, there is no consensus regarding the best screening method for assessing malnutrition in chronic patients. Previously, several tools have been used to evaluate nutritional risks and predict prognosis in patients with COPD, such as the Global Subjective Assessment,<sup>4</sup> Global Leadership Initiative for Malnutrition,<sup>6</sup> Nutritional Risk Screening 2002,<sup>23</sup> Mini Nutritional Assessment-Screening Form<sup>24</sup> and Malnutrition Universal Screening Tool.<sup>25</sup> However, these screening

**Table 2** All-cause mortality HRs for participants according to malnutrition status defined by GNRI (weighted)

Status	Model 1		Model 2		Model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
No malnutrition	1 (Ref)	NA	1 (Ref)	NA	1 (Ref)	NA
Malnutrition	2.30 (1.24 to 4.27)	0.01	2.28 (1.19 to 4.40)	0.01	2.47 (1.36 to 4.50)	0.003

Model 1: No adjustment. Model 2: Age and smoking status were adjusted for statistically significant demographic variables, as determined using univariate Cox analysis. Model 3: Adjusted for all statistically significant variables determined using univariate Cox analysis. Age, smoking status, hypertension and congestive heart failure were adjusted. GNRI, Geriatric Nutritional Risk Index; NA, not available.



tools are cumbersome for general practitioners when managing the nutritional status of numerous patients with stable COPD. Body mass index (BMI) and serum albumin levels are the most commonly used tools in routine clinical practice. However, some non-nutritional factors, such as inflammation, renal dysfunction, fluid status and hepatic congestion, can also affect the accuracy of serum albumin levels and BMI in different ways. Thus, it is neither adequate nor precise to evaluate nutritional risk and associated prognosis based on BMI or albumin status in routine clinical practice. Body weight is an important nutritional marker, and the ratio of current to ideal weight is a good indicator of nutritional status. Fortunately, GNRI values combine ideal weight, current weight and serum albumin, which overcomes the limitations of a single indicator and provides a more precise reflection of nutritional status.<sup>10</sup> Additionally, the GNRI is an objective indicator that can be easily obtained.

The GNRI has been established as a screening tool to detect the risk of morbidity and mortality in hospitalised older patients. It was derived from the nutritional risk index, which was first proposed by Buzby *et al*<sup>26</sup> for young adult surgical patients. However, this is not easy to obtain because of the difficulties in determining the 'usual weight' required by the formula. Therefore, Bouillanne *et al*<sup>10</sup> replaced the usual weight in this formula with the ideal weight according to the Lorentz formula creating a new index called the GNRI, as described above. In recent years, increasing evidence has indicated that the GNRI has a strong prognostic value for different medical populations.<sup>11 12</sup> To the best of our knowledge, this was the first study to evaluate the association between malnutrition and long-term mortality in patients with COPD. Meanwhile, as defined by a low GNRI score, malnutrition was significantly correlated with increased mortality in patients with COPD, as shown in this study.

Nutritional supplement therapy has been demonstrated to improve multiple indicators in patients with COPD, such as body weight, respiratory muscle strength, quality of life and the 6 min walk distance.<sup>27</sup> Multimodal therapy combining rehabilitation, nutritional support and protein supplementation may improve fat-free mass, BMI and exercise performance. Therefore, nutritional support is considered an effective treatment for COPD. However, nutritional support has not consistently been shown to improve lung function.<sup>28 29</sup> Thus, owing to the complexity of nutritional and functional impairment experienced by patients with COPD, there is an urgent need for future interventions to look beyond nutritional imbalance alone, as multisystem diseases are unlikely to respond to a single treatment.

Some limitations of this study should be considered when interpreting the results. First, our primary outcome was restricted to all-cause mortality instead of COPD-related mortality, and there was no time limit for mortality; however, it was an unbiased and

clinically relevant outcome. Second, the sample size of malnutrition defined by a low GNRI was small, which could have led to bias, resulting in reduced credibility of the results. Finally, the severity of the airflow limitation could not be carefully considered in this study because of the lack of spirometric data. In view of these results, further studies with larger sample sizes are required to confirm the predictive value of GNRI scores in patients with COPD before applying it in routine clinical practice.

## CONCLUSION

Our study investigated the impact of different nutritional statuses as classified by GNRI value on the survival of patients with COPD and revealed that poor nutrition is strongly related to a high risk for all-cause mortality in patients. The GNRI is a simple but strong prognostic tool for evaluating the nutritional status of patients with COPD. We believe that it is convenient and effective to use the GNRI to identify and manage malnutrition. When general practitioners and clinicians develop a treatment plan for patients with COPD, their evaluation of nutritional status and consequent recommendation of precautions may contribute to a reduced risk of mortality and improved prognosis.

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**Contributors** XC contributed to the study design, performed statistical analysis, interpreted the results and wrote the manuscript. YC was responsible for the accuracy of data analysis. JC and YL helped with statistical analyses. SG contributed to the study design and provided a critical review and final approval of the manuscript and SG was responsible for the overall content as guarantor.

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**Patient consent for publication** Not applicable.

**Ethics approval** The NCHS Research Ethics Review Board approved the study protocol of the 2013–2018 NHANES (protocols 2011-17 and 2018-01), and all participants provided written informed consent.

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**Data availability statement** Data are available in a public, open access repository.

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