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ORIGINAL RESEARCH

# Comparison of Tools for Nutrition Assessment in Stable Subjects with Chronic Obstructive Pulmonary Disease: Which is the Best Mortality Predictor in Real Clinical Practice?

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**Purpose:** Malnutrition is associated with poor outcomes in chronic obstructive pulmonary disease (COPD), but the prognostic value of different nutritional assessment tools in outpatient settings remains unclear. We aimed to identify which of five commonly used nutritional indicators best predicts all-cause mortality in stable COPD in real-world clinical practice.

**Patients and Methods:** This secondary analysis of a prospective, hospital-based observational cohort included 141 outpatients with stable COPD. Nutritional status was assessed using body mass index (BMI), percent ideal body weight (%IBW), geriatric nutritional risk index (GNRI), prognostic nutritional index (PNI), and controlling nutritional status (CONUT) score. Patients were categorized as malnourished or well-nourished according to established cut-off values, including PNI <45 as a widely used threshold for malnutrition. Associations with all-cause mortality over a median follow-up of 54 months were examined using Cox proportional hazards models. Multivariate analyses adjusted for age, Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage, and COPD Assessment Test (CAT) score, and model fit was compared using Akaike's Information Criterion (AIC).

**Results:** During follow-up, 29 deaths (20.6%) occurred. The proportion classified as malnourished ranged from 7.8% (PNI <45) to 25.5% (CONUT ≥2). In multivariate analyses, only PNI <45 remained significantly associated with mortality (adjusted hazard ratio 3.85; 95% confidence interval 1.33–11.13; p = 0.013) and provided the best AIC among the five tools. Kaplan–Meier curves demonstrated significantly poorer survival in the low PNI group (log-rank p < 0.001).

**Conclusion:** Among five simple nutritional assessment tools, only PNI independently predicted long-term mortality in stable COPD. Given its simplicity, objectivity, and reliance on routinely available laboratory parameters, PNI appears to be a practical marker to support risk stratification and guide proactive management in outpatient COPD care.

**Keywords:** chronic obstructive pulmonary disease, nutrition assessment, mortality, body mass index, ideal body weight

## Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide. Historically, forced expiratory volume in one second ($FEV_1$) was regarded as the most important prognostic marker in COPD. Landmark studies by Burrows and Anthonisen established $FEV_1$ as a central tool for disease classification and outcome prediction.[1–3] However, subsequent research has shown that other factors, including dyspnea, exercise capacity, and physical activity, also contribute importantly to prognosis.[4,5]

Among these systemic manifestations, nutritional status has attracted considerable attention as a potential determinant of clinical outcomes in COPD. The relationship between malnutrition and mortality has been recognized for decades. In 1989, Wilson et al provided early evidence that low body weight, expressed as a percentage of ideal body weight

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(%IBW), was associated with poorer survival in COPD, even after adjustment for other clinical factors.[6] Since then, many studies have supported the prognostic relevance of nutritional depletion,[7–10] with body mass index (BMI) becoming the most frequently used surrogate marker of nutritional status.[11–17]

However, much of the published literature has focused on patients assessed during hospitalization, acute exacerbations, or other acute clinical episodes, often in relation to short-term outcomes or post-discharge mortality.[18–25] These settings differ substantially from the stable outpatient phase, in which long-term clinical management decisions are usually made. In stable COPD, several approaches have been used to define malnutrition or nutritional risk. Although BMI has been the most widely used indicator, the cut-off values have varied across studies.[6,11,13–17,26] Other indices include %IBW, the geriatric nutritional risk index (GNRI),[27] the prognostic nutritional index (PNI),[28] the Malnutrition Universal Screening Tool (MUST),[29] the European Society for Clinical Nutrition and Metabolism (ESPEN) criteria,[26] and the Naples Prognostic Score (NPS).[30] In addition, the European Respiratory Society Task Force proposed definitions of cachexia and pre-cachexia in COPD,[8] further highlighting the importance of nutritional and body composition abnormalities in this disease.

More recently, the Global Leadership Initiative on Malnutrition (GLIM) has proposed standardized criteria that combine phenotypic and etiologic domains to harmonize the diagnosis of malnutrition across clinical settings.[31] Studies applying the GLIM framework in patients with COPD, including Japanese cohorts, have shown that GLIM-defined malnutrition is associated with adverse outcomes such as mortality, hospitalization, and exacerbation.[32,33] Although these comprehensive criteria are valuable for research and specialized care, they are not always practical in routine outpatient settings, where simple and readily available indicators may be more useful.

We therefore hypothesized that, among commonly used nutritional assessment tools, some indices may be more clinically feasible and prognostically informative than others in stable COPD. The aim of this study was to compare five simple nutritional indicators—BMI, %IBW, GNRI, PNI, and CONUT score—and to determine which best predicts all-cause mortality in a real-world outpatient cohort of patients with stable COPD.

# Patients and Methods

## Study Design and Patient Enrollment

This study was conducted as a secondary analysis of an ongoing prospective, hospital-based observational cohort of patients with stable COPD.[34] A total of 175 patients were originally enrolled in the cohort. Data were collected at a single outpatient clinic between February 2015 and February 2022, and follow-up continued until January 2023. The present secondary analysis re-evaluated nutritional indicators for their prognostic value using real-world clinical data. Inclusion criteria were age ≥50 years, a smoking history of ≥10 pack-years, a post-bronchodilator $FEV_1$/forced vital capacity (FVC) ratio of <0.70, and no abnormal findings on chest radiography. Patients were excluded if they had active pulmonary diseases, poorly controlled comorbidities, any exacerbations within the preceding three months, or a past history of asthma. In addition, to ensure clinical stability, participants were required to have received consistent outpatient care for at least six months prior to enrollment, and to have had no changes in pharmacological treatment within the four weeks preceding data collection. Written informed consent was obtained from all participants prior to enrollment. The study adhered to the ethical standards of the Declaration of Helsinki and was approved by the National Center for Geriatrics and Gerontology Ethics Committee (No. 1138–3; updated July 2020).

Participants were instructed to abstain from using bronchodilators for at least 12 hours before visiting the research facility. Spirometry was performed more than one hour after the administration of a dry powder, long-acting bronchodilator, supervised by a physician, using a CHESTAC-8800 spirometer (Chest, Tokyo, Japan). The highest values from three attempts were recorded.[35] All procedures were conducted by trained lab technicians in accordance with the guidelines of the American Thoracic Society and the European Respiratory Society (ERS).[36] The reference values for lung function were provided by the Japanese Respiratory Society.[37] The Japanese versions of the COPD Assessment Test (CAT) were used to assess COPD-specific health status.[38,39] The CAT score ranges from 0 to 40, with higher scores indicating more severe impairment. Survival status was ascertained until mid-January 2023 by direct contact or by

contacting their families or healthcare providers if participants missed follow-up appointments. The period from enrollment to the last follow-up or death was recorded.

## Nutritional Assessments

Nutritional status was assessed using five validated indicators. For each, the presence of malnutrition was defined using established cut-off values reported in the literature. Obesity was not considered in the current analysis. The association between nutritional status and all-cause mortality was evaluated by comparing outcomes between malnourished and non-malnourished groups, as determined by each indicator.

### Body Mass Index (BMI)

BMI was calculated as weight (kg) divided by height ($m^2$). Although BMI has been used frequently in research on COPD, its threshold values used in past research have not been constant.[11–17] The World Health Organization definition was used in this study, with BMI <18.5 $kg/m^2$ considered underweight.[40]

### Percent Ideal Body Weight (%IBW)

IBW was defined as the weight corresponding to a BMI of 22 $kg/m^2$, calculated as height $(m)^2 \times 22$. %IBW was calculated as actual body weight divided by IBW × 100. A %IBW <90% was defined as underweight.[6]

### Geriatric Nutritional Risk Index (GNRI)

Proposed by Bouillanne et al to assess nutritional risk in elderly hospitalized patients,[41] GNRI was calculated as GNRI = 1.489 × serum albumin level (g/L) + 41.7 × (actual body weight (kg)/ideal body weight (kg)). GNRI ≤ 98 is considered to indicate malnutrition or increased nutritional risk.[24,27,41,42]

### Prognostic Nutritional Index (PNI)

Originally developed to predict postoperative complications, PNI has since been validated in various clinical settings, including oncology and chronic diseases.[23,28,43] It is calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (per $mm^3$). Although a universally accepted theoretical cut-off has not been established, a threshold of PNI <45 has been widely adopted in recent studies across various populations—including COPD—to define malnutrition or high nutritional risk.[43] This threshold was used in the current analysis.

### Controlling Nutritional Status (CONUT) Score

The Controlling Nutritional Status (CONUT) score is a nutritional assessment method that scores serum albumin levels, total lymphocyte counts, and total cholesterol levels, with the aim of early detection and continuous control of hospital undernutrition.[44] If serum albumin (g/dL) is 3.5–4.5, 3.0–3.49, 2.5–2.9, or < 2.5, the scores are 0, 2, 4, or 6, respectively. If total lymphocytes (/mL) is > 1600, 1200–1599, 800–1199, or < 800, the scores are 0, 1, 2, or 3, respectively and if cholesterol (mg/dL) is > 180, 140–180, 100–139, or < 100, the scores are 0, 1, 2, or 3, respectively. The total of the three scores is called the CONUT score. The score is 0–1 for normal, 2–4 for mild, 5–8 for moderate, and 9–12 for severe degrees of undernutrition.[14,44]

## Statistical Analysis

Continuous variables are presented as means with standard deviations (SDs) or medians with interquartile ranges (IQRs), depending on their distribution. Categorical variables are expressed as frequencies and percentages. Between-group comparisons were conducted using the Mann–Whitney *U*-test for continuous variables and Fisher's exact test for categorical variables, as appropriate. To evaluate the prognostic value of nutritional indicators, patients were categorized into malnourished and well-nourished groups using predefined thresholds for five nutritional assessment tools: BMI, % IBW, geriatric nutritional risk index, prognostic nutritional index, and CONUT score. Univariate Cox proportional hazards regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for all-cause mortality. Multivariate Cox regression analyses were then performed to adjust for potential confounders, including age, Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage, and CAT score (high vs. low, based on a cut-off of 10 points). Model performance was compared using Akaike's Information Criterion (AIC), with lower values indicating

better model fit. Survival curves were generated using the Kaplan–Meier method, and differences between groups were assessed with the Log rank test. All statistical analyses were conducted using SPSS Statistics, version 28.0 (IBM Corp.), and a two-sided $p$ value < 0.05 was considered statistically significant.

## Results

The participant selection process is summarized in Figure 1. In the original cohort, 175 patients were enrolled. During follow-up, 5 patients were excluded because airflow limitation was no longer present, suggesting reversible airflow limitation rather than persistent COPD. Among the remaining patients, 141 who had complete data for the nutritional indicators evaluated in the present study and who had been enrolled by February 2022 were included in this analysis. These participants were followed for a mean of 54.5 ± 27.5 months (median, 54 months), during which 29 deaths (20.6%) were confirmed.

A total of 141 participants (130 men) were included in the study (Table 1). The mean age was 75.2 years, and the mean $FEV_1$ at baseline was 1.74 L, corresponding to 69.8% of the predicted value. According to the GOLD classification,[45] 43 patients (30.5%) were GOLD 1, 74 (52.5%) were GOLD 2, 19 (13.5%) were GOLD 3, and 5 (3.5%) were GOLD 4. Due to the small sample sizes of the GOLD 3 and 4 groups, they were combined into a single GOLD 3+4 category for analysis. Baseline pharmacological treatment data were also available. At study entry, 77 patients were receiving multiple- or single-inhaler triple therapy, 40 were receiving long-acting muscarinic antagonist (LAMA) monotherapy, 15 were receiving an inhaled corticosteroid/long-acting β2-agonist (ICS/LABA) combination, and 4 were receiving dual bronchodilator therapy (LABA/LAMA), whereas 5 patients were not receiving any of these maintenance inhaled treatments. Based on previously established cut-off values, the number of patients identified as malnourished varied across the five nutritional assessment tools: 12 (8.5%) had a BMI <18.5 kg/m$^2$, 22 (15.6%) had % IBW <90%, 21 (14.9%) had GNRI ≤98, 11 (7.8%) had PNI <45, and 36 (25.5%) had a CONUT score ≥2.

To examine associations with all-cause mortality, univariate Cox proportional hazards analyses were performed (Table 2). Mortality risk was significantly higher in GOLD 3+4 compared to GOLD 1 [HR 4.222, 95% CI: 1.298–13.733, $p$ = 0.017], but not in GOLD 2 [HR 2.658, 95% CI: 0.887–7.961, $p$ = 0.081]. Patients with high CAT scores (≥10) also had significantly higher mortality risk compared to those with lower scores (<9) [HR 2.348, 95% CI: 1.130–4.881, $p$ = 0.022]. Next, patients were categorized into malnourished and well-nourished groups according to each nutritional indicator. Univariate Cox analyses revealed no significant mortality differences based on BMI, %IBW, or GNRI:

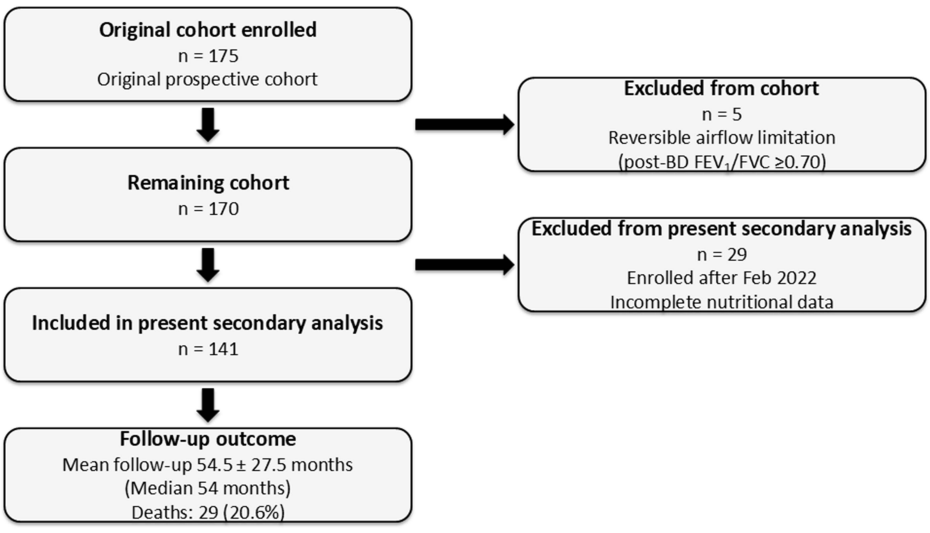


**Figure 1** Flow diagram of participant selection for the present secondary analysis of an ongoing prospective cohort of patients with stable chronic obstructive pulmonary disease (COPD).

**Table 1** Participant Characteristics and Nutritional Assessment in 141 Patients with Chronic Obstructive Pulmonary Disease

| | | Median | IQR | Max | Min |
|---|---|---|---|---|---|
| Age | Years | 75 | 71–80 | 89 | 51 |
| Cumulative Smoking | Pack-years | 54.0 | 37.5–78.0 | 204.0 | 10.0 |
| FVC | % pred. | 98.5 | 86.5–110.2 | 155.7 | 53.5 |
| $FEV_1$ | Liters | 1.74 | 1.42–2.10 | 3.08 | 0.44 |
| $FEV_1$ | % pred. | 72.0 | 56.7–83.7 | 132.5 | 19.5 |
| $FEV_1$/FVC | % | 58.3 | 49.1–64.7 | 69.4 | 24.7 |
| COPD Assessment Test (CAT) score | (0–40) | 7 | 3–12 | 29 | 0 |
| Body mass index (BMI) | kg/m2 | 22.6 | 20.4–24.8 | 35.7 | 14.8 |
| Percent of ideal body weight (%IBW) | % | 102.6 | 93.0–112.8 | 162.5 | 67.3 |
| Geriatric Nutritional Risk Index (GNRI) | - | 106.2 | 100.2–112.4 | 126.9 | 81.7 |
| Prognostic Nutritional Index (PNI) | - | 51.5 | 49.0–54.7 | 71.3 | 38.6 |
| Controlling Nutritional Status (CONUT) score | (0–12) | 1 | 0–2 | 5 | 0 |
| Sex (male/female) | Number (%) | 130 (92%)/11 (8%) | | | |
| GOLD stage (GOLD 1/GOLD 2/GOLD 3+GOLD 4) | Number (%) | 43 (30%)/74 (52%)/24 (17%) | | | |
| CAT<9 vs. CAT≧10 | Number (%) | 93 (66%)/48 (34%) | | | |

**Note**: The numbers in parentheses denote possible score range.
**Abbreviations**: IQR, interquartile range; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

- BMI <18.5 kg/m$^2$: HR 1.619 (95% CI: 0.487–5.379), $p = 0.432$
  %IBW <90%: HR 1.322 (95% CI: 0.504–3.468), $p = 0.571$
- GNRI ≤98: HR 2.335 (95% CI: 0.994–5.484), $p = 0.052$

In contrast, malnutrition defined by the PNI and CONUT score showed significant associations with mortality:

- PNI <45: HR 7.765 (95% CI: 3.259–18.503), $p < 0.001$
- CONUT score ≥2: HR 2.980 (95% CI: 1.437–6.181), $p = 0.003$

To explore potential confounders, baseline covariates were compared between the malnourished and well-nourished groups (Table 3). GOLD disease severity showed significant differences between the malnourished and well-nourished groups divided by four out of five nutritional assessments, and age was also significantly different between the two groups classified by two of five categories. Subsequently, multivariate Cox regression analyses were conducted using age, GOLD stage, and CAT score (high vs. low) as covariates (Table 4).

In the malnourished group classified based on PNI thresholds, the HR was statistically significant when compared to the well-nourished group after adjustment, indicating a significant difference in survival time. However, other indicators (BMI, %IBW, GNRI, CONUT) did not reach statistical significance in the adjusted models. When examining the AIC for the multivariate Cox proportional hazards analyses of the five nutritional assessment indicators, the group classified using the PNI threshold indicated the best model fit. Survival in the malnourished and well-nourished groups based on the PNI was then analyzed using the Kaplan–Meier method, the results of which are shown in Figure 2. According to the Log rank test, there was a significant difference between the two groups ($p < 0.001$).

## Discussion

This study demonstrated that among five nutritional assessment tools—BMI, %IBW, GNRI, PNI, and CONUT score—only the PNI was significantly associated with all-cause mortality in patients with stable COPD. In multivariate analysis adjusted for age, GOLD stage, and CAT score, PNI <45 remained independently associated with mortality and provided the best model fit among the indicators examined. These findings suggest that, in

**Table 2** Association of Clinical Characteristics and Nutritional Assessment with All-Cause Mortality in 141 Participants with Chronic Obstructive Pulmonary Disease Using Univariate Cox Proportional Hazards Analyses

| | Hazard Ratio (95% CI) | p value | AIC |
|---|---|---|---|
| Age (years) | 1.144 (1.067–1.227) | <0.001 | 240.5 |
| GOLD stage defined by airflow limitation | | | |
| GOLD 1 | Reference | NA | |
| GOLD 2 | 2.658 (0.887–7.961) | 0.081 | 251.9 |
| GOLD 3 + GOLD 4 | 4.222 (1.298–13.733) | 0.017 | |
| CAT score | | | |
| CAT score <9 | Reference | NA | |
| CAT score ≧10 | 2.348 (1.130–4.881) | 0.022 | 251.6 |
| Body mass index (BMI) | | | |
| BMI≧18.5 kg/m$^2$ | Reference | NA | |
| BMI<18.5 kg/m$^2$ | 1.619 (0.487–5.379) | 0.432 | 256.1 |
| Percent of ideal body weight (%IBW) | | | |
| IBW≧90% | Reference | NA | |
| IBW<90% | 1.322 (0.504–3.468) | 0.571 | 256.3 |
| Geriatric Nutritional Risk Index (GNRI) | | | |
| GNRI>98 | Reference | NA | |
| GNRI≦98 | 2.335 (0.994–5.484) | 0.052 | 253.4 |
| Prognostic Nutritional Index (PNI) | | | |
| PNI≧45 | Reference | NA | |
| PNI<45 | 7.765 (3.259–18.503) | <0.001 | 241.9 |
| Controlling Nutritional Status (CONUT) score | | | |
| CONUT score≦1 | Reference | NA | |
| CONUT score≧2 | 2.980 (1.437–6.181) | 0.003 | 248.5 |

**Abbreviations**: AIC, Akaike's Information Criterion; GOLD, Global Initiative for Chronic Obstructive Lung Disease; NA, not available.

routine outpatient practice, the PNI may be a more informative prognostic marker than conventional anthropometric indices or other nutrition-related composite tools.

Although the prognostic importance of malnutrition in COPD has long been recognized, the routine incorporation of nutritional assessment into daily practice remains challenging because of the large number of available indices and the overall complexity of COPD care. Clinicians must simultaneously consider airflow limitation, symptoms, comorbidities, frailty, and other systemic manifestations. In this context, the practical value of the PNI lies in its simplicity and wide availability. Because both serum albumin and lymphocyte count are included in standard laboratory testing, the PNI can be calculated easily without additional burden. In outpatient COPD management, a PNI of 45 or higher may suggest relatively preserved nutritional reserve, whereas a lower value may prompt closer clinical review and further nutritional assessment. From a practical perspective, identification of a low PNI in stable COPD may serve as a trigger for more detailed clinical evaluation rather than a stand-alone indication for intervention. In routine outpatient care, a low PNI may prompt clinicians to reassess recent weight change, dietary intake, comorbid conditions, and functional decline, and to consider closer follow-up or multidisciplinary support, including nutritional counseling and pulmonary rehabilitation when appropriate. Although such management strategies were not evaluated in the present study, our findings suggest that the PNI may serve as a simple screening marker to identify patients who may benefit from further assessment and more proactive care.

Our findings should be interpreted in the context of previous studies on nutrition-related prognostic markers in COPD. Although nutritional depletion has long been regarded as an adverse prognostic feature, many earlier studies focused on patients during acute exacerbations or hospitalization rather than during the stable outpatient phase. In contrast, our study specifically evaluated stable COPD, a setting more directly relevant to long-term outpatient management. Within this context, the present study differs from previous reports in that it directly compared five simple and objective nutritional

**Table 3** Comparison of Possible Covariance Between Malnourished and Well-Nourished Groups Divided by the Thresholds of Individual Nutritional Indicators in 141 Patients with Chronic Obstructive Pulmonary Disease

| | | **BMI≧18.5 kg/m$^2$ (n=129)** | **BMI<18.5 kg/m$^2$ (n=12)** | **p value** |
|---|---|---|---|---|
| Age | Years | 75.1 ± 6.8 | 75.9 ± 6.1 | 0.918† |
| Sex (male/female) | N (%) | 121 (94%)/8 (6%) | 9 (75%)/3 (25%) | 0.053§ |
| GOLD stage (GOLD 1/GOLD 2/GOLD 3+GOLD 4) | N (%) | 43 (33%)/66 (51%)/20 (16%) | 0 (0%)/8 (67%)/4 (33%) | 0.015§ |
| CAT<9 vs. CAT≧10 | N (%) | 87 (67%)/42 (33%) | 6 (50%)/6 (50%) | 0.339§ |
| | | **%IBW≧90% (n=119)** | **%IBW<90% (n=22)** | **p value** |
| Age | Years | 75.1 ± 6.7 | 75.8 ± 6.7 | 0.905† |
| Sex (male/female) | N (%) | 112 (94%)/7 (6%) | 18 (82%)/4 (18%) | 0.070§ |
| GOLD stage (GOLD 1/GOLD 2/GOLD 3+GOLD 4) | N (%) | 41 (35%)/62 (52%)/16 (13%) | 2 (9%)/12 (55%)/8 (36%) | 0.009§ |
| CAT<9 vs. CAT≧10 | N (%) | 83 (70%)/36 (30%) | 10 (46%)/12 (56%) | 0.048§ |
| | | **GNRI>98 (n=120)** | **GNRI≦98 (n=21)** | **p value** |
| Age | Years | 74.6 ± 6.5 | 78.8 ± 7.0 | 0.024† |
| Sex (male/female) | N (%) | 113 (94%)/7 (6%) | 17 (81%)/4 (19%) | 0.060§ |
| GOLD stage (GOLD 1/GOLD 2/GOLD 3+GOLD 4) | N (%) | 43 (36%)/59 (49%)/18 (15%) | 0 (0%)/15 (71%)/6 (29%) | <0.001§ |
| CAT<9 vs. CAT≧10 | N (%) | 81 (68%)/39 (33%) | 12 (57%)/9 (43%) | 0.454§ |
| | | **PNI≧45 (n=130)** | **PNI<45 (n=11)** | **p value** |
| Age | Years | 74.6±6.6 | 81.8±4.9 | <0.001† |
| Sex (male/female) | N (%) | 121 (93%)/9 (7%) | 9 (82%)/2 (18%) | 0.206§ |
| GOLD stage (GOLD 1/GOLD 2/GOLD 3+GOLD 4) | N (%) | 42 (32%)/68 (52%)/20 (15%) | 1 (9%)/6 (55%)/4 (36%) | 0.079§ |
| CAT<9 vs. CAT≧10 | N (%) | 86 (66%)/44 (34%) | 7 (64%)/4 (36%) | 1.000§ |
| | | **CONUT score≦1 (n=105)** | **CONUT score≧2 (n=36)** | **p value** |
| Age | Years | 74.6 ± 6.7 | 77.0 ± 6.6 | 0.066† |
| Sex (male/female) | N (%) | 96 (91%)/9 (9%) | 34 (94%)/2 (6%) | 0.729§ |
| GOLD stage (GOLD 1/GOLD 2/GOLD 3+GOLD 4) | N (%) | 38 (36%)/53 (51%)/14 (13%) | 5 (14%)/21 (58%)/10 (28%) | 0.017§ |
| CAT<9 vs. CAT≧10 | N (%) | 73 (70%)/32 (31%) | 20 (56%)/16 (44%) | 0.155§ |

**Notes**: Results are shown as mean ± SD or Number (percent). †Mann–Whitney's *U*-test, §Fisher's exact test.
**Abbreviations**: GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAT, COPD Assessment Test; BMI, body mass index; %IBW, percent of ideal body weight; GNRI, Geriatric Nutritional Risk Index; PNI, Prognostic Nutritional Index; CONUT, Controlling Nutritional Status.

indicators in the same real-world outpatient cohort. Although more comprehensive frameworks such as GLIM are valuable for diagnosing malnutrition, they may be less practical in busy outpatient settings. Our findings therefore suggest that, among readily available nutritional tools, the PNI may offer particular value for pragmatic risk stratification in stable COPD.

The reasons why the PNI outperformed the other indicators in this study are likely multifactorial. Unlike BMI and % IBW, which mainly reflect body size, the PNI incorporates serum albumin and lymphocyte count and may therefore better capture the combined effects of nutritional depletion, systemic inflammation, and impaired physiological reserve. COPD is increasingly recognized as a systemic disease, and nutritional status in these patients is influenced not only by reduced intake and weight loss but also by inflammation, muscle wasting, aging, and comorbid conditions. From this perspective, the PNI may reflect broader biological vulnerability than purely anthropometric indices. The CONUT score also combines nutritional and laboratory variables, but in the present cohort it did not remain significant after multivariable adjustment. This may suggest that the PNI provides a more stable or clinically relevant summary of risk in stable COPD, although this interpretation requires confirmation in larger studies.

Our findings are also broadly consistent with accumulating evidence on the prognostic significance of the PNI in COPD and related settings. Previous reports have shown that lower PNI values are associated with poorer outcomes in elderly patients with COPD and in patients hospitalized with acute exacerbations.[28,46,47] Our results extend this literature by showing that the PNI is also associated with long-term mortality in a real-world outpatient cohort of stable COPD.

**Table 4** Association of Nutrition-Related Indicators with All-Cause Mortality in 141 Participants with Chronic Obstructive Pulmonary Disease Using Multivariate Cox Proportional Hazards Analyses

| | **Model 1 (AIC =238.8)** | | **Model 2 (AIC =238.9)** | |
|---|---|---|---|---|
| | **Hazard ratio (95% CI)** | **p value** | **Hazard ratio (95% CI)** | **p value** |
| Age (years) | 1.154 (1.072–1.241) | <0.001 | 1.154 (1.072–1.241) | <0.001 |
| GOLD 2 (Ref. GOLD 1) | 2.150 (0.706–6.550) | 0.178 | 2.183 (0.718–6.635) | 0.169 |
| GOLD 3 + GOLD 4 (Ref. GOLD 1) | 3.094 (0.897–10.679) | 0.074 | 3.131 (0.906–10.824) | 0.071 |
| CAT score ≧10 (Ref. CAT score <9) | 2.081 (0.919–4.711) | 0.079 | 2.065 (0.908–4.696) | 0.084 |
| BMI<18.5 kg/m$^2$ (Ref. BMI≧18.5 kg/m$^2$) | 1.295 (0.381–4.404) | 0.679 | – | – |
| %IBW<90% (Ref. IBW≧90%) | – | – | 1.111 (0.416–2.969) | 0.834 |
| | **Model 3 (AIC =238.5)** | | **Model 4 (AIC =233.3)** | |
| | **Hazard ratio (95% CI)** | **p value** | **Hazard ratio (95% CI)** | **p value** |
| Age (years) | 1.148 (1.066–1.236) | <0.001 | 1.112 (1.027–1.203) | 0.009 |
| GOLD 2 (Ref. GOLD 1) | 2.064 (0.670–6.355) | 0.207 | 1.852 (0.600–5.715) | 0.283 |
| GOLD 3 + GOLD 4 (Ref. GOLD 1) | 2.885 (0.813–10.234) | 0.101 | 2.366 (0.650–8.615) | 0.191 |
| CAT score ≧10 (Ref. CAT score <9) | 2.096 (0.920–4.772) | 0.078 | 2.428 (1.001–5.891) | 0.050 |
| GNRI≦98 (Ref. GNRI>98) | 1.400 (0.563–3.482) | 0.469 | – | – |
| PNI<45 (Ref. PNI≧45) | – | – | 3.847 (1.330–11.126) | 0.013 |
| | **Model 5 (AIC =236.2)** | | | |
| | **Hazard ratio (95% CI)** | **p value** | | |
| Age (years) | 1.144 (1.064–1.231) | <0.001 | | |
| GOLD 2 (Ref. GOLD 1) | 1.803 (0.579–5.621) | 0.309 | | |
| GOLD 3 + GOLD 4 (Ref. GOLD 1) | 2.695 (0.753–9.646) | 0.128 | | |
| CAT score ≧10 (Ref. CAT score <9) | 1.844 (0.791–4.302) | 0.157 | | |
| CONUT score≧2 (Ref. CONUT score≦1) | 1.933 (0.895–4.173) | 0.093 | | |

**Abbreviations**: AIC, Akaike's Information Criterion; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAT, COPD Assessment Test; BMI, body mass index; %IBW, percent of ideal body weight; GNRI, Geriatric Nutritional Risk Index; PNI, Prognostic Nutritional Index; CONUT, Controlling Nutritional Status.

This distinction is clinically important, because prognostic markers identified during acute exacerbations may not necessarily have the same implications during stable disease. The present findings therefore support the view that the PNI may be useful across different phases of COPD, while also highlighting its particular relevance in routine outpatient follow-up.

Several limitations of this study should be acknowledged. First, this was a secondary analysis of a single-center prospective observational cohort with a relatively small sample size and a limited number of deaths. Although this reflects real-world clinical practice, the statistical power was restricted, and the generalizability of the findings may be limited. Second, the study population was predominantly male, which is typical of many Japanese COPD cohorts but may reduce applicability to female patients. Third, although our multivariable models adjusted for age, GOLD stage, and CAT score, other potentially relevant covariates—including smoking status, comorbidities, physical activity, prior exacerbation history, nutritional counseling, rehabilitation interventions, and treatment-related factors—were not available in a sufficiently standardized form to be incorporated into the analyses. In addition, although baseline pharmacological treatment data were available and are now summarized descriptively, no unified institutional format for nutritional guidance had been established during the study period, and actual participation in exercise therapy or rehabilitation was not systematically recorded. Residual confounding by these variables therefore cannot be excluded. Fourth, we did not assess longitudinal changes in nutritional status, recent weight loss, or cachexia progression, and therefore could not compare our findings directly with cachexia- or pre-cachexia-based classifications. Finally, because inclusion required regular outpatient follow-up, selection bias is possible; patients with unrecognized COPD, minimal symptoms, or severe physical limitation preventing regular visits may have been underrepresented.

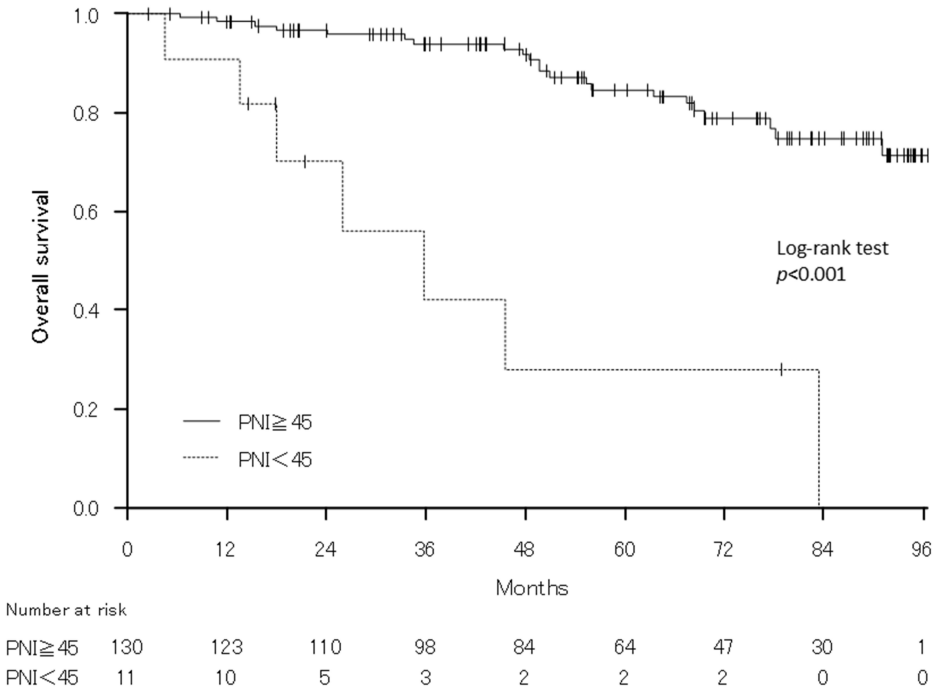


**Figure 2** Kaplan–Meier survival curves based on the malnourished and well-nourished groups classified by Prognostic Nutritional Index (PNI) threshold of 45.

Despite these limitations, the study has several strengths. It directly compared five commonly used nutritional assessment tools within the same stable COPD cohort, used predefined thresholds based on previous literature, and evaluated long-term mortality in a real-world outpatient setting. This design allowed us to assess the relative clinical usefulness of simple nutritional indicators under conditions that are close to everyday respiratory practice.

## Conclusion

In conclusion, among five nutritional assessment tools evaluated in stable COPD, only the PNI was independently associated with all-cause mortality after adjustment for age, GOLD stage, and CAT score. As a simple and objective marker derived from routinely available laboratory parameters, the PNI may be useful for risk stratification in outpatient COPD care. Further multicenter studies with larger and more diverse populations are needed to confirm these findings and to determine how PNI-guided assessment may be integrated with comprehensive nutritional evaluation frameworks in the long-term management of COPD.

## Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the authors used generative AI-based language tools (ChatGPT by OpenAI) to assist in revising sentence structure, improving clarity, and checking grammar and to enhance the readability of the English text. All intellectual content, scientific conclusions, and final decisions were made entirely by the authors, who take full responsibility for the integrity and accuracy of the work.

## Data Sharing Statement

Anonymized participant data will be made available from the corresponding author upon reasonable request.

## Ethics Approval and Consent to Participate

The present study was approved by the Institutional Ethics Committee of the National Center for Geriatrics and Gerontology (No. 1138–3) (updated on 12 July 2020). Written informed consent was obtained from all patients before the study.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

There are no conflicts of interest to declare with respect to any of the authors.

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