Original Article

trd Tuberculosis & Respiratory Diseases

Relationship between the Geriatric Nutrition Risk Index and the Prognosis of Severe Coronavirus Disease 2019 in Korea

https://doi.org/10.4046/trd.2024.0109
ISSN: 1738-3536(Print)/
2005-6184(Online)
Tuberc Respir Dis 2025;88:369-379

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Received Jul. 23, 2024
Revised Nov. 29, 2024
Accepted Jan. 2, 2025
Published online Jan. 6, 2025

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Abstract

Background: Malnutrition exacerbates the prognosis of numerous diseases; however, its specific impact on severe coronavirus disease 2019 (COVID-19) outcomes remains insufficiently explored.

Methods: This multicenter study in Korea evaluated the nutritional status of 1,088 adults with severe COVID-19 using the Geriatric Nutritional Risk Index (GNRI) based on serum albumin levels and body weight. The patients were categorized into two groups: GNRI >98 (no-risk) and GNRI ≤98 (risk). Propensity score matching, adjusted for demographic and clinical variables, was conducted.

Results: Of the 1,088 patients, 642 (59%) were classified as at risk of malnutrition. Propensity score matching revealed significant disparities in hospital (34.3% vs. 19.4%, p<0.001) and intensive care unit (ICU) mortality (31.5% vs. 18.9%, p<0.001) between the groups. The risk group was associated with a higher hospital mortality rate in the multivariate Cox regression analyses following propensity score adjustment (hazard ratio [HR], 1.64; p=0.001). Among the 670 elderly patients, 450 were at risk of malnutrition. Furthermore, the risk group demonstrated significantly higher hospital (52.1% vs. 29.5%, p<0.001) and ICU mortality rates (47.2% vs. 29.1%, p<0.001). The risk group was significantly associated with increased hospital mortality rates in the multivariate analyses following propensity score adjustment (HR, 1.66; p=0.001).

Conclusion: Malnutrition, as indicated by a low GNRI, was associated with increased mortality in patients with severe COVID-19. This effect was also observed in the elderly population. These findings underscore the critical importance of nutritional assessment and effective interventions for patients with severe COVID-19.

Keywords: Geriatric Nutritional Risk Index; COVID-19; Mortality; Malnutrition

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has presented unprecedented challenges to global health systems, characterized by its high morbidity and mortality rates, particularly in patients with severe manifestations requiring intensive respiratory interventions, including high-flow nasal cannula (HFNC) ther-

apy, mechanical ventilation (MV), and extracorporeal membrane oxygenation (ECMO)[1-3]. These severe cases predominantly affect older adults and individuals with pre-existing health conditions, rendering them more susceptible to adverse outcomes[4].

Malnutrition, frequently observed in hospitalized patients, is strongly associated with an increased risk of complications, prolonged hospital stays, and elevated mortality rates[5-7]. Prior studies in Korea have documented a high prevalence of malnutrition among patients with community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP), with rates nearing 40%[8,9]. In these patients, malnutrition correlates with a poor prognosis. Despite these findings, a significant knowledge gap remains concerning the impact of nutritional status on the progression and outcomes of COVID-19[10].

The Geriatric Nutritional Risk Index (GNRI), a validated instrument originally developed to assess nutritional risk in elderly patients, offers a straightforward and effective approach for evaluating nutritional status based on serum albumin levels and body weight[11]. The GNRI has demonstrated predictive capabilities in diverse populations, correlating with preoperative sarcopenia in oncological patients and proving applicable across younger demographics, including adolescents and young adults[12,13]. We hypothesized that patients at risk for malnutrition, indicated by a lower GNRI, experience worse clinical outcomes, such as higher mortality rates, MV, and longer hospitalization durations. We analyzed the association between GNRI and disease prognosis in patients hospitalized with severe COVID-19 within a multicenter Korean cohort using propensity-matched analysis.

Materials and Methods

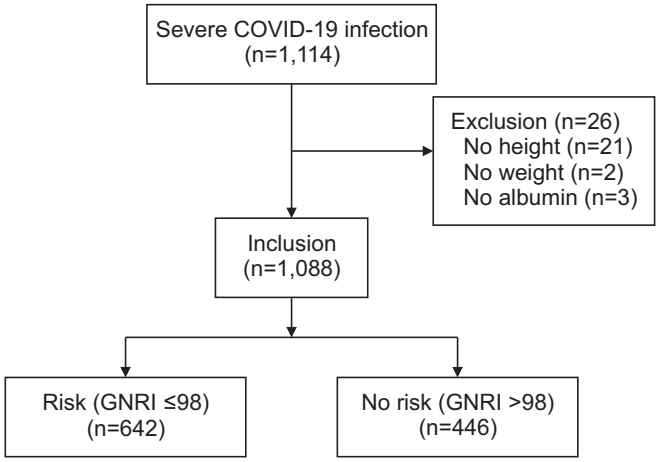
1. Study design and population

This retrospective observational study collected data from patients aged 19 years or older who were diagnosed with severe COVID-19 and respiratory failure. Severe COVID-19 was classified according to the guidelines of the Korea Centers for Disease Control and Prevention (K-CDC), which stipulate that severity requires at least one of the following forms of respiratory support: high-flow nasal oxygen therapy, non-invasive MV, invasive MV, or ECMO. These criteria align with K-CDC standards for assigning dedicated intensive care unit (ICU) beds to severe COVID-19 cases[14]. The classification criteria were applied upon admission to the dedicated ICU beds at participating hospitals. Patients with missing data on height, weight, or albumin levels were excluded from the analysis (Figure 1). Data collection spanned 22 tertiary and university-affiliated hospitals from January 2020 to August 2021. The Institutional Review Board (IRB) of each participating hospital approved this study, including the IRB of Pusan National University Yangsan Hospital (Yangsan, South Korea; approval number: 04-2021-042; approval date: October 7, 2021). Given the study's observational nature and minimal risk, the requirement for informed consent was waived.

2. COVID-19 diagnosis and data collection

COVID-19 was confirmed via a real-time reverse transcription polymerase chain reaction assay, detecting the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in upper respiratory tract specimens. The collected data encompassed demographic details, comorbidities, disease severity (assessed using the Sequential Organ Failure Assessment [SOFA] score and other baseline hemodynamic and laboratory variables), the source and type of infection (both community and hospital-acquired), treatment regimens, resource utilization, and outcome data, including ICU and hospital mortality rates. Patients were identified as having hospital-acquired COVID-19 infections if they tested positive for COVID-19 between 5 and 7 days post-hospitalization, aligning with the typical incubation period. Ventilator-free days (VFDs) during the initial 30 days post-MV initiation were calculated. VFDs represent the number of days a patient remained alive without the need for MV within this pe-

Figure 1. Flowchart of the patient selection process. Of the 1,114 patients with severe coronavirus disease 2019 (COVID-19), 26 with missing data on height (n=21), weight (n=2), and albumin levels (n=3) were excluded. GNRI: Geriatric Nutritional Risk Index.



riod. A VFD value of zero was assigned to patients who died within the initial 28 days. The Clinical Frailty Scale (CFS) was utilized to evaluate functional status prior to hospitalization and upon discharge.

3. Nutritional status assessment

The ideal body weight was calculated using the Lorentz formulas as follows: ideal body weight=height (cm)−100−[(height−150)/4] for men and ideal body weight=height (cm)−100−[(height−150)/2] for women[15]. The GNRI was determined as follows: GNRI=[1.489×serum albumin (g/L)+41.7×(present weight/ideal body weight)][11]. If the patient's current weight exceeded the ideal weight, the present weight-to-ideal body weight ratio was set to 1.

4. Group division and outcome measures

Patients were stratified into no-risk (GNRI >98) and risk (GNRI ≤98) groups based upon their GNRI assessed at admission to a dedicated ICU bed. This stratification was consistently applied to all patients, including those diagnosed with hospital-acquired COVID-19. Hospital mortality was identified as the primary outcome, while secondary outcomes included changes in ICU mortality, MV duration, and CFS scores at discharge.

5. Statistical analysis

Continuous variables are expressed as either the mean±standard deviation or the median and interquartile range (IQR), based on their distribution. Analyses were performed using the Student's t-test or the Mann–Whitney U test as appropriate. Categorical variables were reported as frequencies and percentages and analyzed using the chi-square or Fisher's exact test as appropriate. Propensity score matching (PSM) was utilized to emulate random assignment in both the total cohort and the elderly subset by estimating the likelihood of classification into the risk (GNRI ≤98) group. To ensure balanced comparison between groups, PSM was conducted using the nearest neighbor matching method with a 1:1 ratio. The optimal caliper width was set at 0.2 times the standard deviation of the log-transformed propensity scores, an empirically common threshold to minimize differences between matched pairs while maintaining a sufficiently large number of matched units. Following matching, covariate balance was assessed using the standardized mean difference (SMD), which measures the extent of mean differences between groups relative to the combined standard deviation. Covariates were considered well-balanced if the SMD was below 0.1, indicating negligible imbalance. The matching process, including SMD values for covariates before and after matching, is detailed in Table 1.

The propensity score model incorporated variables that reflected pre-admission characteristics (e.g., age), admission data (e.g., CFS score, site of infection acquisition, and comorbidities such as cardiovascular disease, chronic lung disease, and chronic neurological disease), and post-admission severity markers (e.g., the use of HFNC therapy or MV). This comprehensive approach was adopted to balance baseline characteristics and adjust for confounding variables associated with nutritional risk and mortality[16]. A Cox proportional hazards regression model analyzed factors influencing hospital mortality. To identify independent predictors of hospital mortality, univariate analyses were conducted on all variables presented in Table 1. Variables demonstrating a $p<0.05$ in the univariate analysis were selected for inclusion in the multivariate regression model. We implemented a stepwise backward selection method for the multivariate analysis to systematically identify significant variables, minimizing overfitting risk. This strategy was employed to balance the exploratory nature of the study with the need to identify robust predictors of mortality. Variables retained in the final model were assessed for their biological plausibility and relevance to severe COVID-19 outcomes to confirm their suitability. Risk-adjusted survival curves were generated using the proportional hazards model combined with the mean of the covariate method. Statistical analyses were carried out using SPSS version 27.0 (IBM Corporation, Armonk, NY, USA) and R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). A $p<0.05$ was deemed significant.

Results

1. Patient characteristics

Overall, 1,114 patients with severe COVID-19 were enrolled in the study. After the exclusion of 26 patients due to incomplete height, weight, and albumin data, 1,088 patients were included in the final analysis (Figure 1). Baseline characteristics at ICU admission are displayed in Table 1. Among the included patients, 463 (42.6%) received HFNC therapy alone, while 498 (45.8%) required MV support throughout the duration following the COVID-19 diagnosis. Additionally, 127 patients (11.7%) received both MV and ECMO support. Based on GNRI scores at admission, the patients were categorized into the no-risk group (GNRI >98, n=446) and the risk group (GNRI ≤98, n=642, 59%). The latter group was significantly older (mean age 70.5 years vs. 63.2 years, $p<0.001$), had a higher percentage of elder-

https://doi.org/10.4046/trd.2024.0109

Table 1. Clinical characteristics of the total cohort

Variable	Before PSM			After PSM		
	Risk (GNRI ≤98) (n=642)	No-risk (GNRI >98) (n=446)	SMD, %	Risk (GNRI ≤98) (n=397)	No-risk (GNRI >98) (n=397)	SMD, %
Age, yr	70.5±12.7	63.2±14.3	54.6	66.0±12.0	64.8±11.9	9.9
Elderly (≥65 years)	450 (70.1)	220 (49.3)	43.4	216 (54.4)	207 (52.1)	4.6
Male sex	405 (63.1)	256 (57.4)	11.7	249 (62.7)	230 (57.9)	9.8
BMI, kg/m^2	23.1±3.3	27.3±3.9		23.5±3.2	27.0±3.5	
GNRI	87.7±7.7	107.3±8.7		88.6±7.3	106.5±7.6	
Classification of GNRI						
GNRI <98	0	446 (100)		0	397 (100)	
GNRI 92–98	220 (34.3)	0		153 (38.5)	0	
GNRI 82–92	294 (45.8)	0		183 (46.1)	0	
GNRI <82	128 (19.9)	0		61 (15.4)	0	
CFS before admission	3.0 (2.0–4.0)	3.0 (2.0–3.0)	46.2	3.0 (2.0–3.0)	3.0 (2.0–3.0)	9.9
Location of infection acquisition						
Community-acquired	554 (86.3)	410 (91.9)	18.0	363 (91.4)	365 (91.9)	1.8
Nursing home	12 (1.9)	5 (1.1)	6.6	5 (1.3)	3 (0.8)	4.9
Nursing hospital	38 (5.9)	6 (1.3)	24.9	9 (2.3)	5 (1.3)	7.5
Hospital-acquired	38 (5.9)	25 (5.6)	1.3	20 (5.0)	24 (6.0)	4.4
Duration from COVID-19 diagnosis to ICU admission, day	5.0 (1.0–9.0)	4.0 (1.0–7.0)	8.0	5.0 (1.0–9.0)	4.0 (1.0–8.0)	3.8
Comorbidity						
Hypertension	332 (51.7)	252 (56.5)	9.6	212 (53.4)	230 (57.9)	9.1
Diabetes	206 (32.1)	157 (35.2)	6.6	147 (37)	144 (36.3)	1.5
Cardiovascular disease	87 (13.6)	41 (9.2)	13.9	41 (10.3)	40 (10.1)	0.7
Chronic lung disease	61 (9.5)	26 (5.8)	14.0	26 (6.5)	25 (6.3)	0.8
Chronic neurological disease	112 (17.4)	41 (9.2)	24.3	39 (9.8)	36 (9.1)	2.4
Chronic kidney disease	52 (8.1)	26 (5.8)	9.1	29 (7.3)	24 (6.0)	5.2
Chronic liver disease	18 (2.8)	11 (2.5)	1.9	11 (2.8)	11 (2.8)	0
Immunocompromized	18 (2.8)	8 (1.8)	6.7	11 (2.8)	8 (2.0)	5.2
Connective tissue disease	12 (1.9)	6 (1.3)	4.8	9 (2.3)	6 (1.5)	5.9
Hematologic malignancy	8 (1.2)	7 (1.6)	3.4	4 (1.0)	7 (1.8)	6.8
Solid malignant tumor	55 (8.6)	21 (4.7)	15.7	29 (7.3)	20 (5.0)	9.6

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Table 1. Continued

Variable	Before PSM			After PSM		
	Risk (GNRI ≤98) (n=642)	No-risk (GNRI >98) (n=446)	SMD, %	Risk (GNRI ≤98) (n=397)	No-risk (GNRI >98) (n=397)	SMD, %
SOFA score	5.0±3.2	4.3±2.6	23.6	4.7±3.1	4.4±2.7	9.9
Laboratory finding						
Lactate, mmol/L	1.6 (1.1–2.2)	1.5 (1.1–2.1)	8.1	1.5 (1.0–2.1)	1.5 (1.1–2.0)	7.2
CRP, mg/dL	10 (5.1–17.2)	9.6 (3.5–18.6)	3.6	9.5 (4.1–16.9)	9.0 (3.3–18.5)	1.8
Arterial blood gas analysis						
PH	7.4±0.1	7.4±0.1	9.0	7.4±0.1	7.4±0.1	5.0
PCO_2, mmHg	34.4±8.8	34.3±6.0	1.3	34.8±9.2	34.3±5.8	6.5
PaO_2/FiO_2 ratio	156.8±110.8	173.8±104.6	15.7	161.9±120.6	172.8±105.1	9.6
Pharmacologic treatment						
Remdesivir	465 (72.4)	348 (78)	13.0	302 (76.1)	306 (77.1)	2.4
Dexamethasone	606 (94.4)	431 (96.6)	10.6	379 (95.5)	384 (96.7)	6.2
Tocilizumab	60 (9.3)	34 (7.6)	6.1	46 (11.6)	30 (7.6)	13.6
Respiratory support						
HFNC	245 (38.2)	218 (48.9)	21.7	169 (42.6)	186 (46.9)	8.7
MV	330 (51.4)	168 (37.7)	27.8	172 (43.3)	160 (40.3)	6.1
MV+ECMO	67 (10.4)	60 (13.5)	9.6	56 (14.1)	51 (12.8)	3.8
Rescue therapy						
Prone positioning	144 (22.4)	83 (18.6)	9.4	96 (24.2)	80 (20.2)	9.6
CRRT	83 (12.9)	46 (10.3)	8.1	49 (12.3)	41 (10.3)	6.3
Inhaled NO	30 (4.7)	14 (3.1)	8.3	22 (5.5)	13 (3.3)	10.7

Values are presented as mean±standard deviation, number (%), or median (interquartile range). Variables such as lactate and arterial blood gas analysis (ABGA) values were measured at ICU admission. Data on pharmacologic treatments, respiratory support, and rescue therapies administered throughout the total hospitalization period were presented in Table 1.

PSM: propensity score matching; GNRI: Geriatric Nutritional Risk Index; SMD: standardized mean difference; BMI: body mass index; CFS: Clinical Frailty Scale; COVID-19: coronavirus disease 2019; ICU: intensive care unit; SOFA: Sequential Organ Failure Assessment; CRP: C-reactive protein; HFNC: high-flow nasal cannula; MV: mechanical ventilation; ECMO: extracorporeal membrane oxygenation; CRRT: continuous renal replacement therapy; NO: nitric oxide.

ly individuals (70.1% vs. 49.3%, p<0.001), lower body mass index (BMI) (23.1 vs. 27.3, p<0.001), and higher baseline CFS scores (median 3 [IQR, 2 to 4] vs. 3 [IQR, 2 to 3], p<0.001) (Table 1). This group also exhibited higher rates of infections in nursing homes, nursing hospitals, and hospitals (p<0.001), as well as higher prevalence of comorbidities such as cardiovascular disease, chronic lung disease, chronic neurological disease, and solid malignancy. In terms of clinical management, the malnutrition risk group showed lower utilization of HFNC therapy and greater reliance on MV, indicating more severe respiratory compromise. After PSM, no significant differences remained between the groups, except for BMI and GNRI. The SMD for most covariates was reduced to below 0.1 (10%), indicating that a covariate balance was largely achieved.

1) Primary outcomes

The primary outcome was hospital mortality. The risk group exhibited significantly higher hospital mortality rates compared to the no-risk group (30.7% vs. 19.5%, p<0.001) (Table 2). Despite PSM, hospital mortality remained significantly higher in the risk group (34.3% vs. 19.4%, p<0.001).

2) Secondary outcomes

The secondary outcomes included ICU mortality, MV duration, ICU and hospital length of stay, 30-day VFDs, CFS scores at discharge, and the frequency of tracheostomy. The risk group exhibited higher ICU mortality rates (27.2% vs. 19.3%, p=0.003); these differences persisted after PSM (31.5% vs. 18.9%, p<0.001). The median (IQR) 30-day VFDs were significantly shorter for the risk group compared to the no-risk group (21 [IQR, 1 to 30] vs. 26 [IQR, 11.8 to 30], p<0.001), with a similar pattern observed post-propensity matching (22 days [IQR, 1 to 30] vs. 26 days [IQR, 11 to 30], p=0.033). Additionally, the risk group had significantly higher median CFS scores at discharge (4 [IQR, 3 to 6] vs. 3 [IQR, 3 to 5], p<0.001); however, no difference was noted following propensity matching. The MV durations were longer in the risk group (median 14.5 days vs. 12.5 days, p=0.036), and this significance remained following PSM (MV: 15 days vs. 12 days, p=0.016). The risk group required tracheostomies more frequently (23.4% vs. 14.2%, p<0.001), with a consistent trend after propensity matching (21.2% vs. 14.4%, p=0.012).

2. Cox regression for hospital mortality

Before propensity matching, GNRI did not exhibit a

Table 2. Clinical outcomes

Variable	Before PSM		After PSM	
	Risk (GNRI ≤98) (n=642)	No-risk (GNRI >98) (n=446)	Risk (GNRI ≤98) (n=397)	No-risk (GNRI >98) (n=397)
Tracheostomy	150 (23.4)	63 (14.1)‖	84 (21.2)	57 (14.4)‡
HFNC duration, day*	4.0 (1.0–8.0)	5.0 (1.0–8.0)	5.0 (2.0–8.0)	4.0 (1.0–8.0)
MV duration, day*	14.5 (7.0–34.0)	12.5 (6.3–30)‡	15.0 (80–33.0)	12.0 (6.0–30.0)‡
30-day VFDs	21.0 (1.0–30.0)	26.0 (11.8–30.0)‖	22.0 (1.0–30.0)	26.0 (11.0–30.0)‡
ECMO duration, day*	24.0 (10.0–47.0)	20.0 (10.0–29.0)	25.0 (10.5–47.0)	21.0 (11.0–35.0)
CRRT duration, day*	11 (4–22)	11 (5–23)	11.0 (2.5–24.5)	11.0 (5.0–23.3)
ICU stay, ICU survivors	15 (8–28)	13 (7–21)	13.0 (7.0–22.0)	13.0 (7.0–21.0)
ICU stay, ICU non-survivors	20 (10.3–40)	23 (12–40.3)	21.0 (12.3–40.8)	23.0 (10.5–44.5)
ICU death	172 (27.2)	82 (19.3)§	123 (31.5)	72 (18.9)‖
Hospital stay, hospital survivors	23 (15–42)	19 (13–28)§	19.0 (14.0–31.5)	19.0 (13.0–28.0)
Hospital stay, hospital non-survivors	23 (14–43)	25 (15–45)	25.0 (15.3–44.0)	25.0 (14.0–46.0)
Hospital death	197 (30.7)	87 (19.5)‖	136 (34.3)	77 (19.4)‖
CFS at discharge†	4.0 (3.0–6.0)	3.0 (3.0–5.0)‖	4.0 (3.0–5.0)	3.0 (3.0–5.0)

Values are presented as number (%) or median (interquartile range).
*The duration of HFNC, MV, ECMO, and CRRT was calculated exclusively for patients who received these supports. †CFS calculations at discharge included only patients who survived until discharge. ‡p<0.05. §p<0.01. ‖p<0.001.
PSM: propensity score matching; GNRI: Geriatric Nutritional Risk Index; HFNC: high-flow nasal cannula; MV: mechanical ventilation; VFD: ventilator-free day; ECMO: extracorporeal membrane oxygenation; CRRT: continuous renal replacement therapy; ICU: intensive care unit; CFS: Clinical Frailty Scale.

significant relationship with hospital mortality in both univariate and multivariate Cox regression analyses (Supplementary Table S1). Following propensity adjustment, belonging to the risk group (GNRI ≤98) was significantly associated with increased hospital mortality in both the univariate (hazard ratio [HR], 1.55; 95% confidence interval [CI], 1.17 to 2.05; p=0.002) and multivariate Cox regression analyses (HR, 1.64; 95% CI, 1.24 to 2.18; p=0.001) (Table 3). Both before and after propensity adjusting, a lower GNRI (≤98) correlated with higher mortality rates (Figure 2A: total cohort, χ^2=5.17, p=0.023; Figure 2B: propensity-matched cohort, χ^2=9.71, p=0.002).

3. Subgroup analysis of elderly patients

In this study, 670 elderly patients were examined, and 450 (67.2%) were identified as at risk of malnutrition based on the GNRI score. The risk group was older (mean 77 vs. 74.7, p<0.001) and had a higher proportion of men (60.2% vs. 50.9%, p=0.022) compared to the no-risk group (Supplementary Table S2). Furthermore, the risk group displayed higher CFS scores before admission (median 3 [IQR, 3 to 5] vs. 3 [IQR, 2 to 4], p<0.001) and lower BMI (22.9 vs. 26.7, p<0.001). Moreover, they exhibited a higher rate of infections acquired in care facilities and a higher prevalence of certain comorbidities, such as chronic neurological diseases and solid malignancies. Subsequent to PSM, no significant differences were observed between the groups, except for BMI and GNRI (Supplementary Table S2).

4. Clinical outcomes of elderly patients

Prior to PSM, the risk group exhibited elevated median CFS scores at discharge (5 [IQR, 3 to 7] vs. 4 [IQR, 3 to 6], p<0.001) and elevated tracheostomy rates (24.9% vs. 17.4%, p=0.029) (Table 4). After PSM, the risk group displayed significantly higher rates of hospital (52.1% vs. 29.5%, p<0.001) and ICU mortality (47.2% vs. 29.1%, p<0.001).

5. Cox regression analysis for hospital mortality in elderly patients

In the analysis of the elderly subgroup, GNRI did not demonstrate a significant impact on hospital mortality in either univariate or multivariate Cox analyses prior to propensity matching (Supplementary Table S3). Nonetheless, following propensity matching, being in the risk group (GNRI ≤98) was significantly correlated with increased hospital mortality rates in both univariate (HR, 1.76; 95% CI, 1.30 to 2.39; p<0.001) and multivariate analyses (HR, 1.66; 95% CI, 1.22 to 2.27; p=0.001) (Table 5). Elderly patients in the risk group exhibited a significantly elevated risk of hospital mortality compared to those in the no-risk group (after propensity

Table 3. Hazard ratio for mortality in the propensity-matched cohort determined using the Cox proportional hazards model

Variable	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age, yr	1.06 (1.04–1.07)	<0.001	1.05 (1.03–1.06)	<0.001
GNRI ≤98	1.55 (1.17–2.05)	0.002	1.64(1.24–2.18)	0.001
Cardiovascular disease	2.07 (1.43–2.99)	<0.001		
Chronic lung disease	2.48 (1.64–3.74)	<0.001	2.59 (1.69–3.97)	<0.001
Chronic neurological disease	1.67 (1.16–2.39)	0.005		
Chronic kidney disease	1.78 (1.18–2.68)	0.006		
Solid malignant tumor	2.49 (1.68–3.68)	<0.001	2.52 (1.68–3.79)	<0.001
CFS before admission	1.20 (1.10–1.30)	<0.001		
SOFA score	1.08 (1.05–1.12)	<0.001		
HFNC	0.44 (0.28–0.70)	<0.001	0.55 (0.34–0.89)	0.015
MV	1.41 (1.07–1.86)	0.015		
CRRT	2.89 (2.17–3.84)	<0.001	2.56 (1.90–3.46)	<0.001
CRP, mg/dL	1.00 (1.00–1.00)	0.009	1.00 (1.00–1.00)	0.008

HR: hazard ratio; CI: confidence interval; GNRI: Geriatric Nutritional Risk Index; CFS: Clinical Frailty Scale; SOFA: Sequential Organ Failure Assessment; HFNC: high-flow nasal cannula; MV: mechanical ventilation; CRRT: continuous renal replacement therapy; CRP: C-reactive protein.

Figure 2. Time-to-event curve of hospital mortality by Geriatric Nutritional Risk Index (GNRI) scores in the propensity-matched group. Those at risk for malnutrition had a higher risk of hospital mortality (A: total cohort; generalized Wilcoxon, χ^2=5.17, p=0.023; B: propensity-matched cohort; log rank, χ^2=9.71, p=0.002).

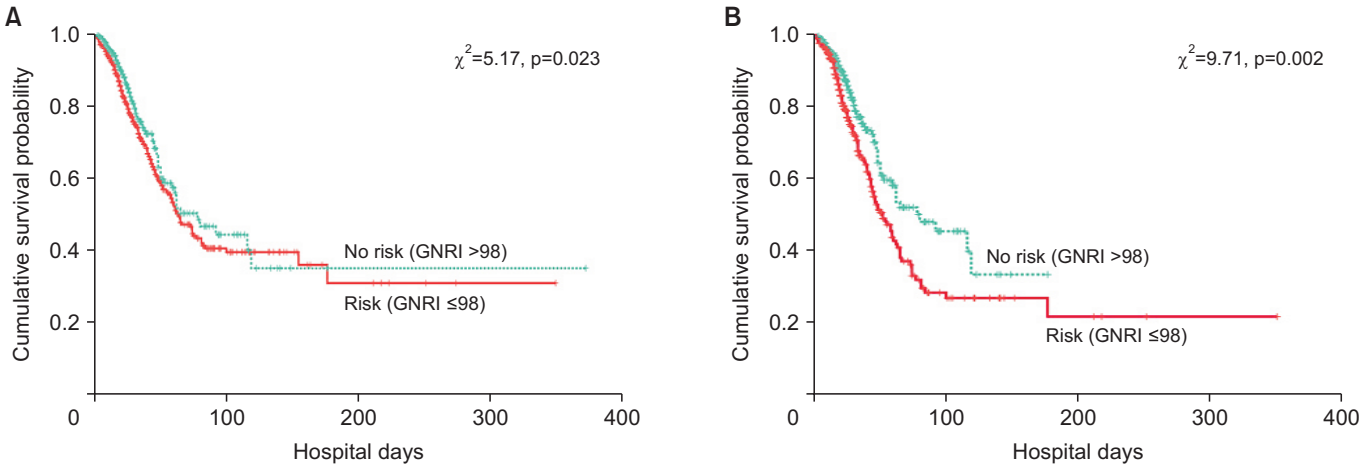

Table 4. Clinical outcomes of the elderly cohort

Variable	Before propensity matching		After propensity matching	
	Risk (GNRI ≤98) (n=450)	No-risk (GNRI >98) (n=220)	Risk (GNRI ≤98) (n=217)	No-risk (GNRI >98) (n=217)
Tracheostomy	112 (24.9)	38 (17.4)*	51 (23.5)	38 (17.7)
HFNC duration	4.0 (1.0–8.0)	4.0 (1.0–8.0)	4.0 (1.0–9.0)	4.0 (1.0–8.0)
MV duration, day	15.0 (7.0–36.0)	14.0 (8.0–32.0)	17.0 (9.0–37.0)	14.0 (8.0–32.0)
30-day VFDs	18.0 (0–30.0)	22.0 (3.0–30)	16 (0–30)	22 (3–30)
ECMO duration, day	27 (12.5–59.5)	20 (10.8–30.5)	36.5 (18.5–61.5)	20 (10.8–30.5)
CRRT duration, day	8 (3.8–21.3)	8.5 (3–23.3)	6.5 (2–23.3)	8.5 (3–23.3)
ICU stay in survivors, day	16 (10–30.8)	16 (9–25)	13 (7–21)	16 (9–25.3)
ICU stay in non-survivors, day	20 (10–36)	20 (10.5–44)	22 (13.5–41.5)	20.5 (11–44)
ICU death	142 (31.8)	61 (29.2)	102 (47.2)	60 (29.1)†
Hospital stay in survivors, day	24 (16–46)	22 (14–35)	20.5 (15–31)	22 (14–35.5)
Hospital stay in non-survivors, day	24.5 (15–41.8)	22 (12.5–46)	27 (16–44)	22.5 (13–46.5)
Hospital death	164 (36.4)	65 (29.5)	113 (52.1)	64 (29.5)†
CFS at discharge	5 (3–7)	4 (3–6)*	4 (3–5)	4 (3–6)

Values are presented as number (%) or median (interquartile range).
*p<0.05. †p<0.001.
GNRI: Geriatric Nutritional Risk Index; HFNC: high-flow nasal cannula; MV: mechanical ventilation; VFD: ventilator-free day; ECMO: extracorporeal membrane oxygenation; CRRT: continuous renal replacement therapy; ICU: intensive care unit; CFS: Clinical Frailty Scale.

matching χ^2=13.65, p<0.001) (Supplementary Figure S1).

Discussion

This multicenter observational study elucidates the significant relationship between malnutrition, as assessed by GNRI, and adverse clinical outcomes in hospitalized patients with severe COVID-19. The study confirms that nutritional status significantly influences the severity and mortality rates of COVID-19 in both general and elderly populations. Subsequent to adjustments for multiple confounding factors, a low GNRI indicative of malnutrition was associated with increased ICU and

Table 5. Hazard ratio for hospital mortality in the elderly cohort determined using the Cox proportional hazards model after propensity matching

Variable	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age, yr	1.05 (1.03–1.08)	<0.001	1.04 (1.02–1.07)	<0.001
GNRI ≤98	1.76 (1.30–2.39)	<0.001	1.66 (1.22–2.27)	0.001
Chronic neurological disease	1.54 (1.06–2.23)	0.025		
SOFA	1.07 (1.02–1.12)	0.004		
CRP	0.99 (0.98–1.00)	0.039	0.99 (0.98–1.00)	0.033
CRRT	2.06 (1.50–2.83)	<0.001	1.78 (1.29–2.47)	0.001

HR: hazard ratio; CI: confidence interval; GNRI: Geriatric Nutritional Risk Index; SOFA: Sequential Organ Failure Assessment; CRP: C-reactive protein; CRRT: continuous renal replacement therapy.

hospital mortality rates, the likelihood of prolonged MV, and tracheostomy rates.

It is noteworthy that 59% of patients with severe COVID-19 in Korea were categorized within the risk group, and this prevalence was notably higher among the elderly population (67.2%). These rates exceed those previously reported for malnutrition in patients with CAP or HAP, underscoring the critical impact of nutritional status on the manifestation of severe COVID-19[8,9]. Among patients with severe COVID-19, those at risk for malnutrition, as indicated by a GNRI of ≤98, exhibited significantly poorer outcomes compared with those not at risk. These findings align with prior studies, highlighting the vulnerability of malnourished elderly patients to severe outcomes of respiratory infections and other critical conditions[17]. GNRI serves as a practical and efficient tool for rapidly assessing nutritional risk in clinical settings, enabling timely interventions for patients with severe COVID-19.

In the context of acute COVID-19, serum albumin, a component of the GNRI, may be heavily influenced by the patient's inflammatory status, rather than exclusively reflecting their nutritional state. In cases of acute COVID-19, albumin levels typically signal systemic inflammation rather than malnutrition. As a negative acute-phase reactant, albumin concentrations decrease as part of the body's response to inflammation, a condition significantly pertinent in acute infections like COVID-19, where inflammation predominates nutritional deficiencies[18]. To address concerns that GNRI may predominantly reflect inflammatory status instead of nutritional status, we incorporated C-reactive protein (CRP) into the PSM process and subsequent Cox regression analysis[19]. Our findings indicate that GNRI remained significantly associated with mortality among hospitalized patients with severe COVID-19, even after controlling for systemic inflammation. CRP levels were well-balanced between the groups post-matching, indicating effective management of the inflammatory component. Despite adjustments for CRP, GNRI maintained a strong correlation with adverse clinical outcomes, suggesting that its prognostic value transcends the impacts of inflammation. Malnutrition, frequently aggravated by systemic inflammation, impairs immune function, prolongs recovery, and heightens the risk of complications. In this setting, CRP and other inflammatory markers could offer further insights in subsequent research. Nevertheless, our results reaffirm GNRI's utility as a reliable prognostic tool, even in acute infections where inflammation is predominant.

In this study, patients in the risk group demonstrated a greater dependency on MV and a more extended duration of ventilator support. This indicates that malnourished patients might encounter more severe respiratory compromise, necessitating prolonged and intensive respiratory support following severe COVID-19 development. Additionally, the incidence of tracheostomy was elevated in the risk group, suggesting a need for extended airway management. At discharge, the risk group exhibited higher median CFS scores, indicating increased frailty and poorer functional recovery. These findings align with those of previous studies, which reported superior functional outcomes in patients with obesity upon discharge[3,20].

Our study supports the finding that lower GNRI scores are associated with higher mortality rates in elderly patients with severe COVID-19. These findings are consistent with those of previous studies, although they contrast with some reports of mixed outcomes. For example, one study indicated that the moderate-to-severe risk category of GNRI was linked to poor prognosis in patients aged >65 years with COVID-19,

with an HR of 9.285[21]. Nevertheless, another study showed that while GNRI was related to a 14-day mortality, it was not associated with a 1-year survival in the same age group[22,23]. Additionally, other relevant studies have demonstrated no connection between malnutrition, defined by the GNRI score, and mortality within the first 3 months in patients aged ≥80 years[10]. These differences may be attributed to variations in patient demographics, malnutrition rates, healthcare settings, and comorbidities. Our results add to the body of evidence suggesting that the GNRI is a significant predictor of short-term outcomes in older adults during acute episodes of severe COVID-19. This observation emphasizes the importance of nutritional assessment in this vulnerable population.

The study had several limitations. Firstly, its observational design restricted our ability to establish causality. Secondly, nutritional status was assessed only at the time of hospital admission, without considering changes during hospitalization. Lastly, the specific nutritional interventions that might have influenced the outcomes were not evaluated. Despite these limitations, the inclusion of a large multicenter cohort enhanced the generalizability of our findings. During the study period, South Korea effectively managed COVID-19 transmission, ensuring that the ICU system was not overwhelmed. This stable healthcare environment ensured that the data were not confounded by health system disruptions, which could have otherwise worsened the outcomes for patients with severe COVID-19. The data were derived from a robust intensive care system that minimized the impact of external variables on patient outcomes. Furthermore, the use of PSM further controlled for confounding factors, providing a clearer understanding of the relationship between GNRI and clinical outcomes.

In conclusion, our study underscores the profound impact of malnutrition, assessed using the GNRI, on the clinical outcomes of patients with severe COVID-19. Malnutrition correlates with elevated mortality rates and the requirement for respiratory support. This issue is particularly alarming due to the escalated risk of severe COVID-19 complications in older adults, attributable to age-related physiological changes and the prevalence of comorbidities. These findings highlight the necessity for systematic nutritional assessment and prompt intervention in the management of patients with severe COVID-19, especially among the elderly. Future research should concentrate on longitudinal evaluation of nutritional status and the efficacy of specific nutritional strategies to enhance outcomes in this susceptible population.

Authors' Contributions

Conceptualization: Yeo HJ. Methodology: Lee D, Chun M, Jang JH. Formal analysis: Yeo HJ. Data curation: Park S, Lee SH, Kim TH. Software: Lee D. Validation: Cho WH. Investigation: Park O. Writing - original draft preparation: Yeo HJ, Lee D. Writing - review and editing: Cho WH. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Funding

This study was supported by the Korean Academy of Tuberculosis and Respiratory Diseases (Grant number KATRD -S-2021-2).

Supplementary Material

Supplementary material can be found in the journal homepage (http://www.e-trd.org).

Supplementary Table S1. Hazard ratios for mortality in the total cohort determined using the Cox proportional hazards modeling.

Supplementary Table S2. Baseline characteristics of the elderly cohort.

Supplementary Table S3. Hazard ratios for hospital mortality in the elderly cohort determined using the Cox proportional hazards model.

Supplementary Figure S1. Time-to-event curve for hospital mortality by Geriatric Nutritional Risk Index (GNRI) score in the elderly cohort.

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