







# Nutrition risk assessed by Nutritional Risk Screening 2002 is associated with in-hospital mortality in older patients with COVID-19

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## Abstract

**Background:** Although numerous studies have been performed to determine predictors of coronavirus disease 2019 (COVID-19) mortality, studies that address the geriatric age group are limited. The aim of this study was to investigate the utility of the Nutritional Risk Screening 2002 (NRS-2002) and the Geriatric 8 (G8) screening tools in predicting clinical outcomes in older adults hospitalized with COVID-19.

**Methods:** Patients aged  $\geq 60$  years who were hospitalized with COVID-19 in the second wave of the pandemic were included in the study. COVID-19 infection was demonstrated by a positive real-time reverse transcriptase–polymerase chain reaction on nasopharyngeal swab or positive radiological findings. Disease severity was determined as defined by the National Institutes of Health. Patient demographics, laboratory values on admission, comorbidities, and medications were recorded. The NRS-2002 and the G8 screening tools were performed for all patients by the same geriatrician. Primary outcome was in-hospital mortality.

**Results:** A total of 121 patients were included. Mean age was  $75 \pm 9$  years, and 51% were female. Mean body mass index was  $27 \pm 4.5$  kg/m<sup>2</sup>. Sixty-nine percent of the patients had nutrition risk according to the NRS-2002. Eighty-nine percent of the patients had a G8 score  $\leq 14$ . In-hospital mortality occurred in 26 (22%) patients. Older age and having nutrition risk as determined by the NRS-2002 were independently associated with a higher risk of in-hospital mortality in older patients with COVID-19.

**Conclusion:** The NRS-2002 tool provides rapid assessment for risk stratification in hospitalized older patients with COVID-19.

## KEYWORDS

COVID-19, hospital mortality, nutrition risk, nutrition status, older adults

## INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by SARS-CoV-2, has overwhelmed healthcare systems around the world and claimed the lives of millions of people, 80% of whom were aged  $\geq 65$  years.<sup>1</sup>

Since the beginning of the pandemic last year, numerous studies aimed to determine mortality predictors for COVID-19. In the meta-analysis by Zheng et al, age of  $>65$  years, male sex, smoking, and comorbidities such as hypertension, diabetes, cardiovascular disease, or respiratory diseases have been associated with poor prognosis.<sup>2</sup> A retrospective cohort study reported that increased age; elevated levels of venous lactate, creatinine, and procalcitonin; and low platelet/lymphocyte counts were associated with higher mortality.<sup>3</sup> The meta-analysis by Rashedi et al, on 504 hospitalized patients with COVID-19 revealed the significance of prognostic nutrition index, which includes peripheral lymphocyte count and serum albumin measurements.<sup>4</sup> However, although they constitute the most vulnerable population among the infected individuals, studies that specifically address older adults are limited.<sup>5–7</sup>

Because of anorexia of aging and reduced food intake, the nutrition state of older adults is frequently compromised.<sup>8</sup> Moreover, the impact of the pandemic on the economy has restricted access to a healthy diet, especially in developing countries.<sup>9</sup> Malnutrition is related to increased rates of infections and mortality in older patients.<sup>10</sup> Poor outcomes have also been reported in the setting of COVID-19 in malnourished patients.<sup>11,12</sup> Hence, early detection of nutrition risk is of utmost importance in patients with COVID-19. The Nutritional Risk Screening 2002 (NRS-2002) is a nutrition screening tool recommended for use in hospitalized older patients with COVID-19.<sup>13,14</sup> Nevertheless, studies investigating the relationship between NRS-2002 and COVID-19 mortality are lacking in number.

The Geriatric 8 (G8) tool is a screening tool incorporating the age variable with seven questions from the Mini Nutritional Assessment (MNA). The evaluated domains are functionality, malnutrition, neuropsychological problems, and age.<sup>15</sup> Numerous studies have shown the validity of the G8 tool in older patients with cancer.<sup>16,17</sup> The validity of G8 has also been demonstrated in geriatric outpatients without malignancy.<sup>18</sup>

Both the NRS-2002 and G8 tools are quick and easy to perform. Moreover, age, which is an acknowledged prognostic factor for COVID-19, is questioned in both screening instruments.

Older adults make up most of the hospitalized patients with COVID-19. A simple prognostic tool in

older patients with COVID-19 would enable risk stratification and early intervention while minimizing the time spent in the patient room. The aim of this study was to investigate the utility of the NRS-2002 and G8 screening tools in predicting clinical outcomes in older adults hospitalized with COVID-19 infection.

## MATERIALS AND METHODS

This cross-sectional study included all patients with COVID-19 aged  $\geq 60$  years and hospitalized in a university hospital from November 2020 to January 2021 (second wave of the pandemic). SARS-CoV-2 infection was demonstrated by a positive real-time reverse transcriptase–polymerase chain reaction results on nasopharyngeal swab or positive radiological findings. Disease severity was determined according to the clinical spectrum of COVID-19 infection as defined by the National Institutes of Health.<sup>19</sup>

- Mild illness: Individuals who do not have shortness of breath, dyspnea, or abnormal chest imaging results
- Moderate illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO<sub>2</sub>)  $\geq 94\%$  on room air
- Severe illness: Individuals who have SpO<sub>2</sub>  $< 94\%$  on room air, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen  $< 300$  mm Hg, respiratory frequency  $> 30$  breaths/min, or lung infiltrates  $> 50\%$
- Critical illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction

All patients were evaluated by the same geriatrician. Patient demographics, laboratory values on admission, comorbidities, and medications were recorded. Primary outcome was in-hospital mortality. Mortality data were obtained from the national mortality database.

The G8 screening tool includes eight questions relating to food intake, weight loss, body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared), motor skills, psychological status, number of medications, and self-perception of health and age (Figure S1).<sup>15</sup> The G8 score ranges from 0 (heavily impaired) to 17 (not impaired), with a threshold value of  $\leq 14$ . A score below 14 indicates the need for further assessment.

NRS-2002 includes questions in two sections: impaired nutrition status and disease severity (Figure S2). A score of  $\geq 3$  points indicates that the patient is nutritionally at risk.

All patients received standard treatment in accordance with national COVID-19 guidelines. The national guidelines recommend treatment with dexamethasone and prophylactic dose anticoagulation for hospitalized patients on supplemental oxygen. Nutrition intervention was planned by the patient's physician for patients with nutrition risk. If nutrition requirements could not be met orally, enteral nutrition was started. Parenteral nutrition was administered when appropriate,<sup>14</sup> either alone or in combination with enteral nutrition. None of the patients were vaccinated for COVID-19 at the time of the study.

## Ethics

Written informed consent was obtained from all participants. For patients with altered mental status, written informed consent was provided by a proxy. The project was authorized by the clinical research ethics committee of the university.

## Statistical analysis

Normality of the variables was investigated using visual (histograms and probability plots) and Kolmogorov-Smirnov tests. Numerical variables were given as mean  $\pm$  SD for normally distributed variables and as median (minimum–maximum) for continuous variables. The chi-square test was run to compare categorical variables. Groups were compared with an independent-sample *t* test or Mann-Whitney *U* test as appropriate. Multicollinearity was checked among the parameters significantly related to mortality. Then, the independent association of variables with mortality was analyzed by multivariate Cox regression analysis. A *P* value of  $<0.05$  was considered significant. SPSS (SPSS Inc) for Windows 21.0 program was used for the analysis.

## RESULTS

A total of 121 patients were hospitalized during the evaluation period. Mean age was  $75 \pm 9$  years, and 51% were female. Mean BMI was  $27 \pm 4.5$ . The three most common comorbidities were hypertension (68%), diabetes mellitus (36%), and coronary artery disease (27%). Sixty-nine percent of the patients had nutrition risk according to the NRS-2002. Eighty-nine percent of the patients had a G8 score of  $\leq 14$ . In-hospital mortality occurred in 26 (22%) patients. Median follow-up time was 16 days (5–68). Demographic and laboratory characteristics of the participants are presented in

TABLE 1 Demographic and laboratory characteristics

Variable	Total (N = 121), n (%)
Sex	
Female	62 (51.2)
Male	59 (48.8)
Age, years <sup>a</sup>	75.1 $\pm$ 9.1
BMI <sup>a</sup>	27.2 $\pm$ 4.5
Active smoking	
Yes	30 (24.8)
No	91 (75.2)
Number of chronic diseases <sup>a</sup>	3 (1–7)
HT	82 (67.8)
DM	44 (36.4)
CAD	33 (27.3)
COPD	22 (18.2)
CKD	21 (17.4)
Dementia	17 (14)
CHF	14 (11.6)
Malignancy	13 (10.7)
COVID-19 diagnosis	
Positive PCR test only	7 (5.8)
Positive radiological findings only	11 (9.1)
Both	103 (85.1)
COVID-19 severity	
Mild	7 (5.8)
Moderate	44 (36.4)
Severe	66 (54.5)
Critical	4 (3.3)
COVID-19 severity	
Mild + Moderate	51 (42.1)
Severe + Critical	70 (57.9)
Number of drugs <sup>a</sup>	4 (1–10)
Hospital stay, days <sup>a</sup>	16 (5–68)
ICU admission	29 (24)
ICU stay, days <sup>a</sup>	6 (1–28)
In-hospital mortality	26 (21.5)
NRS-2002 score <sup>a</sup>	4 (0–7)
NRS-2002	
No malnutrition	38 (31.4)
Nutrition risk	83 (68.6)
G8 score <sup>a</sup>	11 (1.5–17)

(Continues)

TABLE 1 (Continued)

Variable	Total (N = 121), n (%)
Classification of G8	
G8 score > 14	13 (10.7)
G8 score ≤ 14	108 (89.3)
White blood cell, ×10 <sup>3</sup> /μl <sup>a</sup>	7.5 (1.6–23.7)
Lymphocyte, ×10 <sup>3</sup> /μl <sup>a</sup>	1.0 (0.1–3.9)
Neutrophil, ×10 <sup>3</sup> /μl <sup>a</sup>	5.7 (0.9–23.3)
Hemoglobin, g/dl <sup>a</sup>	12.3 (4.1–16.9)
Platelets, ×10 <sup>3</sup> /μl <sup>a</sup>	204 (27–588)
LDH, U/L <sup>a</sup>	367 (105–1329)
Glucose, mg/dl <sup>a</sup>	123 (74–538)
GFR, ml/m <sup>a</sup>	59.7 (4–159)
C-reactive protein, mg/L <sup>a</sup>	78.0 (0.6–333)
Prothrombin time, s <sup>a</sup>	14.6 (10.6–35.3)
INR <sup>a</sup>	1.1 (0.9–2.8)
aPTT, s <sup>a</sup>	29.6 (21.5–75.1)
Fibrinogen, mg/dl <sup>a</sup>	526 (198–999)
D-dimer, mg/dl <sup>a</sup>	1.15 (0.05–20.00)
Ferritin, mcg/L <sup>a</sup>	361 (14–2992)
Procalcitonin, mcg/L <sup>a</sup>	0.14 (0.02–31.4)
Serum albumin level, g/L <sup>a</sup>	3.5 (2.1–4.5)

Abbreviations: aPTT, activated partial thromboplastin time; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; GFR, glomerular filtration rate; G8, Geriatric 8; HT, hypertension; ICU, intensive care unit; INR, international normalized ratio; LDH, lactate dehydrogenase; NRS-2002, Nutritional Risk Screening 2002; PCR, polymerase chain reaction.

<sup>a</sup>Numeric variables were presented as median (minimum–maximum) or mean ± SD. BMI is calculated as weight in kilograms divided by height in meters squared.

Table 1. Factors associated with mortality in the univariate analysis were older age ( $P < 0.001$ ), presence of congestive heart failure (CHF) ( $P < 0.001$ ), admission to the intensive care unit at any point during hospitalization ( $P < 0.001$ ), nutrition risk as determined by the NRS-2002 ( $P = 0.001$ ), higher NRS-2002 scores ( $P = 0.002$ ), and lower G8 scores ( $P = 0.006$ ). As for the laboratory values, lower glucose ( $P = 0.015$ ), glomerular filtration rate (GFR) ( $P < 0.001$ ), and serum albumin levels ( $P = 0.039$ ) and higher prothrombin time (pT) ( $P = 0.049$ ) and procalcitonin levels ( $P = 0.004$ ) were associated with mortality (Table 2).

Factors that were associated with mortality in univariate analysis ( $P < 0.05$ ) were used as independent

factors in multivariate Cox regression analysis. Although sex did not show a statistically significant association with mortality in univariate analysis, it was included in the model because of its clinical relevance. We built separate models for the NRS-2002 and the G8 scores to assess the factors independently associated with mortality (Tables 3 and 4). In the regression analysis of mortality with the NRS-2002 score (Table 3), model 1 included the NRS-2002 score, age, and sex. Model 2 included model 1 plus CHF. Model 3 included model 2 plus five laboratory parameters (glucose, GFR, procalcitonin, serum albumin level, and pT). In model 1, higher NRS-2002 scores and age were independently associated with mortality (odds ratio [OR] = 1.33; 95% CI, 1.03–1.73 [ $P = 0.032$ ]; and OR = 1.12; 95% CI, 1.06–1.19 [ $P < 0.001$ ], respectively). In model 2, only age was associated with mortality (OR = 1.13; 95% CI, 1.06–1.20;  $P < 0.001$ ). In model 3, again, higher NRS-2002 scores and age were independently associated with mortality (OR = 1.45; 95% CI, 1.95–2.01 [ $P = 0.025$ ]; and OR = 1.14; 95% CI, 1.05–1.25 [ $P = 0.002$ ], respectively). In the regression analysis of mortality with the G8 score (Table 4), model 1 included the G8 score, age, and sex, in which older age was independently associated with mortality (OR = 1.11; 95% CI, 1.05–1.17;  $P < 0.001$ ). Model 2 included model 1 plus CHF. Again, only older age was independently associated with mortality (OR = 1.11; 95% CI, 1.05–1.18;  $P < 0.001$ ). Model 3 included model 2 plus five laboratory parameters (glucose, GFR, procalcitonin, serum albumin level, and pT). In model 3, only older age was independently associated with mortality (OR = 1.11; 95% CI, 1.03–1.20;  $P = 0.005$ ).

## DISCUSSION

In this study, older age and nutrition risk as determined by the NRS-2002 were independently associated with a higher risk of in-hospital mortality in older patients with COVID-19.

With increasing age, a physiological change defined as immunosenescence compromises the cellular and the humoral immunity. In addition, comorbidities associated with older age make the geriatric age group more susceptible to infection with COVID-19. Although the geriatric age group is defined as aged ≥65 years, research has shown that increasing age, rather than age above a certain threshold, is associated with a worse prognosis.<sup>3,20,21</sup> The structured literature review by Wolff et al,<sup>20</sup> has linked higher age with poor COVID-19 outcome. Chen et al,<sup>21</sup> have discussed aging, immunity, and COVID-19, again, without indicating a specific age. Singhal et al,<sup>5</sup> have reviewed the clinical characteristics

**TABLE 2** Univariate analysis of in-hospital mortality

	<b>Survivors (N = 95), n (%)</b>	<b>Nonsurvivors (N = 26), n (%)</b>	<b>P value</b>
Sex			0.558
Female	50 (52.6)	12 (46.2)	
Male	45 (47.4)	14 (53.8)	
Age, years <sup>a</sup>	73.1 ± 8.9	82.4 ± 5.5	<0.001*
BMI <sup>a</sup>	27.5 ± 4.6	25.8 ± 4.1	0.058
Active smoking	24 (25.3)	6 (23.1)	0.818
Number of chronic diseases <sup>a</sup>	3 (1–7)	4 (1–7)	0.080
HT	63 (66.3)	19 (73.1)	0.508
DM	35 (36.8)	9 (34.6)	0.834
CAD	25 (26.3)	8 (30.8)	0.654
COPD	16 (16.8)	6 (23.1)	0.475
CKD	14 (14.7)	7 (26.9)	0.163
Dementia	12 (12.6)	5 (19.2)	0.406
CHF	5 (5.3)	9 (34.6)	<0.001*
Malignancy	11 (11.6)	2 (7.7)	0.557
COVID-19 severity			0.292
Mild	7 (7.4)	0 (0.0)	
Moderate	35 (36.8)	9 (34.6)	
Severe	50 (52.6)	16 (61.5)	
Critical	3 (3.2)	1 (3.8)	
COVID-19 severity			0.380
Mild + Moderate	42 (44.2)	9 (34.6)	
Severe + Critical	53 (55.8)	17 (65.4)	
Number of drugs <sup>a</sup>	3.5 (1–10)	4 (1–8)	0.840
Hospital stay, days <sup>a</sup>	15 (5–68)	23.5 (6–67)	0.244
ICU admission	13 (13.7)	16 (61.5)	<0.001*
ICU stay, days <sup>a</sup>	5 (2–27)	6 (1–28)	0.676
NRS-2002 score <sup>a</sup>	3 (0–7)	4 (2–7)	0.002*
NRS-2002			0.001*
No malnutrition	36 (37.9)	2 (7.7)	
Nutrition risk	59 (62.1)	24 (92.3)	
G8 score <sup>a</sup>	11 (1.5–17)	9 (2.5–16)	0.006*
Classification of G8			0.157
G8 score >14	12 (12.6)	1 (3.8)	
G8 score ≤14	83 (87.4)	25 (96.2)	
White blood cell, ×10 <sup>3</sup> /μl <sup>a</sup>	7.7 (2.7–23.7)	7.4 (1.6–14.3)	0.803
Lymphocyte, ×10 <sup>3</sup> /μl <sup>a</sup>	1.0 (0.1–3.9)	1.05 (0.2–2.7)	0.815
Neutrophil, ×10 <sup>3</sup> /μl <sup>a</sup>	5.6 (1.3–23.3)	5.9 (0.9–13.2)	0.798

TABLE 2 (Continued)

	Survivors (N = 95), n (%)	Nonsurvivors (N = 26), n (%)	P value
Hemoglobin, g/dl <sup>a</sup>	12.4 (4.1–16.9)	11.7 (8–16.6)	0.598
Platelets, ×10 <sup>3</sup> /μl <sup>a</sup>	211 (35–558)	179 (27–414)	0.298
LDH, U/L <sup>a</sup>	366 (149–1192)	386 (105–1329)	0.852
Glucose, mg/dl <sup>a</sup>	127 (74–538)	105 (76–269)	0.015*
GFR, ml/m <sup>2</sup>	76.2 (4.2–159.6)	39.2 (11.7–90.0)	<0.001*
C-reactive protein, mg/L <sup>a</sup>	80 (0.6–333)	77 (3.3–300)	0.514
Prothrombin time, s <sup>a</sup>	14.5 (10.6–28.3)	15.5 (11.6–35.3)	0.049*
INR <sup>a</sup>	1.1 (0.91–2.2)	1.2 (0.9–2.8)	0.054
aPTT, s <sup>a</sup>	29.5 (21.5–75.1)	31.2 (21.8–44.4)	0.090
Fibrinogen, mg/dl <sup>a</sup>	519 (199–999)	563 (198–877)	0.802
D-dimer, mg/dl <sup>a</sup>	1.1 (0.2–20)	1.9 (0.2–5.3)	0.311
Ferritin, mcg/L <sup>a</sup>	368 (29–2992)	319 (14–1656)	0.779
Procalcitonin, mcg/L <sup>a</sup>	0.12 (0.02–30.0)	0.48 (0.02–31.4)	0.004*
Serum albumin level, g/L <sup>a</sup>	3.6 (2.1–4.5)	3.2 (2.6–4.0)	0.039*

Abbreviations: aPTT, activated partial thromboplastin time; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; GFR, glomerular filtration rate; G8, Geriatric 8; HT, hypertension; ICU, intensive care unit; INR, international normalized ratio; LDH, lactate dehydrogenase; NRS-2002, Nutritional Risk Screening 2002.

<sup>a</sup>Numeric variables were presented as median (minimum–maximum) or mean ± SD. BMI is calculated as weight in kilograms divided by height in meters squared.

\*P < 0.05.

TABLE 3 Multivariate Cox regression analysis of in-hospital mortality with the NRS-2002 score

	Model 1		Model 2		Model 3	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.12 (1.06–1.19)	<0.001*	1.13 (1.06–1.20)	<0.001*	1.14 (1.05–1.25)	0.002*
Sex (male)	1.93 (0.84–4.43)	0.120	1.52 (0.61–3.77)	0.364	0.89 (0.32–2.47)	0.829
NRS-2002 score	1.33 (1.03–1.73)	0.032*	1.29 (0.99–1.68)	0.055	1.45 (1.95–2.01)	0.025*
CHF			0.51 (1.89–1.35)	0.173	0.44 (0.13–1.53)	0.199
Glucose					0.99 (0.98–1.01)	0.729
Procalcitonin					1.06 (0.99–1.14)	0.110
GFR					0.99 (0.98–1.02)	0.736
Serum albumin level					0.51 (0.18–1.40)	0.192
Prothrombin time					1.12 (0.99–1.24)	0.057

Note: Model 1 included sex, age, and the NRS-2002 score; model 2 included model 1 plus CHF; model 3 included model 2 plus five laboratory values.

Abbreviations: CHF, congestive heart failure; GFR, glomerular filtration rate; NRS-2002, Nutritional Risk Screening 2002; OR, odds ratio.

\*P < 0.05.

of older adults (aged ≥60 years) with COVID-19, in which older age was related to disease severity. Similarly, we included adults aged ≥60 years and found that older age was associated with mortality.

Our in-hospital mortality rate of 22% was somewhat higher than previous studies,<sup>5,22</sup> since our study population consisted of older patients with multiple comorbidities, 58% of whom had been hospitalized for severe or

**TABLE 4** Multivariate Cox regression analysis of in-hospital mortality with the G8 score

	<b>Model 1</b>		<b>Model 2</b>		<b>Model 3</b>	
	<b>OR (95% CI)</b>	<b>P value</b>	<b>OR (95% CI)</b>	<b>P value</b>	<b>OR (95% CI)</b>	<b>P value</b>
Age	1.11 (1.05–1.17)	<0.001*	1.11 (1.05–1.18)	<0.001*	1.11 (1.03–1.20)	0.005*
Sex (male)	1.71 (0.75–3.93)	0.204	1.38 (1.05–3.33)	0.478	0.85 (0.31–2.33)	0.758
G8 score	0.95 (0.85–1.07)	0.392	0.96 (0.85–1.07)	0.436	0.99 (0.88–1.13)	0.911
CHF			0.45 (0.18–1.15)	0.094	0.39 (0.12–1.24)	0.111
Glucose					0.99 (0.98–1.01)	0.385
Procalcitonin					1.06 (0.98–1.14)	0.385
GFR					0.99 (0.98–1.01)	0.659
Serum albumin level					0.58 (0.23–1.47)	0.249
Prothrombin time					1.05 (0.96–1.14)	0.319

Note: Model 1 included sex, age, and the G8 score; model 2 included model 1 plus CHF; model 3 included model 2 plus five laboratory values.

Abbreviations: CHF, congestive heart failure; GFR, glomerular filtration rate; G8, Geriatric 8; OR, odds ratio.

\* $P < 0.05$ .

critical disease. Also of note is that the study was conducted in a tertiary care center.

Although previous studies have shown a male predominance among nonsurvivors, we failed to show such an association.<sup>2,23</sup> Similarly, comorbidities, such as hypertension, diabetes mellitus, and cardiovascular disease have been shown to affect the prognosis of COVID-19, possibly through damage to the vascular structure. Moreover, the inflammatory state is known to aggravate cardiovascular incidents in the predisposed individual. In the present study, although the presence of CHF was associated with increased mortality in univariate analysis, comorbidities were not significantly associated with mortality in multivariate analysis. Similarly, laboratory values were not significantly different among survivors and nonsurvivors in multivariate analysis. Decreased statistical power due to the relatively small sample size may account for our findings.

In our study, nutrition risk assessed by the NRS-2002 was highly prevalent (67%) at hospital admission for COVID-19, which was in line with the literature.<sup>24,25</sup> In a study by Bedock et al, the prevalence of malnutrition according to the Global Leadership Initiative on Malnutrition (GLIM) criteria was shown to reach 66.7% in hospitalized patients with COVID-19.<sup>24</sup> Li et al, have found that among older adults hospitalized for COVID-19, 27.5% were at risk for malnutrition and 52.7% were malnourished based on the MNA.<sup>25</sup> It is not only the lack of appetite, anosmia, dysgeusia, and nausea (hence, the reduced food intake) that lead to malnutrition in COVID-19; disease-related malnutrition has been defined to include an inflammatory component as

well.<sup>26</sup> Acute inflammatory response increases energy and protein requirements by increasing resting energy expenditure. Subsequently, acute infections cause lean body mass catabolism.<sup>26</sup>

Among the most widely used malnutrition screening tools—namely, Malnutrition Universal Screening Tool (MUST), NRS-2002, MNA-Short Form (MNA-SF), and Nutrition Risk Index (NRI)—NRS-2002 was the best predictor of malnutrition in hospitalized older adults with COVID-19.<sup>27</sup> In a systematic review by Silva et al,<sup>28</sup> NRS-2002 was found to be highly sensitive compared with other nutrition screening tools and had the best predictive validity for the length of hospital stay. According to the retrospective study by Mendes et al, higher NRS-2002 scores were likewise associated with prolonged hospital stay.<sup>11</sup>

An association between nutrition status and in-hospital mortality has already been reported in patients without COVID-19.<sup>29,30</sup> With the advent of the pandemic, the possible role of nutrition status as a predictor of COVID-19 mortality has also been investigated.<sup>31,32</sup> Indeed, both the American Society for Parenteral and Enteral Nutrition (ASPEN) and the European Society for Clinical Nutrition and Metabolism (ESPEN) recommend nutrition intervention for all older adults hospitalized with COVID-19.<sup>14,33</sup> Leukocyte response, B-lymphocyte antibody production, and cytokine production are impaired in the setting of malnutrition.<sup>34</sup> Furthermore, the immunomodulatory function of micronutrients relates malnutrition to disease severity. It has, therefore, been hypothesized that vitamins C, D, and E;  $\omega$ -3 fatty acids; zinc; and selenium may be beneficial during SARS-CoV-2 infection.<sup>35</sup> Malnutrition

is also associated with sarcopenia, which affects muscles throughout the body, including the respiratory muscles. Hence, sarcopenia caused by malnutrition may lead to increased mortality through poor respiratory muscle function. In the present study, the NRS-2002 was associated with in-hospital mortality in patients with COVID-19. Nutrition risk assessed by Controlling Nutritional Status (CONUT) score, which is based on serum albumin level, peripheral blood lymphocyte count, and cholesterol concentration, has also been related to COVID-19 prognosis.<sup>31</sup> Recinella et al, have shown that malnutrition evaluated using the Geriatric Nutritional Risk Index (GNRI) is associated with in-hospital mortality in older adults hospitalized for COVID-19.<sup>32</sup> However, both the CONUT score and the GNRI are more complex and, therefore, more difficult to implement in the COVID-19 ward compared with the NRS-2002. Ideally, we should have used the GLIM<sup>36</sup> criteria for malnutrition diagnosis. However, the GLIM criteria include muscle mass measurements, which we had to omit to minimize the time spent in the patient room. Recently, a prospective study on oropharyngeal dysphagia in patients with COVID-19 revealed no significant difference in mortality between patients with and without malnutrition.<sup>22</sup> Similarly, in the study by Bedock et al, nutrition status was not associated with mortality.<sup>24</sup> It should be noted that these studies were not conducted specifically in the geriatric population and that malnutrition may have a stronger predictive value over mortality in older age.

In our study, although the G8 score showed an association with mortality in univariate analysis, we lost this significance in multivariate analysis. The G8 score was not significant even when we built a model that excluded the age variable. However, in the study by Kananen et al, the MNA-SF, which is very similar to the G8 tool, was correlated with in-hospital COVID-19 mortality.<sup>37</sup> The patient population in the aforementioned study had a very low mortality rate and a median Charlson Comorbidity Index of 1. The inconsistency between the two studies might be explained by the multimorbidity and disease severity of our patient population, which is questioned in the NRS-2002 but not in the MNA-SF. Generally, the MNA-SF is recommended for use in the outpatient setting. The authors of the NUTRI-COVID19 study<sup>38</sup> have argued that reduced self-reported food intake is the most important determinant of poor prognosis. Both the G8 and the NRS-2002 tools assess dietary intake; however, the NRS-2002 additionally assesses disease severity, which might explain its significant relationship with mortality. It is also of note that we set out to investigate in-hospital mortality. The predictive value of the G8

screening tool for long-term mortality merits further investigation.

The study by Kananen et al,<sup>37</sup> revealed that being underweight (BMI < 18.5) increased the risk of in-hospital mortality in patients with COVID-19 after adjusting for age, sex, comorbidity, frailty, and polypharmacy. In the present study, however, BMI itself was not independently associated with mortality. Most of our patients were overweight and 30 patients were obese (BMI ≥ 30). The scarcity of underweight individuals in our sample may have resulted in a lack of relationship between underweight and mortality. It is also plausible that the overall nutrition status is more predictive than BMI measurements alone. Possibly through increased coagulation and cardiac injury, obesity has been associated with high mortality in patients with COVID-19.<sup>39</sup> However, similar to the results of our study, Kananen et al,<sup>37</sup> have failed to show a correlation between obesity and COVID-19 mortality. They argue that in older age, obesity—in the absence of comorbid diseases—may even be protective (obesity paradox).

This study has some limitations. First, the study sample was small, which decreased the statistical power. Second, to minimize aerosol exposure, we did not obtain data on body composition. Notwithstanding these limitations, to the best of our knowledge, this is the first study supporting the predictive role of the NRS-2002 in older patients with COVID-19.

In conclusion, the NRS-2002 tool, which incorporates the assessment of nutrition status with disease severity, provides rapid assessment for risk stratification in hospitalized older patients with COVID-19. Our findings underline the significance of early nutrition assessment in the setting of COVID-19. Nutrition intervention may be lifesaving and should be part of the standard inpatient COVID-19 treatment for older adults.

#### AUTHOR CONTRIBUTIONS

Busra Can, Nurdan Senturk Durmus, and Asli Tufan contributed to the conception and design of the research; Sehnaz Olgun Yildizeli and Derya Kocakaya equally contributed to the acquisition and analysis of the data; Birkan Ilhan, Nurdan Senturk Durmus, and Asli Tufan contributed to the interpretation and analysis of the data; and Busra Can drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

#### CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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