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Significance of Screening Frailty, Sarcopenia, and Malnutrition in Hospitalized Patients with COVID-19: A One-Year Follow-Up Study

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ABSTRACT

Objective: This study aimed to explore the effect of sarcopenia, malnutrition, and frailty screening tools on one-year mortality in hospitalized adult patients with coronavirus disease 2019 (COVID-19).

Materials and Methods: Patients, 18 years of age, who were admitted to the COVID-19 clinic were enrolled in this prospective study. The clinical frailty scale (CFS) and SARC-F questionnaire were used for frailty and sarcopenia screening. Nutrition Risk Screening (NRS-2002) and Mini Nutritional Assessment–Short Form (MNA-SF) were performed to screen for malnutrition. The survival of all participants was investigated by using the Turkish national death registry. Multivariable logistic regression analyses were performed.

Results: A total of 72 subjects were enrolled in this study. The rate of patients with sarcopenia risk, malnutrition risk (via MNA-SF), malnutrition risk (via NRS-2002), and living with frailty were 75%, 93.8%, 81.3%, and 50.0% in the deceased group, respectively. Conversely, the rates of patients with sarcopenia risk, malnutrition risk (via MNA-SF), malnutrition risk (via NRS-2002), and living with frailty were 23.2%, 71.4%, 60.7%, and 16.1% in the alive group, respectively. SARC-F score (OR 1.331, p=0.006), MNA-SF score (OR 1.695, p=0.002), NRS-2002 score (OR 1.580, p=0.024), and CFS (OR 1.639, p=0.009) score were independently associated with one-year mortality after adjusting for sex and age.

Conclusion: MNA-SF, SARC-F, and CFS may be used for mortality risk estimation after discharge from the hospital who were admitted for acute disease.

Keywords: Frailty, sarcopenia, malnutrition, MNA-SF, clinical frailty scale.

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INTRODUCTION

Frailty, sarcopenia, and malnutrition are closely interrelated conditions that cause and exacerbate significant health issues, particularly in hospitalized patients. Frailty is a condition that impacts multiple physiological systems and causes susceptibility to stressors; its prevalence among older patients is high.[1] It is associated with mortality, hospital readmission, and adverse health outcomes.

There are numerous evaluation instruments for frailty. The clinical frailty scale (CFS) is one of the most widely used, particularly during the coronavirus disease 2019 (COVID-19) pandemic period. Hence, it is simple to execute. Although it was designed for older patients, recently, it has been administered to patients of all ages.[2–4]

Sarcopenia, which is characterized by a decrease in muscle strength and mass, can result in severe morbidity and mortality. Therefore, it may occur secondary to systemic disease (especially for inflammatory processes). COVID-19 is a systemic disease that provokes a severe inflammatory response. Moreover, sarcopenia in patients with COVID-19 should be evaluated and managed. The sarcopenia working group (EWGSOP2) suggests using SARC-F for sarcopenia screening. After the screening, muscle strength, muscle mass, and physical performance should be assessed.[5]

Malnutrition is defined as "a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat-free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease." It can be due to inflammation and is referred to as disease-related malnutrition.[6,7] Especially for hospitalized patients, its prevalence is underestimated. Several malnutrition diagnostic instruments are currently available.[8] Mini Nutrition Assessment–Short Form (MNA-SF) and NRS-2002 (Nutrition Risk Screening 2002) are often used for malnutrition screening.[9,10]

In this study, we planned to screen sarcopenia, malnutrition, and frailty in hospitalized adult patients admitted for COVID-19. Additionally, we assessed the contribution of screening tests on one-year mortality.

MATERIALS AND METHODS

Study Design

The Hacettepe University Clinical Research Ethics Committee approved the current study on June 29, 2021 (approval number: GO 21/817). All patients provided a signed, informed consent form.

Patients, who were 18 years and older, admitted to a university hospital because of COVID-19 disease between June 2021 and December 2022 were enrolled in this study. Those who were hemodynamically unstable and had difficulties speaking were excluded. All measurements were obtained within 48 h of hospitalization. Medical records of patients were obtained. Laboratory values, taken within 24 h of admission, include white blood cell ($\times 10^3$/μL), lymphocyte ($\times 10^3$/μL), fasting plasma glucose (mg/dL), total cholesterol protein (mg/dL), albumin (g/dL), C-reactive protein (mg/dL), ALT (U/L), creatinine (mg/dL), AST (U/L), ferritin (μg/L), D-dimer (mg/L), and fibrinogen (mg/dL) were recorded. SARS-CoV-2 polymerase chain reaction tests were taken by a health professional (both combined oropharyngeal and nasopharyngeal samples). Computed tomography (CT) findings were categorized as no infiltration, typical infiltration, and indeterminate infiltration previously reported by a radiologist. Patients were diagnosed with COVID-19 either using a positive test or positive CT findings.

Nutritional Status

Both MNA-SF and NRS-2002 were performed within 48 h of hospital admission. MNA-SF included questions regarding body mass index (BMI), food intake, neuropsychological problems, weight loss, mobility, and psychological stress or acute disease. Patients were categorized as malnourished, at risk, and normal.[11,12] NRS-2002 consisted of four questions that assess reduced dietary intake, BMI, weight loss, and severe illness. If at least one of these questions was answered with an affirmative response, the second and final screening phase was conducted. The patients were deemed "nutritionally at risk" if their score was 3 or greater.[10,13]

Sarcopenia Screening

It was recommended that the SARC-F questionnaire be used for sarcopenia screening. This questionnaire inquired about assistance with walking, rising from a chair, climbing stairs, falls, and strength.[14,15]

Frailty Screening

CFS was used to screen frailty based on the patient's condition prior to COVID-19 infection. Using CFS, comorbidity, cognitive impairment, and disability with physical infirmity are evaluated. The score ranges from 1 (very fit) to 9 (terminally ill). A score of 4 is considered to be pre-frail, whereas a score ≥5 is considered to be frail.[1,16]

Objective

The primary objective of this study was to define the effects of screening tests on one-year all-cause mortality. The survival of the participants was recorded by using the Turkish national death registry.

Statistical Analysis

The histograms, probability plots, and Kolmogorov–Smirnov were used to define the distribution of data. Categorical variables were shown in terms of counts and percentages. Continuous variables were written as means and standard deviations (SDs) or interquartile range (25^{th}–75^{th} percentiles) based on their distributions. Mann–Whitney U test and independent sample t-test were performed for group comparisons between alive and deceased patients. The Kaplan–Meier survival analysis was performed for the groups of SARC-F, CFS, MNA-SF, and NRS-2002. The associations of SARC-F, MNA-SF, NRS-2002, and CFS with one-year mortality were determined by using

Table 1. Baseline characteristics of participants

Age	60.2±16.3
Female	39 (54.2)
Length of stay	11.5 (7–25.7)
Comorbidities	
Hypertension	23 (31.9)
Diabetes mellitus	18 (25)
Hyperlipidemia	5 (6.9)
Atrial fibrillation	5 (6.9)
Coronary arterial disease	12 (16.7)
Chronic kidney disease	8 (11.1)
Heart failure	4 (5.6)
Chronic obstructive pulmonary disease	2 (2.8)
Hematological malignancies	5 (6.9)
Solid tumors	16 (22.2)
Rheumatologic disease	6 (8.3)
ICU admission rate	12 (16.7)
SARS-CoV-2 RT-PCR+	61 (84.7)
SARS-CoV-2 RT-PCR–, radiologically+	11 (15.3)
Chest CT	
Normal, no infiltration	19 (26.4)
Typical infiltration	25 (34.7)
Indeterminate infiltration	22 (30.6)
CT not performed	6 (8.3)
COVID-19 severity	
Mild	25 (34.7)
Moderate	35 (48.6)
Severe	12 (16.7)
Fasting plasma glucose, mg/dL	119 (96–155)
Lymphocyte, $\times10^3/\mu L$	0.8 (0.6–1.4)
Albumin, g/dL	3.6 (3.2–3.9)
C-reactive protein, mg/dL	7.6 (2.2–13.8)
D-dimer, mg/L	0.8 (0.4–1.8)
Ferritin, µg/L	295 (12–600)
Height, cm	166±9.8
Weight, kg	75.2±16.6
Body mass index, kg/m^2	27.1±5.4
MNA-SF ≤11	55(76.4)
NRS-2002 ≥3	47 (65.3)
CFS ≥5	17 (23.6)
SARC-F ≥4	25 (34.7)

Continuous variables were presented as medians (25^{th}–75^{th} percentiles) or means±SDs according to their distribution. Categorical variables were given as n (%). CFS: Clinical frailty scale; ICU: Intensive care unit; CT: Computed tomography; SARC-F: Strength, assistance with walking, rising from a chair, climbing stairs, and falls; MNA-SF: Mini Nutritional Assessment–Short Form; NRS-2002: Nutrition Risk Screening 2002.

Table 2. Characteristics of patients according to one-year survival

	Deceased (n=16)	Alive (n=56)	p
Age	64.9±12.1	58.9±17.2	0.126
Sex, female	8 (50%)	31 (55.4%)	0.704
Length of stay	15 (10–46)	10 (7–23)	0.028
COVID-19 severity			0.490
Mild	25.0%	37.5%	
Moderate	50.0%	48.2%	
Severe	25.0%	14.3%	
Comorbidities			
DM	6 (37.5)	12 (21.4)	0.204
HT	6 (37.5)	17 (30.4)	0.589
AF	1 (6.3)	4 (7.1)	0.901
CAD	4 (25.0)	8 (14.3)	0.446
CHF	1 (6.3)	3 (5.4)	0.891
COPD	1 (6.3)	1 (1.8)	0.397
Asthma	0 (0)	7 (12.5)	0.336
Body mass index, kg/m^2	24.9±5.21	27.7±5.3	0.065
SARC-F score	6 (1–8)	0 (0–3)	<0.001
SARC-F ≥4	12 (75%)	13 (23.2%)	<0.001
MNA-SF score	6(5–9)	10 (8–12)	0.001
MNA-SF ≤11	15 (93.8%)	40 (71.4)	0.095
NRS-2002 score	4 (3–5)	3 (0–4)	0.009
NRS-2002 ≥3	13 (81.3%)	34 (60.7)	0.128
CFS score	4 (4–6)	3 (2–4)	0.001
CFS ≥5	8 (50%)	9 (16.1%)	0.007
Crp, mg/dL	10.0 (4.4–16.4)	7.2 (2.1–13.3)	0.324
D-dimer, mg/L	1.74 (1.00–3.38)	0.76 (0.42–1.45)	0.008
Ferritin, ng /mL	573 (217–2189)	261 (112–467)	0.008
Albumin, g/dL	3.4 (2.9–3.8)	3.6 (3.4–4.0)	0.141
Lymphocyte, $\times10^9/L$	0.76 (0.39–1.32)	0.87 (0.68–1.56)	0.140
Hemoglobin, g/dL	10.5 (9.4–11.8)	12.2 (10.6–14.0)	0.090

Continuous variables were presented as medians (25^{th}–75^{th} percentiles) or means±SDs according to their distribution. Categorical variables were given as n (%). DM: Diabetes mellitus; HT: Hypertension; AF: Atrial fibrillation; CAD: Coronary artery disease; CHF: Chronic heart failure; COPD: Chronic obstructive pulmonary disease; SARC-F: Strength, assistance with walking, rising from a chair, climbing stairs, and falls; CFS: Clinical frailty scale; MNA-SF: Mini Nutritional Assessment-Short Form; NRS-2002: Nutrition Risk Screening 2002.

binary univariate and multivariate logistic regression analyses with the backward method. All of them were adjusted for age and sex. The Hosmer–Lemeshow test (p>0.05) was checked to evaluate the model. The significance level was defined as p<0.05 for all tests. Statistical Package of Social Science 23.0 (SPSS Inc., Chicago, IL) was employed.

RESULTS

Study Population

A total of 72 patients were enrolled in the study. The mean (±SD) age of the participants was 60.2±16.3 (range 20–88) years, and 54.2% were female. Table 1 provides the main characteristics of patients. Sixteen (22.2%) patients had died within 1 year of follow-up. Age (p=0.126) and sex (p=0.704) were not different between the deceased and alive groups. Length of stay was longer in the deceased group (p=0.028). The median SARC-F, CFS, NRS-2002, and MNA-SF scores were worse in the deceased group. The rate of patients with sarcopenia risk, malnutrition risk (via MNA-SF), malnutrition risk (via NRS-2002), and living with frailty were 75%, 93.8%, 81.3%%, and 50.0% in the deceased group, respectively. Conversely, the rates of patients with sarcopenia risk, malnutrition risk (via MNA-SF), malnutrition risk (via NRS-2002), and living with frailty were 23.2%, 71.4%, 60.7%, and 16.1% in the alive group, respectively. Table 2 details the comparison of the two groups.

All-cause Mortality

Table 3 shows the binary univariate logistic regression model. Only SARC-F, MNA-SF, and CFS scores were statistically different (p<0.05). Figure 1 shows the graphs of Kaplan–Meier survival analysis according to the SARC-F, CFS, MNA-SF, and NRS-2002. SARC-F score (OR 1.331, 95% CI 1.001–1.072, p=0.006), MNA-SF score (OR 1.695, 95% CI 0.554–0.872, p=0.002), NRS-2002 score (OR 1.580, 95% CI 1.062–2.350, p=0.024), and CFS (OR 1.639, 95% CI 1.133–2.369, p=0.009) score were independently associated with one-year mortality after adjusting for sex and age (Table 4).

Table 3. Binary univariate logistics regression analysis

Variables	One-year mortality	
	Exp (B) (95% CI)	p
Age	1.025 (0.987–1.064)	0.198
Sex	1.240 (0.408–3.773)	0.705
BMI	0.897 (0.798–1.008)	0.067
D-dimer	1.161 (0.938–1.437)	0.171
Ferritin	1.001 (1.000–1.002)	0.038
Hemoglobin	0.875 (0.724–1.058)	0.168
CRP	1.017 (0.957–1.081)	0.580
Albumin	0.451 (0.159–1.281)	0.135
Lymphocyte	0.576 (0.225–1.473)	0.249
SARC-F score	1.225 (1.079–1.392)	0.002
MNA-SF score	0.778 (0.672–0.900)	0.001
NRS-2002	1.565 (1.100–2.229)	0.013
CFS score	1.487 (1.157–1.910)	0.002

CI: Confidence interval; BMI: Body mass index; CFS: Clinical frailty scale; SARC-F: Strength, assistance with walking, rising from a chair, climbing stairs, and falls; MNA-SF: Mini Nutritional Assessment–Short Form; NRS-2002: Nutrition Risk Screening 2002.

Table 4. Binary multiple logistics regression analysis

Variables	One-year mortality	
	Exp (B) (95% CI)	p
SARC-F score*	1.331 (1.001–1.072)	0.006
MNA-SF score*	0.695 (0.554–0.872)	0.002
NRS-2002*	1.580 (1.062–2.350)	0.024
CFS score*	1.639 (1.133–2.369)	0.009

*: Adjusted for sex and age; CI: Confidence interval; CFS: Clinical frailty scale; SARC-F: Strength, assistance with walking, rising from a chair, climbing stairs, and falls; MNA-SF: Mini Nutritional Assessment–Short Form; NRS-2002: Nutrition Risk Screening 2002.

DISCUSSION

This prospective, observational cohort study aimed to screen hospitalized patients with COVID-19 for frailty, sarcopenia, and malnutrition. After screening the patients, their vital status within 1 year from discharge was monitored and the effects of screening tests on one-year mortality were examined. CFS, SARC-F, MNA-SF, and NRS-2002 scores were significantly different between deceased and alive groups. Furthermore, their effects on mortality are significant regardless of sex and age. This study plays an important role for hospitalized patients. First, it put forward the importance of screening malnutrition, sarcopenia, and frailty in hospitalized patients who were admitted for acute illnesses. Second, it presented the effects of CFS, SARC-F, MNA-SF, and NRS-2002 regardless of age and sex. Each one-point increase in CFS, NRS-2002, and SARC-F increases the risk of mortality. Therefore, each one-point decrease in the MNA-SF score increases the risk of mortality.

CFS was developed by Rockwood for patients aged 65 years and older.[1] Recently, CFS has gained popularity not only for older patients but also for adult patients. As it is easy to perform, CFS has been used in so many areas. In this study, we showed the relationship between CFS and one-year mortality in acute hospitalized patients. These data are in line with the other studies. In a recently published systematic review and meta-analysis, CFS indicated frailty was found to be associated with 30-day mortality in patients with COVID-19.[17] Another systematic review and meta-analysis, which included 3817 patients from seven studies, found a relationship between CFS and mortality in older patients with COVID-19.[18] Therefore, Kastora et al.[19] revealed the association between CFS and COVID-19 irrespective of age.

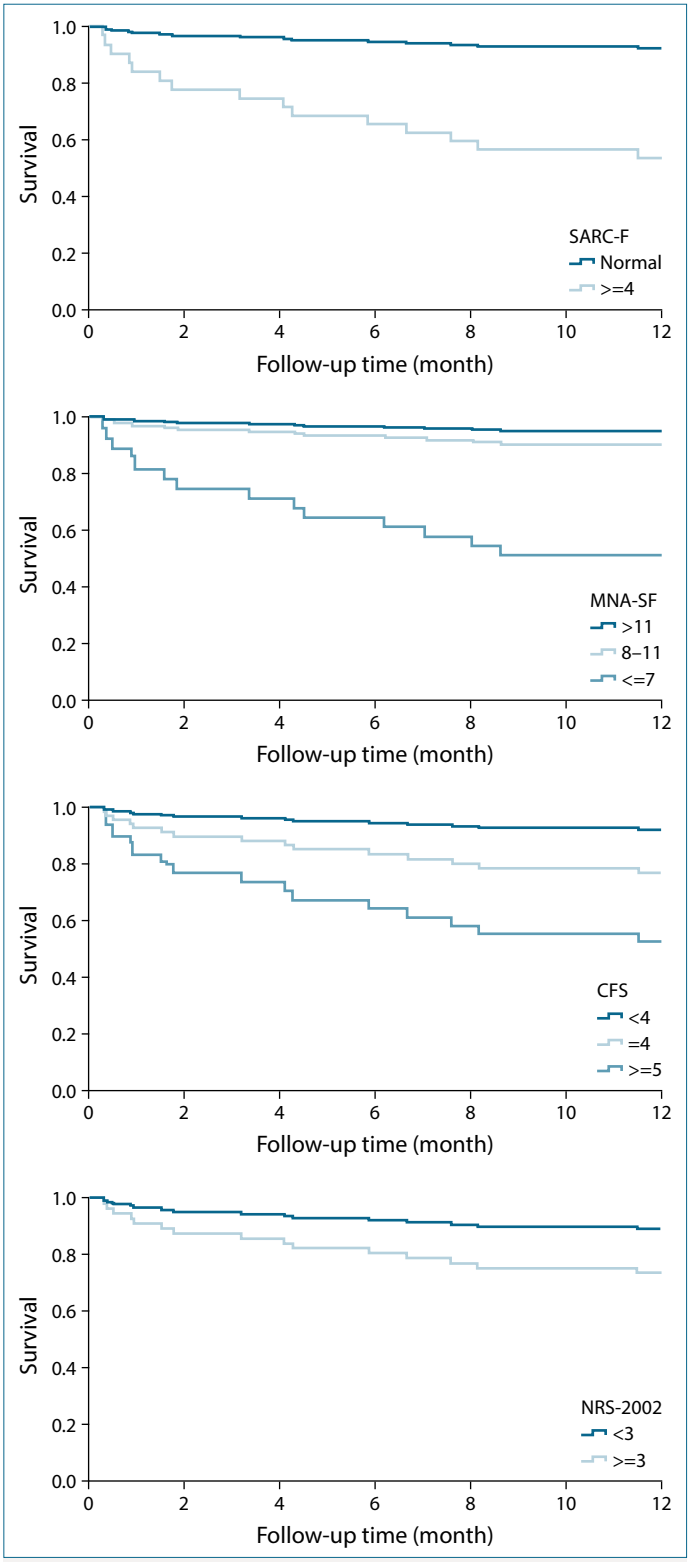

Figure 1. Kaplan–Meier survival estimations according to SARC-F, clinical frailty scale, Mini Nutritional Assessment–Short Form, and Nutrition Risk Screening 2002 categories.

The SARC-F score was developed by Malmstrom et al., and it is recommended to screen sarcopenia via EWGSOP2.[5,20] In our study, we also showed the association between the SARC-F score and one-year mortality. Ueshima et al.[21] revealed SARC-F as a beneficial prognostic indicator for older adults to predict in-hospital mortality. Thus, the relationship between SARC-F and mortality was shown in a meta-analysis.[22] Mori et al.[23] showed SARC-F as a practical predictor of prognosis for cancer patients who were receiving palliative care. Trussardi Fayh et al.[24] presented its association with a longer length of stay and hospital readmission after a cardiovascular event. Another important study was conducted by Bahat et al.,[25] who showed the predicting capacity of SARC-F to define frailty. This study supports the data interaction between them.

NRS-2002 and MNA-SF are malnutrition screening tools that are frequently utilized. However, NRS-2002 is usually recommended for hospitalized patients, and MNA-SF is recommended for older outpatients. However, MNA-SF is usually performed at hospitalized as well, not only for older but also for adult patients.[26–28] In our study, we assessed both the NRS-2002 and MNA-SF for hospitalized patients with COVID-19. We found that NRS-2002 and MNA-SF are related to one-year mortality. In our previous study, we reported the estimating capacity of MNA-SF for long-term mortality in older outpatients as well.[29]

Our study has limitations and strengths. It had a small sample size, and we only perform screening tests in response to the quarantine measurements at that time. However, only patients with COVID-19, who had all acute and inflammatory diseases, were included. In addition, the importance of screening exams, even in isolation, was demonstrated. Thus, all SARC-F, MNA-SF, NRS-2002, and CFS in one study were assessed, and their crucial roles were highlighted. In the future, prospective studies with large sample sizes may develop a combined risk screening tool.

CONCLUSION

In conclusion, even if the underlying acute problems are resolved during hospitalization, their long-term effects due to frailty, sarcopenia, and malnutrition may persist. Hospitalized patients must be screened for, prevented from, and treated for frailty, sarcopenia, and malnutrition. For hospitalized patients admitted with acute maladies, screening for malnutrition, sarcopenia, and frailty using MNA-SF, SARC-F, and CFS is simple and fast. Therefore, these tools for screening can be used to predict mortality across all age groups. However, they may be used to identify patients who require close post-discharge monitoring.

Peer-review: Externally peer-reviewed.

Ethics Committee Approval: The Hacettepe University Clinical Research Ethics Committee granted approval for this study (date: 29.06.2021, number: GO 21/817).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Author Contributions: Concept – YÖ, MGH, MG, AOB, MK, SC; Design – YÖ, MGH, MG, AOB, MK, SC; Supervision – YÖ, MGH, MÖ, OAU; Resource – YÖ, MÖ, OAU; Materials – YÖ, MÖ, OAU; Data Collection and/or Processing – YÖ, MG, AOB, MK, SC; Analysis and/or Interpretation – YÖ, CB, BBD, MC, MGH; Literature Search – YÖ, CB, BBD, MC; Writing – YÖ; Critical Reviews – CB, BBD, MC, MGH.

Conflict of Interest: The authors have no conflict of interest to declare.

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