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Impact of Nutritional Status on Prognosis in Non-critically ill Patients with COVID-19 Pneumonia

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What is known on this subject?

The current studies have shown that malnourished patients had higher treatment costs and worse prognosis and a longer duration of the hospitalization. Several tools such as nutritional risk screening-2002 (NRS-2002), malnutrition universal screening tool, and mini nutritional assessment-short form (MNA-SF) have been developed and used to assess the nutritional status in hospitalized patients. The NRS-2002, MNA-SF, and the nutritional risk index have been reported to be useful and practical for the NRS-2002 in the coronavirus disease-2019 (COVID-19). The NRS-2002 was found to be more effective than body mass index in predict the prognosis of the COVID-19, especially in elderly patients.

What this study adds?

We suggest that a simple, user-friendly NRS-2002 tool should be performed to evaluate the nutritional risk in COVID-19 pneumonia in routine clinical assessments. Performing NRS-2002 more than once in the hospitalization process may help the physicians in the early treatment of malnutrition and improve the prognosis of the disease.

ABSTRACT

Objective: The study assessed the nutritional status of non-critically ill coronavirus disease-2019 (COVID-19) patients with pneumonia using the nutritional risk screening 2002 (NRS-2002) score and evaluate ıts impact on prognosis.

Material and Methods: The clinical presentation of COVID-19 disease varies widely from asymptomatic or mild upper respiratory infection to severe life-threatening pneumonia and respiratory failure. Malnutrition negatively affects impair prognosis in COVID-19 patients, but few studies have evaluated the prognostic value of nutritional risk in COVID-19. In this retrospective observational study, non-critically ill COVID-19 patients who were divided into two groups considering their nutritional risk (NRS-2002 score < or ≥3) were compared to each other. Data analysis was performed using SPSS version 22 (Chicago, IL, USA).

Results: A total of 142 non-critically ill patients with COVID-19 were included in the study. The patients with the nutritional risk (NRS-2002 score ≥3) were older and had higher mortality and intensive care unit (ICU) requirement rates than those without the nutritional risk. The groups did not differ regarding gender distribution, body mass index, and length of hospital stay. Compared with survivors, patients who died (n=11, 7.75%) were older and had significantly higher NRS-2002 scores and C-reactive protein levels and lower oxygen saturation and albumin level.

Conclusion: The NRS-2002 test is a practical tool that can help assess the need for ICU admission and mortality in patients with COVID-19 pneumonia. The application of the test early during the disease should be considered for risk assessment, particularly in elderly patients.

Keywords: SARS-CoV, pneumonia, malnutrition, prognosis

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Introduction

Coronavirus disease-2019 (COVID-19) disease is caused by a newly identified type of coronavirus called severe acute respiratory syndrome-coronavirus-2. The virus was first discovered in December 2019, in China and led to a global pandemic that presents with a broad spectrum of clinical manifestations ranging from asymptomatic or mild upper respiratory infection to severe life-threatening pneumonia and respiratory failure. Like almost every viral disease, fever due to acute inflammatory process, anorexia, and subsequent weight loss are common in COVID-19 disease (1).

The first COVID-19 case in Turkey was reported on March 11, 2020 (2). Since then, as in other countries in the world, the number of infected people has increased rapidly. The mortality of the COVID-19 infection was found especially high in elderly patients. Comorbidities such as hypertension, diabetes mellitus (DM), chronic obstructive pulmonary disease, malnutrition, and cancer have been reported as risk factors for the progression of the COVID-19 in the previous studies (3). These studies reported a higher prevalence of DM and malnutrition in older patients with the COVID-19 than in the general population. The results of the studies conducted in Italy and the USA were in contrast with observations from China and those studies pointed out that the severity of COVID-19 was closely related to obesity (4,5). The diagnosis and treatment of malnutrition are crucial for a better prognosis of the COVID-19 disease (6). Malnutrition is a clinic phenomenon that is mostly underdiagnosed and defined simply as imbalanced feeding, under or overfeeding, and affects both thin and obese people (7).

The current studies have shown that malnourished patients had higher treatment costs and worse prognosis and a longer duration of the hospitalization (3). Several tools such as nutritional risk screening (NRS-2002), malnutrition universal screening tool (MUST), and mini nutritional assessment-short form (MNA-SF) have been developed and used to assess the nutritional status in hospitalized patients (3,8). The NRS-2002, MNA-SF, and the nutritional risk index have been reported to be useful and practical for the NRS-2002 in the COVID-19 disease (9). The NRS-2002 was found to be more effective than BMI in predict the prognosis of the COVID-19, especially in older patients (10). To our knowledge, the prognostic value of the nutritional risk in the COVID-19 (disease) was evaluated specifically in several studies, but there is a need for more studies besides the current studies (11). We assess the nutritional status of non-critically ill COVID-19 patients with pneumonia using the NRS-2002 test and evaluate its impact on the prognosis of the disease.

Material and Methods

Subjects

Patients admitted to the hospital and treated with a diagnosis of COVID-19 pneumonia between March 2020 and June 2020 were included in our study. The records of the patients consisting of demographic features, co-morbidities, and laboratory findings were noted. The diagnosis of COVID-19 was reached by polymerase chain reaction (PCR) testing of the oronasal swab for the presence of reminiscent lesions as predominantly peripheral ground-glass opacities at lower lung zones suggesting COVID-19 on chest computed tomography, history of contact with an infected patient, or fever (>37.3°C), cough, sputum, or presence of gastrointestinal symptoms, lymphopenia, and ruling out other causes led us to a diagnosis of COVID-19 PCR negative.

The patients and the criteria for hospitalization, infection severity, admission to an intensive care unit (ICU), and discharge were managed according to the Turkish Ministry of Health's COVID-19 management guidelines (2). According to the rules of the Turkish Ministry of Health, evaluation and recording of the nutritional status of all in-patients by the nursing staff using NRS-2002 is mandatory. The first part of NRS-2002 was filled by in-service nurses within the first 24 h of admission; if NRS-2002 score ≥3, the second part is filled by the physicians.

The NRS-2002 were evaluated by asking the following 4 questions:

- Is the body mass index (BMI) <20.5 kg/m^2?

- Has the patient lost weight within the last week?

- Has the patient had a reduced dietary intake during the last week?

- Is the patient severely ill?

A patient was "not at risk" if BMI is ≥20.5 kg/m^2, food intake was normal, the weight has not been declining and the current illness was not severe (i.e., no increased stress metabolism). If at least one of these criteria was met, and the assessment results in by giving a score from 0-3 concerning BMI, recent weight loss, and food intake during the previous weeks. Furthermore, stress metabolism was evaluated with a 0-3 score according to the illness category. Finally, the patients aged 70 years and older get one extra point. Patients with an NRS-2002 score ≥3 were accepted as risky nutritionally according to the European Society of Clinical Nutrition and Metabolism (ESPEN) (7). BMI was classified into the following categories: underweight (<18.5 kg/m^2), healthy weight (18.5-24.9 kg/m^2, overweight (25-29.9 kg/m^2), and

obesity ≥30 kg/m^2). Therefore, according to the presence or absence of nutritional risk, our patients were separated into two groups. The demographic features, comorbidity, laboratory findings, length of stay (LOS), and mortality rate in the hospitalization, the requirement of ICU was compared between the two groups. Those under 18 years of age and pregnant were excluded from the study. This study was approved by the University of Health Sciences Turkey, Istanbul Training and Research Hospital Ethical Committee (12.06.2020-2400). The study was performed appropriate to the rules in the Helsinki Declaration.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation or median (range) and categorical data as percentages as appropriate. Differences between the groups were assessed using a Student's t-test. Categorical data were compared using the X^2 test: a p value of <0.05 was accepted as significant. The risk factors for mortality were evaluated with cox regression analysis. Results are presented as an odds ratio (OR) with confidence intervals (CI) of 95%. Data analysis was performed using SPSS version 22(SPSS Inc., Chicago, IL, USA).

Results

A total of 142 COVID-19 patients 82 (57.7%) males and 60 (42.2%) females and the median age was 55 and interquantil range was (42.7-66.2). The minimum age was 21 years, and the maximum was 94 years. The most common associated condition was DM with 31 cases (21.8%). Eleven cases (7.7%) die, and 13 cases (9.2%) required ICU admission. In 59 (41.5%) cases, the PCR test was positive.

The BMI of patients was classified according to the World Health Organization. In the current study, underweight, normal, overweight, and obese were found in 1.4%, 38.4%, 37.3%, and 23.2% of cases, respectively.

According to NRS-2002, 11 patients (7.7%) had an NRS-2002 score of 3 and over, and were considered as nutritionally at-risk. NRS-2002 score 0:60 (42.3%), score 1:37 (26.1%), score 2:34 (23.9%), score 3:7 (4.9%), score 4:3 (2.1%), and score 6:1 (0.7%).

They were elder and had higher mortality rates, and higher ICU requirement rate than cases with a nutritional risk score of <3. Four of eleven cases had normal BMI, but the rest of the group were overweight and obese. There was not any statistically significang difference between the albumin levels, BMI, BMI class, length of hospital stays, and gender distribution of these 2 groups (Table 1). The NRS-2002 score of 3 or more was higher in patients aged over 65 than under 65 (17.5% vs. 3.9%, respectively). In other words, the malnutrition risk in the aged ≥65 age group was 5 times more than in patients under 65 years of age (OR: 5.1 , 95% CI: 1.43-18.8 ; p value=0.006).

Eleven (7.75%) cases died. Deceased patients were elderly, had significantly higher NRS-2002 scores, and C-reactive protein (CRP), also had lower oxygen saturation and albumin levels than the patients who survived. Gender, BMI, and weight distribution were not different between the groups (Table 2).

The NRS-2002 score was significantly correlated with albumin, age, CRP, oxygen saturation, severity of diseases, LOS, admission to an ICU, and mortality (Table 3).

When the factors affecting the mortality were evaluated with cox regression analysis, albumin and CRP level was found statistically, NRS-2002 test, age, O_2 saturation, and severity of diseases were not found (Table 4).

Table 1. The characteristics of cases with and without nutritional risk according to NRS-2002

	NRS-2002 <3 (n=131)	NRS-2002 ≥3 (n=11)	p value
Age (mean)	54.2±11.4	65.7±13.5	0.02
LOS (day)	10.2±5.1	11.8±13.3.1	0.40
Mortality +/-	5 (3.8%)/126 (96.1%)	6 (54.5%)/5 (45.4%)	0.001
ICU need +/-	4 (3%)/127 (97%)	9 (95.3%)/2 (4.6%)	0.001
Mean of BMI	27.6±4.5	28.2±5.9	0.40
Sex M:F	77 (58.7%)/54 (41.2%)	5 (45.4%)/6 (54.5%)	0.39
Albumin (g/L)	41.6±3.7	36.1±0.6	0.64
Age 65 (below/above)	98/33 (96.1%-82.5%)	4/7 (3.9%-17.5%)	0.001
Class of BMI			
Healthy (n=56)	52 (39.7%)	4 (36.4%)	0.81
Overweight (n=86)	79 (60.3%)	7 (63.6%)	

LOS: Length of stay, ICU: Intensive care unit, M: Male, F: Female, BMI: Body mass index, NRS: Nutritional risk screening

Discussion

We performed a nutrition risk evaluation with the NRS-2002 test in non-critical COVID-19 patients in our study. 7.7% of patients were found with a nutritional risk. The patients with NRS-2002 score ≥3 had an older age and higher mortality and admission to the ICU than NRS-2002 score <3.

In our study, DM was found in one of the five patients followed up with the diagnosis of non-critical COVID-19 pneumonia, and obesity was found in one of the three patients. The patients with a normal BMI ve even obese patients had a nutritional risk. The evaluation of the nutritional status of the patients is crucial because malnutrition increases the infection risk (12).

MNA, subjective global ass (SGA), MUST, and NRS-2002 were designed to evaluate the nutritional risk. MUST has been used mostly as a screening test. SGA, MNA, and NRS-2002 were assessed in hospitalized patients. NRS-2002 test is remarkable with a design to perform easier and faster than other tests. The NRS-2002 test was validated by the ESPEN and suggested for NRS-2002 of hospitalized COVID-19 patients (8,13). Furthermore NRS-2002 was showed as a valid and reliable test in hospitalized patients in a thesis study in our country (14).

In previous studies, although the nutritional risk ratios were found to be lower according to NRS-2002 compared with tests such as MUST and MNA-SF, NRS-2002 was reported to be more effective in predicting the clinical outcomes of the nutritional status of the patients (15).

A nutritional risk for 77-92% was reported in studies which were performed with the NRS-2002 test in COVID-19 pneumonia and those findings were evaluated to be related to the high amount of old patients (16,17). The NRS-2002 test had a high sensitivity and low specificity to predict the LOS and the need of ICU in COVID-19 patients (16).

Table 2. The comparison of mortality and survival of the cases

	Non-survivor (n=11)	Survivor (n=131)	p value
NRS-2002	2.64±1.7	0.87±0.9	0.001
Age (mean)	66.4±13.1	54.2±16.4	0.01
BMI (mean)	25.5±5.1	27.2±4.6	0.23 NS
Sex M:F	8/3	74/57	0.29 NS
Weight	70.3±12.7	77.3±15.4	0.14 NS
Median of CRP (mg/L)	164±102.5	60.9±65.3	0.001
Age 65 (below/above)	5/6 (4.9%/15.0%)	97/34 (95.1%/85%)	0.04
O_2 saturation % (room air)	85.0±6.6	92.8±3.9	0.001
Mean of albumin (g/L)	28.7±8.0	39.0±4.9	0.001
DM +/-	3/8 (27.3%/76.6%)	28/103 (21.4%/ 78.5%)	0.64 NS
Obesity +/-	9/2 (81.8%/18.1%)	70/59 (54.3%/45.6%)	0.07 NS
Severity of diseases +/-	10/1 (32.3/0.9%)	21/110 (67.7/99.1%)	0.000

BMI: Body mass index, CRP: C-reactive protein, NRS: Nutritional risk screening, NS: Non-significant, M: Male, F: Female, DM: Diabetes mellitus

Table 3. The correlation of NRS-2002 score with clinical and laboratory parameters

Variable	Correlation with NRS-2002	p value	
Age	0.401	0.000	S
Albumin	-0.277	0.001	S
BMI	-0.153	0.70	NS
CRP	0.236	0.05	S
O_2 saturation (air room)	-0.618	0.001	S
Severity of diseases	0.579	0.001	S
LOS (length of stay)	0.200	0.018	S
ICU	-0.590	0.001	S
Mortality	-0.420	0.001	S

S: Significant, NS: Non-significant, BMI: Body mass index, CRP: C-reactive protein, LOS: Length of stay, ICU: Intensive care unit, NRS: Nutritional risk screening

Table 4. The evaluation of factors affecting mortality according to cox regression analysis

Variable	B	SE	Wald	Df	Sig	Exp (ß)	95% CI (min-max)	
Albumin	-0.209	0.089	5.50	1	0.019	0.812	0.682	0.966
CRP	0.017	0.008	4.68	1	0.030	1.01	1.00	1.03
Age	0.056	0.118	0.227	1	0.634	1.05	0.839	1.33
Oxygen saturation	-0.033	0.149	0.049	1	0.825	0.968	0.723	1.29
NRS-2002	0.020	1.57	0.000	1	0.990	1.02	0.047	22.12
Severity of diseases	0.045	1.02	0.193	1	0.661	1.57	0.209	11.79

CRP: C-reactive protein, NRS: Nutritional risk screening, CI: Confidence interval, SE: Standard error, Df: Degrees of freedom

In our study, our nutritional risk rate was found to be 7.7%, lower than that reported in the literature. We think that this migth be due to the younger average age of our patient group and the fact that the patients were screened for malnutrition with the NRS-2002 test at admission and the test was not repeated during hospitalization.

In a study conducted on 182 patients over 65 years of age with COVID-19 pneumonia, the risk of malnutrition was found to be 27.5% and to be associated with DM, albumin level, and arm circumference measurement (9). In our study, the nutritional risk rate was found to be 17% in the group over 65 years of age and it was 5 times higher than the group under 65 years of age. Higher predisposition to infections due to the increasing malnutrition risk with older age and impaired immune functions is been known.

Furthermore older age was reported as a risk factor in COVID-19 patients in many studies. Factors affecting the prognosis in COVID-19 pneumonia are reported as advanced age, DM and male gender, and obesity (6). The prevalence of obesity in COVID-19 patients varies between 10-75.8% in studies. Obese patients infected with COVID-19 required more ICU admission and longer hospital stay (5). In our study, our DM rate was 21.8% and our obesity rate was 23%. Although the rate of underweight cases was very low, the rate of obesity was compatible with the literature. We found that there was a nutritional risk not only in patients with normal weight but also in obese patients but DM and obesity were not found to be significant in terms of nutritional risk and mortality.

In this study, the average age, need for ICU admission, and mortality in the nutritional risk group were higher than the group without the nutritional risk. The sex, length of hospital stays, and BMI were not different between the two groups. There was no difference between the groups with and without the nutritional risk in terms of the length of the hospitalization stay rates. We think that it migth be due to the reasons that COVID-19 pneumonia is an acute disease, the rapid progression of the patients, and their discharge to ICU or death may have affected the hospitalization days.

In our study, the mean of BMI and weight of the cases were lower in the non-survivor patients than in the survivor group; however, but the difference was not significant statistically. Also, the sex distribution was not different between the dead and alive patients.

NRS-2002 scores of the patients who died were higher than those who survived, their albumin and oxygen saturation levels were lower, and CRP values were higher. Differences between the groups were statistically significant. Serum albumin level alone may sufficiently reflect malnutrition in hospitalized COVID-19 patients, especially in highly vulnerable individuals (13). Serum albumin level and CRP were reported as independent risk factors for mortality in COVID-19 patients, and an odd ratio was found 0.94 and 1.006 respectively (18). In our study, albumin levels were significantly lower in non-survived patients. Hypoalbuminemia was associated with a poor prognosis of COVID-19 (16). Even the mechanism is unclear, hypoalbuminemia was thought to be caused by increased capillary permeability and liver damage because of the cytokine storm (19).

In a study of elderly hospitalized patients in Brazil, NRS-2002 was found to be more effective than MNA and a MUST in predicting mortality, and it was reported as area under the curve (AUC): 0.78 for death (15). In another study, AUC was reported to be 0.86 to predict death for NRS-2002 (20). The prognostic value of NRS-2002 has been investigated in cancer, COPD, and critical illness (21). NRS-2002 was found to be more effective in predicting clinical prognosis and mortality.

Malnutrition was associated with disease progression and ICU need and mortality in hospitalized patients with COVID-19 pneumonia (11,13).

The NRS-2002 score was significantly correlated with albumin, age, CRP, oxygen saturation, severity of diseases, LOS, admission to an ICU, and mortality. Besides the factors affecting the mortality were evaluated with cox regression

analysis and albumin and CRP level were found statistically, NRS-2002 test, age, oxygen saturation, and severity of diseases were not found.

Many risk factors affect their nutritional status. It has been reported that factors such as socio-economic status, daily dietary intake and lifestyle, exposure to viral load, and time of initiation of treatment affect the nutritional status of patients with COVID patients (16). Since we did not evaluate the nutritional habits of the patients before hospitalization, the gastrointestinal tract symptoms due to viral load, and the side effects of the drugs used in our study, we cannot make any implications about the effect on nutritional risk. Nutrition is a dynamic process, and since the NRS-2002 evaluation is made within the first 24 h of hospitalization, we do not know whether a risk develops in the following days in patients who are not at risk, we think that these reasons have affected our results. Our study was conducted during the first wave of the pandemic, and the majority of the patients had mild-to-moderate infection. We think that the NRS-2002 test may have reduced its effectiveness in evaluating the prognosis of patients with COVID-19 pneumonia.

Malnutrition, frequently overlooked, is defined simply as imbalanced feeding, under or over feeding, and affects both thin and obese people. It is commonly seen in hospitalized patients, affects the prognosis adversely, increases both hospital stay and costs (20). Our results showed that the coexistence of advanced age and nutritional risk as a negative prognostic factor was supported by the finding of high nutritional risk and increased mean age in the non-survivor cases. Even our study did not show any association between the NRS-2002 score and mortality and admission to ICU in non-critical COVID-19 pneumonia, the NRS-2002 score was significantly correlated with albumin, age, CRP, oxygen saturation, severity of diseases, LOS, admission to an ICU, and mortality.

The limitations of the study, single-center and retrospective design of the study, limited data about the physical activity and eating habits affecting the nutritional status of the cases, and evaluation of sarcopenia with BMI. Furthermore, nutritional support products were not assessed because they were excluded from the study. Also, due to the sample size of the study, which was relatively small, our findings could not be generalized to all hospitalized patients.

Despite its limitations, we think that the use of NRS-2002, which is a non-invaziv method with lower costs to assess the nutritional risk of COVID-19, helps contribute to the prognosis of the disease.

As a conclusion, the results indicated that the use of the NRS-2002 test in cases with COVID-19 pneumonia was very helpful to assess the need for ICU and mortality. It should be the first step to assess risky patients, especially the elderly and those having acute or chronic diseases. Malnutrition seems to be a problem for viral pandemics in the 21st century and after.

In the future, in a viral pandemic, we might confront a problem named two-sided malnutrition, under and overfeeding, which aggravates the severity of the disease. More studies with nutritional support products are needed.

Study Limitations

The limitations of our study were the single-center setting and retrospective study design as well as the absence of data about physical activity and eating habits of patients, which might have affected the nutritional status of the cases and of evaluation for sarcopenia in addition to BMI. Furthermore, we did not collect information about the use of nutritional support products in our study. Because to the relatively small size of our patient population, our findings can not be generalized. Overall, our results showed that NRS-2002 helped predict the need for ICU admission and the risk of mortality in COVID-19 pneumonia, particularly in older patients.

Conclusion

We suggest that a simple, user-friendly NRS-2002 tool should be performed to evaluate the nutritional risk in COVID-19 pneumonia in routine clinical assessments. Performing NRS-2002 more than once in the hospitalization process may help the physicians in the early treatment of malnutrition and improve the prognosis of the disease.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Istanbul Training and Research Hospital Ethical Committee (12.06.2020-2400).

Informed Consent: An informed consent form was signed by each patient included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.B., B.P.Y., Design: A.B., B.P.Y., H.A., C.A., Data Collection or Processing: A.B., B.P.Y., H.A., Analysis or Interpretation: A.B., B.P.Y., A.D.A., C.A., Literature Search: A.D.A., C.A., Writing: A.B., B.P.Y., C.A.

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