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Grip strength as a predictor of disease severity in hospitalized COVID-19 patients



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ABSTRACT

Background: Grip strength is one of the main components for the physical functioning in sarcopenia and physical frailty.

Objectives: To explore the role of grip strength measurement at admission for predicting disease severity in COVID-19.

Methods: Demographic data, smoking status, comorbidities, COVID-19 related symptoms, grip strength, laboratory and computed tomography (CT) findings at admission were all noted. Using a Smedley hand dynamometer, the maximum grip strength value (kg) after three measurements on the dominant side was recorded. Low grip strength was defined as two standard deviations below the gender-specific peak mean value of the healthy young adults (<32 kg for males, <19 kg for females). Patients were categorized into three groups according to clinical and CT findings. Severe illness group had pneumonia with a respiratory rate >30/min, oxygen saturation ≤90%, or extensive lung involvement in CT. Moderate illness group had pneumonia with CT score ≤11. Mild illness group had normal CT findings.

Results: The study population included 312 patients (140 F, 172 M). The distribution of mild, moderate and severe disease groups were 36.9%, 51.0% and 12.2%, respectively. Cough, fever, dyspnea, hypertension, obesity, cardiovascular disease (CVD) and chronic obstructive pulmonary disease (COPD) were most frequent, and C-reactive protein (CRP), ferritin, D-dimer, and neutrophil levels were highest in the severe group (all $p < .05$). Absolute grip strength values were lowest and the frequency of having low grip strength were highest in the severe group (both $p < .01$). Since we found that the significant differences were stemming from the severe group, we combined the mild and moderate group as non-severe, and compared severe vs. non-severe groups with binary logistic regression analyses. When age, gender, body mass index, smoking status, presence of comorbidities and low grip strength, and abnormal laboratory findings were taken into analyses; age (odds ratio [OR]: 1.054 [95% confidence interval (CI): 1.020–1.089]), obesity (OR: 2.822 [95% CI: 1.143–6.966]), COPD (OR: 5.699 [95% CI: 1.231–26.383]), CRP level (OR: 1.023 [95% CI: 1.010–1.036]) and low grip strength (OR: 3.047 [95% CI: 1.146–8.103]) were observed to be independent predictors for severe COVID-19 disease (all $p < .05$).

Conclusions: In addition to the well-known independent risk factors (i.e. age, obesity, COPD, and CRP level), low grip strength independently increased (about three times) the severity of COVID-19.

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Introduction

Determining the possible risk factors for disease severity - as well as for worse prognosis - among inpatients with COVID-19 is

important. It is reported that increased age and comorbidities - especially hypertension, cardiovascular disease (CVD), obesity, diabetes mellitus (DM), and chronic respiratory diseases including chronic obstructive pulmonary disease (COPD) and bronchial asthma - are related with higher rates of severe disease and mortality in COVID-19.¹ Likewise, a recent study investigating the predictors of in-hospital mortality among older patients with COVID-19 has shown that non-survivors were more often frail with worse functional status and higher comorbidity burden.² In this sense, a simple but powerful predictor to stratify the risk of frail COVID-19 patients (particularly due to aging, comorbidities such as CVD, DM, obesity, COPD, bronchial

Abbreviations: BMI, Body mass index; COPD, Chronic obstructive pulmonary disease; CRP, C-reactive protein; CT, Computed tomography; CVD, Cardiovascular disease; DM, Diabetes mellitus; SpO₂, Oxygen saturation

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asthma, sarcopenia, low physical activity, malnutrition, and vitamin D deficiency) would be noteworthy.³⁻⁵

Frailty is defined as 'a biological syndrome of decreased reserve and resistance to stressors, resulting from cumulative decline across multiple physiological systems - causing vulnerability to adverse outcomes.'⁶ It has been reported that five indicators of physical functioning i.e. weight loss, exhaustion, slowness, low grip strength, and low levels of physical activity are interrelated within a frailty cycle.⁷ Grip strength (one of the main determinants of sarcopenia and physical frailty) can be used to assess overall muscle strength/function and impairments.⁸ Yet, it is a predictor of future morbidity, disability, and even mortality in young, middle-aged and older adults.⁹ In addition, a longitudinal multicenter study found that grip strength can predict all-cause, particularly cardiovascular, morbidity and mortality even better than systolic blood pressure.⁹ Similarly, grip strength was also found to be related with the respiratory muscle strength and pulmonary function tests.^{10,11} To this end, together with the other potential risk factors, we aimed to investigate the possible relationship between handgrip strength and disease severity in adult patients with COVID-19.

Methods

Study protocol and subjects

This clinical cross-sectional study encompassed polymerase chain reaction (PCR) positive COVID-19 patients who were being monitored and treated in our inpatient adult clinics between 1 April - 1 July 2020. Our 270-bed university-affiliated hospital was designated as a 'COVID-19 hospital' by the Turkish Ministry of Health which (in addition to the local Ethics Committee) approved the current study protocol. All participants were informed about the study procedure and they gave informed consent to participate.

Pediatric patients, adult patients who had neuromuscular or rheumatic diseases affecting the handgrip strength measurements, and critically ill patients who admitted initially to the intensive care units were excluded. Demographic data, smoking status, comorbidities (e.g. hypertension, DM, CVD, bronchial asthma and COPD), COVID-19 related symptoms, clinical and handgrip strength values at admission were all noted. A body mass index (BMI) >30 kg/m² was considered as obese.

Disease severity

Patients were categorized into three groups according to their clinical and computed tomography (CT) findings. Severe illness group had clinical signs of pneumonia (fever, cough, dyspnea and tachypnea) together with a respiratory rate >30/min, an oxygen saturation (SpO₂) ≤90% on room air,¹² or extensive lung involvement in CT (i.e. CT score >11).^{13,14} Moderate illness group had pneumonia confirmed by clinical and radiological findings (i.e. CT score ≤11) together with a respiratory rate ≤30/min and SpO₂ >90% on room air. Mild illness group had normal chest CT and/or radiographic findings.

Computed tomography

Scans were obtained while patients were in supine position at the end of inspiration, using GE Brightspeed 16-Slice CT Scanner (GE Healthcare, Chicago, Illinois, United States). A radiologist with 10 years of experience evaluated the CT findings i.e. the presence and patterns of infiltrations as ground glass opacities, pulmonary consolidation, and crazy paving.¹⁵ The anatomic distribution of the infiltrations was coded for the right upper, middle and lower lobes, and left upper and lower lobes. A semi-quantitative CT severity scoring system¹⁶ which was firstly defined to correlate radiological and pathological findings for primary pulmonary fibrosis was applied for each lobe. This method has

been widely used for quantifying radiological findings in various diseases including COVID-19.^{13,14} An important study¹⁴ has shown that CT scoring >11 was found to be associated with COVID-19 disease severity. The extent of anatomic involvement was coded as 0 (absent), 1 (<5%), 2 (5-25%), 3 (26-50%), 4 (51-75%), and 5 (>75%). The total CT score was computed as the sum of each lobe's scores between 0 to 25. CT findings were also given as follows: normal vs. pathological, maximum chest CT scores >11 vs. ≤11,¹⁴ multilobar vs. unilobar involvement, and unilateral vs. bilateral involvement.

Handgrip strength

Handgrip strength was measured (in kg) using an electronic Smedley hand dynamometer (Baseline, Model 12-0286, Guangdong, China). Patients were seated placing their arms by their sides with the elbow flexed to 90°, the forearm in mid-prone and the wrist in neutral positions. Patients were asked to grip the dynamometer with maximal effort using standard verbal encouragement. In keeping with the most commonly used protocols for grip strength assessment in the literature,¹⁷ the maximum value of three repetitions from the dominant side were measured (with 30-second rests between trials) and recorded in kg. Low grip strength was defined as two standard deviations below the gender-specific peak mean value of the healthy young adults i.e. <32 kg in males and <19 kg in females.¹⁸

Statistical analyses

Statistical analyses were done using SPSS 20.0 (SPSS Inc., Chicago, IL, USA). Kolmogorov Smirnov or Shapiro-Wilk test was used to test normal distribution. Numerical variables are expressed as mean± standard deviation or median (min-max) values, where appropriate. Categorical variables are given as numbers and percentages. Numerical variables were compared with One-way analysis of variance (ANOVA) or Kruskal Wallis test (with Bonferroni or Tukey corrections), while categorical variables were compared by Chi-square or Fisher's exact tests. For binary logistic regression analysis (with backward likelihood ratio selection), COVID-19 patients were categorized into two groups according to disease severity as non-severe (i.e. mild and moderate) and severe. For predicting severe disease, demographic and significant clinical variables were taken into analyses. Statistical significance was set at *p*<0.05.

Results

The study population included 312 patients (140 F, 172 M) with a mean age of 46.1±14.8 (20-90) years. Their most common symptoms were cough (n=135, 43.3%), fever (n=108, 34.6%) and myalgia (n=79, 25.3%) whereby 72 patients (23.1%) were asymptomatic. Patients with comorbidities (N=164) comprised 52.6% of the study population. Only 35 patients (11.2%) were older adults (≥65-year-old). The most common comorbidities were hypertension (N=78, 25.0%), obesity (N=60, 19.2%), DM (N=37, 11.9%) and bronchial asthma (N=34, 10.9%). Among them, 16 patients (5.1%) required intensive care treatment. Median length of hospital stay was 9 (2-30) days.

Distribution of mild, moderate and severe disease groups were 36.9%, 51.0% and 12.2%, respectively. Clinical findings according to disease severity are given in Table 1. Mean age and length of hospital stay were higher in the severe vs. other groups (both *p*<.001). All severe patients were older than 40 year, and 26/38 (68.4%) were older than 55 years. BMI was lower in the mild vs. other groups (*p*<.01). Other than the frequency of smoking (being highest in the mild group), frequencies of cough, fever, dyspnea, hypertension, obesity, CVD and COPD were highest in the severe group (all *p*<.05). According to the laboratory findings on admission; the C-reactive protein (CRP), ferritin, D-dimer, and neutrophil levels were highest, while lymphocyte count was lowest in the severe vs. other groups

(all $p < .05$). Mean grip strength values were lower and frequency of low grip strength was higher in the severe vs. other groups (both $p < .01$). Gender, presence of other symptoms and comorbid diseases, and hemoglobin levels were similar among the groups (all $p > .05$).

Of 312 patients, 12 (3.8%) patients had no chest CT images in the picture archiving and communication system of the study center (but they had pneumonia on CT reports at other hospitals). Those patients were grouped as severe (N=1) and moderate (N=11) according to their clinical findings (only one patient had clinically severe disease and needed intensive care treatment), CT reports and chest radiographs. Remaining 300 patients had chest CT examinations. Among those, 115 (38.3%) patients had normal CT examinations, whereas 185 (61.7%) patients had pathological involvements i.e. ground glass opacities in 141 (76.2%), consolidations in 39 (21.1%), and crazy paving in 5 (2.7%) patients. Overall median CT score was 2 (0-19), and 26 (8.7%) patients had high (>11) CT scores. The anatomical distribution of chest involvement (on CT) is given in Table 2. The most common location was left lower lobe, followed by right lower lobe. Findings were unilateral in 36 (19.5%) and bilateral in 149 (80.5%) patients; unilobar in 30 (16.2%) and multilobar in 155 (83.8%) cases.

There were no significant differences between the mild and moderate groups as regards clinical findings for COVID-19, and the statistically significant differences (i.e. length of hospital stay, symptomatology, comorbid diseases, laboratory findings, and low grip strength) appeared to stem from the severe group (Table 1). As such, data from the mild and moderate groups were combined as non-severe and binary logistic regression analyses were performed as severe vs. non-severe groups. Low grip strength was present in 25 patients (9.1%) in the non-severe group and in 15 patients (39.5%) in the severe group ($p < 0.001$). When age, gender, BMI, smoking status,

presence of comorbidities, low grip strength and abnormal laboratory findings were taken into analyses (Table 3); age, obesity, COPD, CRP level and low grip strength were found to be independent predictors for severe disease (all $p < .05$).

Discussion

The COVID-19 pandemic is ever mounting as a global emergency that continues to still threaten the healthcare systems in many dimensions. Emerging research investigates various patient factors e.g. demographic, clinical, laboratory and radiographic findings that may help clinicians to predict the severity and mortality of COVID-19. In this regard, a recent review reported that age >55 years, multiple comorbidities, hypoxia, CT findings with extensive lung involvement, various laboratory abnormalities, and biomarkers of end-organ dysfunction were predictive for COVID-19 severity and/or mortality.¹

Table 2
Chest computed tomography findings of the patients (N=300)

Anatomical location	N	%	CT score
Lung involvement	185	61.7	5 (1-19)
Right upper lobe	123	68.5	1 (0-4)
Right middle lobe	112	62.9	1 (0-4)
Right lower lobe	154	84.3	1 (0-4)
Left upper lobe	147	79.5	1 (0-3)
Left lower lobe	172	93.0	1 (0-5)
No involvement	115	38.3	0
Total	300	100.0	2 (0-19)

N; number

Table 1
Clinical and demographic characteristics of the study population (N=312)

Characteristic	Mild (N=115)	Moderate (N=159)	Severe (N=38)	P
Age, year	39 (21-74)	46 (20-90)	61 (42-90)	<0.001
Gender, female	50 (43.5)	73 (45.9)	17 (44.7)	0.923
BMI, kg/m²	26.8±5.3*	29.3±5.4	30.5±6.6	0.002
Smoking	39 (33.9)	21 (13.2)	8 (21.1)	<0.001
Hospital stay, day	8 (2-19)	8 (3-21)	18 (6-30)*	<0.001
Symptoms, n (%)				
Cough	41 (35.7)	71 (44.7)	23 (60.5)*	0.024
Fever (>37.8 C)	30 (26.1)	54 (34.0)	24 (63.2)*	<0.001
Myalgia	29 (25.2)	39 (24.5)	11 (28.9)	0.853
Fatigue	13 (11.3)	23 (14.5)	5 (13.2)	0.747
Dyspnea	13 (11.3)	24 (15.1)	33 (86.8)*	<0.001
Headache	13 (11.3)	16 (10.1)	2 (5.3)	0.557
Anosmia/ageusia	11 (9.6)	16 (10.1)	0 (0)	0.127
Diarrhea	7 (6.1)	6 (3.8)	0 (0)	0.250
Asymptomatic	36 (31.3)	36 (22.6)	0 (0)	<0.001
Comorbidities, n (%)				
Hypertension	21 (18.3)	37 (23.3)	20 (52.6)*	<0.001
Obesity	15 (13.0)	32 (20.1)	13 (34.2)	0.015
Diabetes Mellitus	15 (13.0)	14 (8.8)	8 (21.1)	0.098
Bronchial Asthma	11 (9.6)	20 (12.6)	3 (7.9)	0.599
Hypothyroidism	12 (10.4)	10 (6.3)	2 (5.3)	0.373
Cardiovascular Disease	6 (5.2)	10 (6.3)	8 (21.1)*	0.004
COPD	2 (1.7)	2 (1.3)	5 (13.2)*	<0.001
Laboratory, median (IQR)				
C-reactive protein, mg/L	5.0 (1.6-9.2)	7.5 (2.2-14.0)	34.5 (13.8-81.3)*	<0.001
Ferritin, µg/L	60 (23-125)	110 (38-206)	276 (130-396)	<0.001
D-dimer (µg/mL)	0.25 (0.19-0.35)	0.36 (0.21-0.56)	0.59 (0.33-1.08)*	<0.001
WBC, 10³/µL	5.6 (4.1-7.3)	5.2 (4.1-5.9)	5.4 (4.7-6.8)	0.042
Lymphocyte, 10³/µL	1.7 (1.2-2.2)	1.5 (1.2-2.0)	1.3 (1.0-1.9)	0.037
Neutrophil, 10³/µL	3.1 (2.2-4.7)	3.0 (2.2-3.9)	3.7 (2.9-4.5)*	0.022
Hemoglobin, g/dL	14.5 (13.2-15.5)	14.3 (13.0-15.2)	13.9 (12.8-14.5)	0.099
Grip strength, kg	35.1±11.2	34.7±11.1	26.5±12.4*	0.006
Low grip strength, n (%)	11 (9.6)	14 (8.8)	15 (39.5)*	<0.001

Data are given as mean±SD, median (min-max), median (IQR) or n (%).

Statistically significant variables are shown as bold.

BMI; body mass index, IQR; interquartile range, WBC; white blood cell; COPD, Chronic Obstructive Pulmonary Disease.

* The statistical difference is caused from this value.

Table 3
Binary logistic regression analyses (N=312) for predicting severe disease

Dependent variable	Independent variable*	Exp (β)	95% CI	p
Severe disease (N=38)	Age	1.054	1.020-1.089	0.002
	Obesity	2.822	1.143-6.966	0.024
	COPD	5.699	1.231-26.383	0.026
	C-reactive protein	1.023	1.010-1.036	0.001
	Low grip strength	3.047	1.146-8.103	0.026

β ; standardized coefficients, CI; confidence interval, COPD; chronic obstructive pulmonary disease

* Age, gender, smoking status, obesity, hypertension, diabetes mellitus, cardiovascular disease and COPD, and low grip strength and abnormal laboratory findings.

The results of this current study have shown that other than biological aging, comorbidities such as obesity and COPD and CRP levels, low muscle strength/function (i.e. grip strength) seem to be an independent predictor for COVID-19 disease severity.

A recent study conducted in 100 COVID-19 patients (mean age of 66 years) evaluated the inpatient rehabilitation for post-acute care and reported that grip strength was positively/moderately correlated with Barthel index (assessing overall strength and physical functioning), and negatively/moderately correlated with the duration of intensive care unit stay.¹⁹ Another study recruiting 150 hospitalized COVID-19 patients (mean age of 53 years) compared the musculoskeletal findings (including grip strength) and revealed that female (but not male) patients with severe COVID-19 disease had lower grip strength as compared to non-severe ones.²⁰ In our relatively larger study (N=312) with younger subjects (mean age of 46 years), we found that low grip strength independently increased (about three times) the risk of severe disease course in COVID-19.

The most common COVID-19 related symptoms included cough (43.3%), fever (34.6%) and myalgia (25.3%) in our study and these findings are in line with the pertinent literature whereby fever, cough and fatigue are similarly reported.¹ Additionally, our most common chest CT finding was ground glass opacities whereby the most commonly involved lobes were the right and left lower lobes - again consistent with the literature.²¹ Patients with CVD, chronic lung diseases (especially COPD), DM, hypertension and obesity have an unfavorable COVID-19 disease course including intubation and death.^{22,23} It has been reported that obesity (BMI > 30 kg/m²) is also a strong predictor for severe COVID-19.²³ Additionally, a large case-control study found that COVID-19 patients with at least one comorbidity (obesity followed by DM and hypertension) are more likely to suffer severe disease course.²³ Although the most common comorbidities were hypertension (25.0%), obesity (19.2%), DM (11.9%), and bronchial asthma (10.9%) in our study, we found that only the presence of obesity and COPD were independent risk factors for severe COVID-19. Although it has been reported that DM is a predictor for COVID-19 severity,¹ possibly owing to the fact that our data were obtained from relatively young/healthy adult patients (almost half of them with no comorbid diseases) admitted in the first phase of the pandemic; there were low frequencies of stable DM (12%) and severe COVID-19 disease (12%). Likewise, older patients with multimorbidity leading end-organ failure such as advanced diabetes mellitus, cardiovascular disease, immunosuppression, chronic renal/liver, heart failure and cancer patients who had required intensive care unit treatment were not present. Second, the relatively young Turkish population as well as early admission of restriction and social isolation for older adults (≥ 65 -year-old) in our country resulted in low infection and hospital admission rates in these groups. Third, the healthcare system in Turkey for COVID-19 patients is free and easily accessible especially at the beginning of the pandemic due to the lack of experience and feedback for its management.

Certain laboratory markers may predict COVID-19 prognosis. Elevated D-dimer, CRP, and cardiac troponin I levels are commonly reported in relation with poor outcome in COVID-19.^{1,23,24} In

addition, increased white blood cells and neutrophils, and lymphopenia may also be used to predict disease severity.^{1,25-27} Further, elevated CRP - suggested as a predictor of COVID-19 severity - is also related with severe abnormal CT findings.^{26,27} According to our results, although most of the COVID-19 related laboratory findings were statistically higher in the severe group, only elevated CRP levels were independently associated with severe disease. This finding might have been due to the fact that our study population included relatively younger and healthier patients.

This study has some limitations. First, it was performed during an early period of the pandemic. Therefore, an important portion of the hospitalized patients were asymptomatic (23.1%) and had no comorbid diseases (47.4%) - possibly owing to the fact that our study population included relatively younger and healthier patients. Second, we did not have enough patients (only 17 F, 21 M) with severe COVID-19 disease to analyze each gender separately. Third, we did not evaluate the other pre-existing frailty components (i.e. slowness, weight loss, exhaustion and low levels of physical activity) due to the pandemic conditions. Nevertheless, our results were significant enough to demonstrate the importance of grip strength.

Conclusions

Grip strength - the "vital sign" of the neuromusculoskeletal examination - can be used as a convenient tool to predict overall muscle strength/function including physical and respiratory functioning all of which significantly impact the severity/mortality in COVID-19. As being simple, objective, cheap and reliable; measuring grip strength of COVID-19 patients would seemingly be important during this pandemic, especially in aging adults with comorbid diseases. Future studies with larger and older samples are needed to support our results.

Declaration of competing interest

There are no conflicts of interest

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None.

Authors' contribution

Substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data: OK, MK, MEA, LO

Drafting the article or revising it critically for important intellectual content: OK, MK, MEA, LO

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