The effect of body composition on prognosis in critically ill COVID-19 patients

Sarcopenia in ICU patients diagnosed with COVID-19

Ismail Beypinar¹, Murat Bayav², Anil Ucan³, Serdar Efe⁴
¹Department of Medical Oncology, Eskişehir City Hospital
²Department of Radiology, Eskişehir City Hospital
³Department of Internal Medicine, Eskişehir City Hospital
⁴Department of Intensive Care, Eskişehir City Hospital, Eskişehir, Turkey

Abstract

Aim: Although limited risk factors were observed with the accumulated evidence during the SARS-CoV-2 (COVID-19) pandemic, there is still a lack of evidence for markers distinguishing asymptomatic-mild disease from severe disease. In this study, we aimed to evaluate the prognostic impact of sarcopenia and visceral adipose tissue in ICU patients treated for COVID-19.

Material and Methods: The study designed as a retrospective cross-sectional study for evaluating the effect of prognostic radiologic features in COVID-19 infected patients. The patient characteristics, intubation status and dates, transfer to ICU, and last control or death dates were recorded. Axial CT images, including all abdominal muscles, total skeletal muscle area, were calculated. The total and psoas sarcopenia index (PSI) was calculated by dividing the square of the patient's height by the square meter (cm²/m²). Also, axial CT images of the body fat subcutaneous adipose and visceral adipose tissue distribution areas were calculated in cm² using threshold values of -30 to -190 for adipose tissue.

Results: In the study population, there were nine deaths that occurred among male patients. In univariate analysis, chronic obstructive pulmonary disease and PSI were found to be related to prognosis. The median survival was 14 days in PSI low group. The prognostic effect of the PSI was still valid in the male population. Other factors had no relationship with survival in univariate analysis. In multivariate analysis, the prognostic effect of TSI and PSI was related to prognosis, while COPD lost its prognostic effect.

Discussion: In this study, we found a new prognostic factor in critically ill COVID-19 patients, which may be a new area of interest. In contrast to other studies, we found no effect of BMI and visceral adipose tissue on mortality in COVID-19 patients treated in ICU. This feasible method needs further evaluation and validation with prospective studies in a large patient population.

Keywords
COVID-19; Mortality; Sarcopenia; Visceral adipose tissue; Prognosis; Critically ill patients

DOI: 10.4328/ACAM.20383    Received: 2020-10-25    Accepted: 2020-11-24    Published Online: 2020-12-05    Ann Clin Anal Med 2021;12(6):680-684

Corresponding Author: Murat Bayav, Eskişehir City Hospital, Department of Radiology, Eskişehir, 26080, Turkey
E-mail: muratbayav@hotmail.com    P: +90 5356171747
Corresponding Author ORCID ID: https://orcid.org/0000-0002-8210-4182
Introduction
SARS-CoV-2 (COVID-19) is a single-stranded RNA spherical virus which has glycoprotein spikes [1]. Multiple subtypes of coronaviruses have the capability of infecting humans. The major subgroups which have severe infection capacity are COVID-19, MERS, and SARS-CoV-1 [2]. The primary target of the COVID-19 is angiotensin-converting enzyme-2 (ACE-2) located on the alveolar and ciliated bronchial epithelium. Airborne droplets were shown to be the direct dissemination way of the viral particles [3]. Cough, fever, and shortness of breath are the most frequent symptoms of the disease. It has been reported that myocardial damage, respiratory and renal failure are the leading reasons for death in COVID-19 patients [4]. Approximately 200,000 deaths, confirmed by the World Health Organization, occurred related to COVID-19 till April 25, 2020 worldwide [5].

According to the literature, the groups most affected by COVID-19 were immunocompromised and older adults. High rates of respiratory failure during the disease are the major problem in COVID-19 infection [6]. Although limited risk factors with the accumulated evidence were observed during the pandemic, there is still a lack of evidence for markers distinguishing asymptomatic-mild disease from severe disease [7].

Catabolism of the main skeletal muscle proteins is a frequent phenomenon for chronic conditions such as cancer and chronic obstructive lung disease [8]. Also, cachexia is known to be related to increased mortality in cancer patients [9]. Differences in body composition between males and females have been observed in previous studies in both healthy subjects, patients with cirrhosis, or cancer. Muscle tissue was enlarged in males, while females had enlarged adipose tissue [10]. Sarcopenia is one of the new areas of interest in cancer patients in relation to a clinical marker [11]. Obesity, according to body mass index (BMI), is associated with a decreased treatment response in breast cancer patients [12]. Obese patients are not uniform; some patients remain metabolically stable, which is called the ‘obesity paradox’ [13]. In addition, sarcopenia can be masked by increased BMI, which leads to the phenomenon of sarcopenic obesity [14]. For these reasons, BMI is not a reliable marker for estimating body composition and disease prognosis.

A new study reported that increased BMI might be related to increased mortality in patients hospitalized for COVID-19 [15]. Computed tomography (CT) is a reliable method to evaluate the muscle quality and adipose tissue [16].

To our knowledge, there are no studies investigating the prognostic effect of sarcopenia in critically ill patients hospitalized for COVID-19. In this study, we try to evaluate the prognostic impact of sarcopenia and visceral adipose tissue in ICU patients treated for COVID-19.

Material and Methods
Study Participants
The archive records of patients, who were diagnosed with COVID-19 between 11th March 2020 and 15th June 2020 at the Eskişehir City Hospital Intensive Care Unit, were retrospectively analyzed. Patients with COVID-19 were diagnosed using PCR. Oropharyngeal and nasal swabs were obtained in PCR samples.
was still valid in the male population. (p=0.007) Gender, DM, HT, CAD, TSI, VAT, BMI (categorized for both 25 and 30 kg/m²) had no relationship with survival in univariate analysis (Table 2). In multivariate analysis, the prognostic effect of TSI and PSI was related to prognosis, while COPD lost its prognostic effect (p=0.044; p=0.035; p=0.33).

Table 1. The comparative features of the study population according by gender

| Features                              | Male (%) | Female (%) | p-value |
|---------------------------------------|----------|------------|---------|
| Gender                                | 28 (77)  | 8 (23)     | N/A     |
| Age (years)                           | 72       | 66         | 0.16    |
| Weight (kg)                           | 80       | 80         | 0.74    |
| Height (m)                            | 1.75     | 1.60       | 0.008   |
| BMI (kg/m²)                           | 25.6     | 30.3       | 0.22    |
| DM                                    | 11/28 (39.3) | 4/8 (50)     | 0.58 |
| HT                                    | 7/28 (25) | 4/8 (50)     | 0.17    |
| Coronary Artery Disease               | 5/28 (17.9) | 2/8 (25)     | 0.65 |
| COPD                                  | 8/28 (28.6) | 0/8 (0)      | 0.08 |
| Rheumatic Disease                     | 1/28 (3.6) | 1/8 (12.5)   | 0.06 |
| Chronic Corticosteroid Utility       | 1/27 (3.7) | 1/8 (12.5)   | 0.34 |
| Typical CT images                     | 27/28 (96.4) | 7/8 (87.5)   | 0.33 |
| Total adipose tissue (mm²)            | 432.3    | 504.5      | 0.22 |
| Visceral adipose tissue (mm²)         | 244.3    | 216.5      | 0.68 |
| Subcutaneous adipose tissue (mm²)     | 173.6    | 247.4      | 0.22 |
| Total muscle area (mm²)               | 144.5    | 99.2       | 0.045 |
| Psoas muscle area (mm²)               | 13.7     | 7.5        | 0.006 |
| Total Sarcopenia index                | 45.9     | 38.1       | 0.22 |
| Total Psoas index                     | 4.1      | 2.7        | 0.26 |

BMI: Body Mass Index, DM: Diabetes Mellitus, HT: Hypertension, COPD: Chronic Obstructive Pulmonary Disease, CT: Computed Tomography

Table 2. Univariate analysis of the features of the study population

| Features                              | Male | Female | p-value |
|---------------------------------------|------|--------|---------|
| Median OS (days)                      | NR   | NR     | 0.13    |
| DM                                    | Yes  | No     | 0.45    |
| Median OS (days)                      | 47   | NR     | 0.45    |
| HT                                    | Yes  | No     | 0.74    |
| Median OS (days)                      | NR   | 47     | 0.67    |
| CAD                                   | Yes  | No     | 0.001   |
| Median OS (days)                      | 12   | NR     | 0.010   |
| PSI                                   | Low  | High   |         |
| Median OS (days)                      | 14   | NR     | 0.18    |
| TSI                                   | Low  | High   |         |
| Median OS (days)                      | NR   | NR     | 0.46    |
| VAT                                   | Low  | High   |         |
| Median OS (days)                      | NR   | NR     | 0.4     |
| VAT                                   | Low  | High   |         |
| Median OS (days)                      | NR   | NR     | 0.46    |

DM: Diabetes Mellitus, HT: Hypertension, CAD: Coronary Artery Disease, COPD: Chronic Obstructive Pulmonary Disease, PSI: Psoas Sarcopenia Index, TSI: Total Sarcopenia Index, VAT: Visceral Adipose Tissue, BMI: Body Mass Index, NR: Not Reached
Sarcopenia in ICU patients diagnosed with COVID-19

Discussion
To our knowledge, this is the first study that evaluates the prognostic effect of sarcopenia in ICU patients. In our research, TSI and PSI were found to be an independent risk factor in COVID-19 infected ICU patients.

COVID-19 is known to have high mortality in the geriatric population. Conditions such as sarcopenia and frailty are frequently seen in the elderly [17]. Sarcopenia is defined as the loss of a prominent muscle tissue that is related to increased vulnerability to stressors [18]. Previous studies have shown a relationship between sarcopenia and ICU mortality [19]. Interestingly, COVID-19 infection was found to induce weight loss in animal models via interferon-gamma and tumor necrosis factor-alpha. This effect disappeared after the treatment [20]. Regulations, including social isolation during the pandemic, were strictly applied, especially to the elder population, which may accelerate muscle loss in a short period. Also, chronic conditions such as DM and COPD are responsible for sarcopenia in this group [21]. Although some new reports have been published, which have shown a relationship between high BMI and poor outcome in COVID-19 infection, no literature is available investigating sarcopenia in this condition. The death rates were higher in countries with a high prevalence of obesity, such as the United States of America (USA), Canada, the United Kingdom, and Mexico. This phenomenon was speculated to be related to sarcopenia, DM, CAD, increased function of the renin-angiotensin-aldosterone system (RAAS), obstructive sleep apnea, and deficiency of vitamin D. In the USA, a single-center experience showed that obesity and male gender are independent risk factors for COVID-19 infection [15]. In addition, a study investigating patient outcomes in China reported more symptoms and a severe disease course with increasing BMI [23]. In contrast to this literature, we did not found a significant relationship between BMI and COVID-19 infection, which might be related with sarcopenic obesity phenomenon. This result was supported by increased BMI but low mortality in female patients in the study population. Also, increased visceral adipose tissue was speculated to be a reservoir to the virus, which might induce an abnormal cytokine release and cause a poor outcome [24].

In our study, we found no relationship between visceral adipose tissue and increased mortality in critically ill patients. Although obstructive sleep apnea might be related to increased mortality due to obesity, no data were available in our study [25]. The limitations of this study were the small sample size, and the retrospective nature of the study made it hard to evaluate the outcomes. Although the first images were used to assess sarcopenia on CT images, the early period of the disease might affect the body composition. No deaths were observed in female patients, which might inflect the strong prognostic effect of sarcopenia in this patient group.

Conclusion
In this study, we found a new prognostic factor in critically ill COVID-19 patients, which may be a new area of interest. In contrast to other studies, we found no effect of BMI and visceral adipose tissue on mortality in COVID-19 patients treated in ICU. This comfortable and applicable method needs further evaluation and validation with prospective studies in a large patient population.
Sarcopenia in ICU patients diagnosed with COVID-19

(COVID-19) in golden Syrian hamster model: implications for disease pathogenesis and transmissibility. Clin Infect Dis. 2020; DOI:10.1093/cid/ciaa325.

21. Dent E, Morley JE, Cruz-Jentoft AJ, Arai H, Kritchevsky SB, Guralnik J, et al. International Clinical Practice Guidelines for Sarcopenia (ICFSR): Screening, Diagnosis and Management. J Nutr Heal Aging. 2018; DOI:10.1007/s12603-018-1139-9.

22. Zores F, Rebeaud ME. COVID and the Renin-Angiotensin System: Are Hypertension or Its Treatments Deleterious? Front Cardiovasc Med. 2020; DOI:10.3389/fcvm.2020.00071.

23. Cai Q, Chen F, Wang T, Luo F, Liu X, Wu Q, et al. Obesity and COVID-19 Severity in a Designated Hospital in Shenzhen, China. Diabetes Care. 2020; DOI:10.2337/dc20-0576.

24. Ryan PMD, Caplice NM. Is Adipose Tissue a Reservoir for Viral Spread, Immune Activation, and Cytokine Amplification in Coronavirus Disease 2019? Obesity. 2020; DOI:10.1002/oby.22843.

25. Pazarlı AC, Ekiz T, İlik F. Coronavirus disease 2019 and obstructive sleep apnea syndrome. Sleep Breath. 2020; DOI:10.1007/s11325-020-02087-0.

How to cite this article:
Ismail Beypinar, Murat Bayav, Ani Ucan, Serdar Efe. The effect of body composition on prognosis in critically ill COVID-19 patients. Ann Clin Anal Med 2021;12(6):680-684