

## **Original Article**

## Risk of sarcopenia, fear of COVID-19, anxiety, depression and physical activity levels: Associations across patients on hemodialysis within Greece

Maria Tsekoura<sup>1</sup>, Nikolaos Kalampakos<sup>1</sup>, Konstantinos Fousekis<sup>1</sup>, Konstantinos Mylonas<sup>1</sup>, Pavlos Angelopoulos<sup>1</sup>, Charalampos Matzaroglou<sup>1</sup>, Theodora Bita<sup>2</sup>, John Gliatis<sup>3</sup>, Elias Tsepis<sup>1</sup>, Evdokia Billis<sup>1</sup>

<sup>1</sup>Department of Physiotherapy, School of Health Rehabilitation Sciences, University of Patras, Rio, Greece; <sup>2</sup>Filoxenia hemodialysis centre, Aigio, Greece; <sup>3</sup>Department of Medicine, School of Uselth Sciences, University of Patras, Pio, Patras, Greece;

<sup>3</sup>Department of Medicine, School of Health Sciences, University of Patras, Rio, Patra, Greece

## Abstract

**Objectives**: The purpose of this multicenter cross-sectional study was to investigate the association between SARC-F, fear of COVID 19, anxiety, depression and physical activity in patients undergoing hemodialysis. **Methods**: This study was conducted in 3 hemodialysis centers in Greece during the period of the COVID-19 pandemic. Sarcopenia risk was assessed using the Greek version of SARC-F ( $\geq$ 4). Demographic and medical history were collected from the patient's medical charts. The participants were also asked to fill the Fear of COVID-19 Scale (FCV-19S), the Hospital Anxiety and Depression Scale (HADS), and the International Physical Activity Questionnaire (IPAQ) questionnaire. **Results**: A hundred and thirty-two (132) patients on hemodialysis (92 men, 70.75±13.14 years) were enrolled. Sarcopenia risk (utilizing the SARC-F) was found in 41.7% of patients on hemodialysis. The average duration of hemodialysis was 3.94±4.58 years. The mean score values for SARC-F, FCV-19S and HADS were 3.9±2.57, 21.08±5.32, and 15.02±6.69, respectively. The majority of patients were physically inactive. The SARC-F scores were strongly associated with age (r=56; p<0.001), HADS (r=0.55; p<0.001), levels of physical activity (r=0.5; p<0.001), but not with FCV-19S (r=0.27; p<0.001). **Conclusion**: A statistically significant relationship was recorded between sarcopenia risk and age, anxiety/depression and levels of physical inactivity in patients on hemodialysis. Future studies are necessary in order to evaluate the association of specific characteristics of patients.

Keywords: SARC-F, Fear of COVID-19, Sarcopenia risk, Anxiety, Depression

## Introduction

Sarcopenia is a muscular disease (muscle failure) associated with low muscle quantity and quality<sup>1</sup>. Sarcopenia is highly prevalent in patients undergoing hemodialysis, leading to poor outcomes<sup>2</sup> such as poor quality of life, falls, fractures, loss of independence, fatigue and mortality<sup>3,4</sup>. The prevalence of sarcopenia in patients with chronic kidney disease is higher compared to the general population<sup>4-6</sup>. Aging, comorbidities, physical inactivity, chronic inflammation, inadequate protein intake, nutrient loss during dialysis, accumulation of non-dialyzable uremic toxins, metabolic acidosis, excess angiotensin II, insulin and insulin-like growth factor resistance are some reasons justifying the high prevalence

rates of sarcopenia and this group of patients<sup>2,7</sup>.

Early diagnosis of sarcopenia would help improve the overall healthcare management for these patients, may prevent adverse health outcomes, and will also

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**Corresponding author:** Maria Tsekoura. Department of Physiotherapy, School of Health Rehabilitation Sciences, University of Patras, Rio, Greece

E-mail: mariatsekoura@upatras.gr

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reduce the economic impact on the health care system<sup>8</sup>. While knowledge about sarcopenia pathophysiology has improved, diagnosis remains challenging among health professionals<sup>9</sup>. Diagnosis may be overlooked in clinical practice apparently due to the complexity of determining what variables to measure. In 2O18, the European Working Group on Sarcopenia in Older People (EWGSOP2) published a definition based on low muscle strength as the key characteristic and the primary parameter of sarcopenia<sup>1.8</sup>. The EWGSOP2 algorithm has incorporated the SARC-F questionnaire as a screening tool for sarcopenia and it is proposed to be used as an initial screening tool in order to identify people at risk of sarcopenia<sup>1</sup>. SARC-F is focusing on strength, walking assistance, rising from a chair, climbing stairs, and falling<sup>10</sup>.

In addition, patients on hemodialysis affected by SARS-CoV-2 may be at high risk for musculoskeletal health impairments, such as sarcopenia<sup>11</sup>. The new coronavirus (COVID 19) infection, which has started in the Wuhan region of China in 2019, has become a pandemic<sup>12</sup> and large numbers of chronic kidney disease (CKD) patients, are more vulnerable to COVID 19 complications<sup>13</sup> due to the several comorbidities (from their disease), and their impaired immune response. COVID-19 can infect the kidney, and the presence of chronic kidney disease constitutes a higher risk of negative prognosis, severe complications<sup>14,15</sup> and often increased severity and mortality from COVID-19<sup>16</sup>. The COVID-19 pandemic is an important factor affecting the health of people worldwide, as well as their fear, stress, and anxiety<sup>17</sup>. The fear of the patients increases due to the risk of Covid-19 and its complications<sup>12,13</sup>.

Considering the high prevalence of sarcopenia in patients with CKD (20-55%)<sup>18</sup>, the difficulties in diagnosis<sup>1</sup> and the importance of optimal care for patients with this disease during the pandemic, it seems important to investigate the level of association of sarcopenia in patients on hemodialysis. There is limited data regarding the use of SARC-F in patients undergoing chronic hemodialysis. Thus, the objective of this study was to investigate the association between SARC-F, fear of COVID-19 and other inter-related variables in these patients.

## **Methods**

## Study population and design

The participants involved in this cross-sectional study were recruited from 3 hemodialysis centers: i) "Filoxenia" located in Aegio city, western Greece; ii) "Euromedica Kyanous Stavros" located in Thessaloniki city, northern Greece and iii) "Nephroxenia" located in loannina city, north west Greece. Any patient from these centers was requested to participate in the study.

Eligible participants had to be aged over 18 years old on hemodialysis, and be able to read in Greek and understand the purpose of the study. The exclusion criteria included cognitive impairment and no willingness to participate. All

Variable								
Mean ± SD								
Age (years)	70.7±13.1							
BMI (kg/m²)	26.06±4.64							
Drugs (number)	4.89±2.58							
Comorbidities (number)	5.1±1.8							
Years on hemodialysis	3.94±4.58							
SARC-F score	3.9±2.57							
HADS total score HADS Anxiety HADS Depression	15.02±6.69 6.91.±3.69 8.11.±4.13							
FCV-19S total score	21.08±5.32							
Number and percentage (%)								
Gender Women Men	40 (30.3%) 92 (69.7%)							
Smoking Number of cigarettes per day	30 (22.7%) 7							
Levels of physical activity/IPAQ Inactivity Moderate activity level High activity level	92 (69.7%) 38 (28.8%) 2 (1.5%)							

BMI: Body Mass Index; HADS: Hospital Anxiety and Depression Scale; IPAQ: International Physical Activity Questionnaire; FCV-19S: Fear of COVID 19 scale

 Table 1. Participants' characteristics.

participants were informed about the aim of this study and signed an informed consent form prior to their inclusion.

## Procedure

The study and all measurements were completed in a single visit for each participant. After consent, patient data were collected by a trained clinical researcher (KN). Demographics and medical history (including cognitive diagnosis) were obtained by the patient's medical records. All patients fulfilled 4 questionnaires.

- a. SARC-F: This tool includes five items based on cardinal features or consequences of sarcopenia: deficiencies in strength, assistance in walking, rising from a chair, climbing stairs, and falls<sup>10</sup>. The total score range is from O points to 10 points. SARC-F ≥4 indicate a risk of having sarcopenia<sup>8,19</sup>. SARC-F has been translated and cross-culturally adapted in Greek language<sup>20</sup>.
- b. Fear of COVID 19 scale (FCV-19S): This 7-item score was developed to assess the fear of COVID-19. The total score of FCV-19S is calculated by adding up each item score and ranges from 7 to 35<sup>21</sup>. The scale has been officially crossculturally adapted into Greek<sup>22</sup>.
- c. Hospital Anxiety and Depression Scale (HADS): This

	FCV-19S	IPAQ	Age	HADS total	Depression (HADS-D)_	Anxiety (HADS-A)	Years on he- modialysis	BMI	Gender
SARC-F	r=0.27; p=0.02	r=0.5; p≤0.001	r=0.56; p≤0.001	r=0.55; p≤0.001	r=0.6; p≤0.001	r=0.25; p=0.02	r=0.05; p=0.5	r=0.11; p=0.2	r=0.13; p=0.5

FVS: Fear of COVID 19 scale; HADS: Hospital Anxiety and Depression Scale; IPAQ: International Physical Activity Questionnaire; BMI: Body Mass Index.

Table 2. Association of SARC-F and other variables.

questionnaire measures anxiety and depression<sup>23</sup>. HADS comprises 14 questions, and takes 2–5min to complete<sup>23,24</sup>. It consists two subscales: anxiety subscale (HADS-A) and the depression subscale (HADS-D). The cut-off scores for the total score and subscales are as follows: a) 0–7 normal, b) 8–10 mild/doubtful, and c) >10 moderate-severe (clinical anxiety or depression)<sup>25</sup>. HADS Greek version has good psychometric properties and has proven useful to clinicians and health professionals for assessing anxiety and depression<sup>26</sup>.

d. International Physical Activity Questionnaire-short form (IPAQ): IPAQ was developed in the late 1990s to assess physical activity levels. It is a 7-item instrument. It consists of six questions that participants are asked to record the number of days and the minutes per day of their participation in all kinds of physical activity during the last seven days<sup>27</sup>. IPAQ was cross-culturally adapted into Greek and showed excellent reliability properties<sup>28</sup>.

#### Statistical analysis

Descriptive statistics and analysis of data were performed using IMB SPPS Statistics 28.0. T-test was used to compare SARC-F between genders. The association between variables was calculated using Pearson's r correlation coefficients. Pearson-r categorization was made according to Cohen (r=0.10 small, r=0.30 medium and r=0.50 large)<sup>29</sup>. Statistical results were considered significant at the 5% critical level (p<0.05).

#### Results

A hundred and thirty-two (132) participants (71.6 $\pm$ 7.8 years; 92 men and 40 women) were included in the study. The response rate is 91%. The average duration of hemodialysis was 3.94 $\pm$ 4.58 years. 49 patients were recruited from the Thessaloniki dialysis center, 35 from Aigio and 48 from the loannina dialysis center. Fifty-five patients on hemodialysis (41.7%) were found to have sarcopenia risk by the SARC-F. All participants were vaccinated for COVID-19. Table 1 presents the participants' characteristics.

SARC-F total score showed no significant statistical differences across gender in Greek patients (women:  $3.49\pm2.7$ ; men:  $3.57\pm2.61$ ; p>0.05). No significant differences were also recorded for FCV-19S results across gender (women:  $21\pm5.6$ ; men:  $21.45\pm4.69$ ; p>0.05).

A Pearson's correlation coefficient matrix for SARC-F and all variables was performed. Strong correlations were recorded with age (r=0.56; p≤0.001), HADS total score (r=0.55; p≤0.001), depression (r=0.6; p≤0.001), and activity levels (r=0.5; p≤0.001). All the other variables had low correlations with the SARC-F score, including the FCV-19S. Table 2 presents the correlations between SARC-F and all other variables.

#### Discussion

To our knowledge, this is the first study to examine sarcopenia risk and fear of COVID-19 in patients on hemodialysis in Greece. Sarcopenia risk by the SARC-F was found in 41.7% (n=55) patients on hemodialysis. Yamamoto et al., (2019) showed that 26.7% of patients that underwent hemodialysis in two dialysis centers in Japan had SARC-F  $\geq$ 4. In Japan, the study was conducted from April 2017 to July 2018<sup>30</sup>. The present study was performed during the second year of the pandemic and that factor could perhaps explain the higher results (41.7 vs 26.7%).

In the present study, SARC-F was used in order to measure the risk for sarcopenia<sup>1</sup>. SARC-F is an easy, simple and one of the best instruments for sarcopenia assessment in everyday clinical practice<sup>20,30</sup>. It has been translated in Greek language and has shown satisfactory psychometric characteristics<sup>20</sup>. Researchers suggest that this tool may provide easy opportunities for physicians to screen sarcopenia and physical limitations in clinical practice. SARC-F provides early results and does not require any instrumentation<sup>30</sup>. In future studies, measures of hand grip strength, muscle mass and physical performance should be added in order to assess sarcopenia and its severity, as all these constitute a thorough assessment of sarcopenia.

Literature shows that patients with CKD are more likely to experience high results of muscle loss because of a combination of multiple factors (e.g. metabolic acidosis, oxidative stress, inflammation)<sup>30</sup>. Prevalence on sarcopenia in patients on hemodialysis range from  $13.7\%^{32}$  to  $42.2\%^{33}$ . Sarcopenia, is of importance clinically and should be accounted for in research studies in patients with CKD<sup>1.34</sup>. In this study SARC-F was strongly associated with age (r=0.56; p≤0.001). Sarcopenia is an age related disease<sup>1</sup> and CKD is described as a model of "accelerated ageing"<sup>34</sup>, and is a chronic catabolic condition. Literature shows that there is evidence for the molecular mechanism of muscle wasting, especially uremic toxin-induced muscle wasting in patients on hemodialysis. Oxidative stress and inflammation seems to be contributors to the muscle wasting. Identifying early patients with sarcopenia risk with the SARC-F point to the importance of developing potential therapeutic agents<sup>35</sup>.

Inactivity may be an important factor for sarcopenia risk. In the present study the majority of the participants are not physically active (69.7%). Patients on hemodialysis in general are not very active, and COVID-19 presents a number of risks for further reductions in activity levels<sup>36</sup>. In this study, SARC-F was strongly associated with levels of physical activity (r=0.5; p≤0.001) in this group of patients. Physical inactivity in CKD patients can contribute to the progression of sarcopenia. Results of a study recorded that 2 weeks of inactivity may decrease muscle mass and significant change body composition in healthy older adults<sup>37</sup>. There is evidence that people with various chronic conditions decrease their levels of physical activity and are more likely to be hospitalized during the pandemic<sup>38,39</sup>. A significant point is that the researchers in this study received no records regarding physical activity levels before the pandemic. Promoting physical activity and exercise strategies from gualified health professionals may decrease physical inactivity and improve sarcopenia<sup>40-42</sup>.

Patients with advanced CKD have also shown to be vulnerable to mental health problems, such as anxiety and depression. It is also not surprising that patients with sarcopenia are concomitant with depression, because there are many known factors relevant to both medical conditions. In addition, patients with a depressive mood are likely to have physical inactivity, which is a well-recognised cause of sarcopenia<sup>43,44</sup>. Results of a recent study in 126 patients in Denmark showed that the majority of patients (n=55, 67%) reported to be more anxious about COVID-19 because of their kidney diseases<sup>44</sup>. In the present study HADS mean anxiety score was 6.91.±3.69, much higher than the Dutch patients. It is important to mention that people living in different countries may have different feelings and perceptions of the COVID-19 situations and related policies45,46.

HADS total score was  $15.02\pm6.69$  indicating moderate to severe anxiety/depression. In addition, FVS mean score was  $21.08\pm5.32$  indicating that fear of the participants was moderate to severe. In addition results recorded weak correlations between SARC-F and fear of COVID-19. This study conducted in Greece was performed during the second year of the pandemic. All participants were vaccinated for COVID-19. On hypothesis was that vaccination may lower anxiety, depression and fear levels. However, fear of COVID-19 is expected for most people<sup>21</sup>. It seems normal to fear the unknown, especially if it affects our health and that of our loved ones<sup>47</sup>. Excessive and prolonged fear, though, could reduce functionality and impair mental health<sup>21</sup>. In a study conducted in Spain by Carcia Liana et al., (2022), researchers investigated the impact of COVID-19 vaccination on anxiety and depression scores in patients with CKD. Results showed no significant differences for depression, anxiety, and healthrelated quality of life scores among the different groups of patients before and after vaccination<sup>48</sup>. Future studies should address this issue. Results of this study recommend that health professionals use the FCV-19S in clinical practice to design and perform appropriate interventions to reduce fear in different patients<sup>21</sup>. FCV-19S had strong features in its brevity with satisfactory psychometric properties shown in different language versions<sup>49</sup>.

# Clinical relevance and significance of this study

The results of this multi-centered cross-sectional study provide important data of a group of patients not previously studied in Greece and show that early detection of patients at high risk of sarcopenia seems necessary. Early detection of sarcopenia may minimize morbidity and mortality rates<sup>50</sup>. Using the Greek version of SARC-F by health professions will contribute the detection of sarcopenia in patients on hemodialysis. Clinicians should propose the most appropriate treatment strategies to improve physical and functional levels of their patients. Although results showed weak correlations between SARC-F and fear of COVID-19, the total score of FCV-19S records moderate to severe fear among patients on hemodialysis. Therapeutic exercise programmes could also help with the psychological effects and fears of COVID-19 in these group of patients.

## Limitations

This study was performed on patients on hemodialysis, and most of the participants were men; thus, any generalization of its results should be limited to this group of patients. In addition, the presence of household income or education that may influence the association between sarcopenia risk and other variables was not recorded. Finally, it seems necessary for future studies to investigate not only sarcopenia risk but the severity of sarcopenia in order to establish valid comparisons.

## Conclusions

In summary, SARC-F was strongly associated with age, anxiety, and physical activity in patients on hemodialysis. The SARC-F questionnaire can be easily and rapidly administered to patients on hemodialysis in order to assess sarcopenia risk. More research is needed to clarify the precise association of specific characteristics of patients on hemodialysis with sarcopenia and COVID-19.

#### Ethics approval

The study obtained ethical approval from the Ethical Committee of the University of Patras (approval no. 7725).

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