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## Measuring Sarcopenia on MRI among Turkish Female Breast Cancer Patients

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### ABSTRACT

**Background:** Since the presence of sarcopenia in breast cancer patients is associated with increased postoperative complications, it is crucial to know its frequency in the prechemotherapy period. It has been suggested that there are many factors associated with sarcopenia. This study focused on the frequency of sarcopenia over the pectoralis muscle area obtained in routine breast MRI among Turkish females who were newly diagnosed with breast cancer.

**Methods:** In a prospective study, pectoralis muscle was manually contoured bilaterally, and the cross-sectional area on breast MRI was calculated in newly diagnosed breast cancer patients. The 'Core slices' program was used while calculating SMI. We accepted 7.4 kg/m<sup>2</sup> as the threshold value for sarcopenia.

**Results:** Overall, 17 patients (17 %) were sarcopenic. The analysis regarding the detection of sarcopenia in the patient groups < 65 and ≥ 65 years of age was not statistically significant (P<0.156). The relationship between the groups with BMI < 25 and ≥ 25 sarcopenia was statistically significant (P<0.001). Sarcopenia was found significantly more frequently in patients with metastasis (P<0,0001).

**Conclusion:** This study recruited Turkish females who were newly diagnosed breast cancer. It is the first study in the literature to include the same race, gender, and malignancy in which sarcopenia was investigated. It was shown that breast MRI which is radiation-free can be used in the evaluation of sarcopenia in patients with breast cancer. This result is important for being prepared for possible complications before treatment.

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### INTRODUCTION

Sarcopenia is an age- and disease-related decrease in muscle mass and performance. Cancer is probably the most important pathological condition leading to the loss of muscle mass and is an important cause of sarcopenia.<sup>1-5</sup> According to 2018 data from the World Health Organization, breast cancer is the most common cancer in women worldwide. Sarcopenia is accepted as a strong predictor of poor survival among breast cancer patients.<sup>1-5</sup>

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It has been reported that the prevalence of sarcopenia in cancer patients varies significantly depending on the various types of cancer and disease stages and the tools to measure it. Usually, low muscle mass can be identified by examinations such as dual X-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), or a computed tomography (CT) scan. Because CT allows the measurement of muscle area and density, it is considered as the gold standard in the evaluation of sarcopenia. Additionally, it is possible to determine low muscle strength by hand grip strength, while the timed get-up and go test and gait speed must measure impaired physical performance.<sup>6-9</sup>



Routine staging evaluations in women with breast cancer with different techniques such as mammography, ultrasound, tomosynthesis, and magnetic resonance imaging (MRI) focus on regional disease. A study was conducted to measure muscle mass in breast cancer patients with breast MRI, which did not involve radiation and was obtained within the general approach to the patient algorithm.<sup>10</sup> In this study, it has been shown that total psoas muscle in CT and pectoral muscle measurement in breast MRI are correlated, and muscle mass can be measured over the pectoral muscle in breast MRI.

Additionally, positron emission tomography (PET-CT) is preferred for staging breast cancer, and the indications for CT alone have decreased. In early-stage breast cancer, both tests may not be obtained. In cases where CT cannot be obtained, having an alternative such as MRI is a significant advantage.

Breast MRI is the most sensitive test for detecting breast cancer.<sup>11</sup> It is used to screen for cases with dense breast parenchyma and in high-risk populations. It is also widely used as a problem solver in addition to conventional examinations. It is frequently preferred in evaluating multifocal-multicentric disease, invasion of surrounding tissues, and nipple involvement.

The European Working Group on Sarcopenia in Older People (EWGSOP) has developed an easy to apply clinical definition and diagnostic criteria for sarcopenia. As far as we know, the only study determining the cut-off value in healthy adult women (18–39 years old) for the Turkish population is that of Bahat *et al.*<sup>12</sup> In this study, the cut-off sarcopenia value for women was 7.4kg/m<sup>2</sup>, and we used this value in our study.

In another study by Oflazoğlu *et al.*, in which sarcopenia was determined in newly diagnosed cancers for the Turkish male and female populations, where all cancers were evaluated together.<sup>13</sup> They were used to assess muscle resistance BIA and handgrip dynamometer tools and to obtain the specific cut-off values for women and men. The specific SMI value for female cancer patients in the Turkish population was calculated at 6.76 kg/m<sup>2</sup>.

Since the presence of sarcopenia in breast cancer patients is associated with increased postoperative complications, chemotherapy toxicity, and disease-free survival, it is crucial to determine the frequency of sarcopenia in breast cancer patients.<sup>5,14-16</sup> In previous research, we could not find a study in which sarcopenia was evaluated by pectoral muscle measurement on MRI for newly diagnosed breast cancer patients.

In our study, we discussed the determination, frequency, and practical implications of sarcopenia

over the pectoral muscle area obtained in routine breast MRI with female newly diagnosed breast cancer patients and its related factors in the Turkish population.

## METHODS

The local ethics committee approved the prospective study protocol (ID:180 / April 2021). This study included all newly diagnosed breast cancer patients who did not undergo surgery and had received no chemotherapy or radiotherapy between April and December 2021 at our university hospital. We excluded patients with breast cancer who had breast MRIs during or after treatment and those with pectoral muscle invasion and those who had a previous operation that disrupted their pectoral muscle integrity. Those patients' pretreatment height, weight, age, body mass index, and demographic data were recorded.

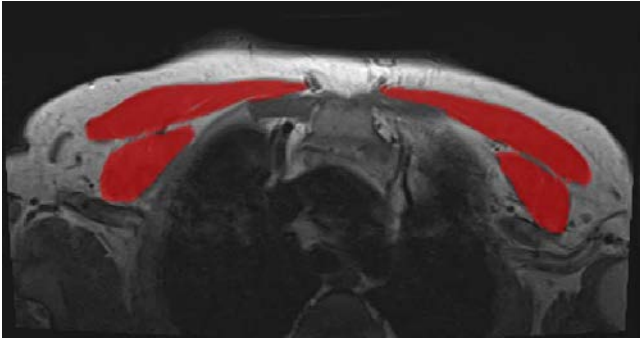
### *Images analysis: MRI*

All patients were examined with a 1,5 Tesla (T) MRI device (General Electric Signa HDx, Medical Systems, USA). A dedicated 8-channel phased-array breast surface coil was used. The standard MRI images were obtained using the following techniques: Axial fat-suppressed T2 and T1-weighted with a slice thicknesses of 4 mm with a 1,2-mm intersection gap without contrast. The gadolinium-based contrast agent was administered at a dose of 0,1 mmol/kg using an automatic syringe, and this injection was followed by a 15–20 cc of saline flush. Consecutive post-contrast dynamic sequences were taken at 60-second intervals.

The aim was to calculate the PMA cross-sectional area on MRI axial pre-contrast T1-weighted fat-suppressed images. The pectoralis muscle was identified at the level of the sternal angle of Louis at the level of the second costal cartilage in the manubriosternal joint.<sup>10</sup> The pectoral muscle is an easily measurable thoracic muscle, which is assessed on routinely obtained breast MRIs. Pectoralis muscle was manually contoured bilaterally, and the cross-sectional area on axial pre-contrast T1-weighted fat-saturated images was calculated (Figure 1). PMA was calculated by two observers (G.S, more than 15 years of experience in breast imaging, K.A.S, and a 3-year radiology resident) on MRI images by consensus. The 'Core slices' program (a free and open-source web-based interface that allows the measurement of analytic morphomics) was used while calculating SMI. When the muscle area was marked from the appropriate localization, the program automatically calculated the SMI. We accepted 7.4kg/m<sup>2</sup> as the threshold value for sarcopenia.<sup>12</sup> We



grouped the patients with BMI indexes below 25, 25, and above.



**Figure 1.** A 48 year- old, newly diagnosed breast cancer Turkish patient. The pectoralis muscle was identified at the level of the sternal angle of Louis used as a bony landmark. The pectoralis muscle (major and minor) area was countered bilaterally (red area) on axial pre-contrast T1-weighted MRI.

#### Statistical analysis

Statistical analysis was performed using statistical software (SPSS, version 22. 0). We used the Mann–Whitney U test, which is a non-parametric test, to analyze the relationship between the different groups (Table 1). The chi-squared test for categorical variables was used to compare metastatic and non-metastatic groups with or without sarcopenia. P-values<0.05 were considered as the statistical significance.

**Table 1.** Analysis of the relationship between different groups

	Sarcopenia n=17	No sarcopenia n=83	P values*
Age	55 (14.5)	50 (20)	< 0.156
Weight	61 (9.5)	73 (17)	< 0.001
BMI	24.8 (4.2)	29.3 (7.6)	< 0.001
SMI	6.4 (1.5)	10.8 (3.8)	< 0.001

Data are presented as median (interquartile range) values, \*Mann-Whitney U test

SMI, skeletal muscle mass index; BMI, body mass index

#### RESULTS

Among all patients, 17 patients (17 %) were sarcopenic. The mean age of the patients with sarcopenia was  $52 \pm 8.4$  (range 37-67), and the mean age of those without sarcopenia was  $54.4 \pm 11.7$  (range 34-84). The number of patients over 65 years was 18% (n=18). Among all patients, 72% were categorized as having BMI  $\geq 25$  (n=72). The analysis regarding the detection of sarcopenia in the patient groups <65 years of age and  $\geq 65$  years of age was not statistically significant (P<0.156). The relationship between the groups with BMI 25 < and

25  $\geq$  and sarcopenia was statistically significant (P <0.001). In other words, the risk of sarcopenia decreased as the BMI increased.

T<sub>1-4</sub>N<sub>1-3</sub>M<sub>0</sub> was detected in 73% of the patients, and T<sub>1-4</sub>N<sub>1-3</sub>M<sub>1</sub> in 23%. All patients with distant metastases also had axillary metastases. Also, 4 % of the patients (T<sub>1</sub>N<sub>0</sub>M<sub>0</sub>) had no nodal or distant metastases. A statistically significant correlation was found between sarcopenia and metastasis (P<0.0001).

#### DISCUSSION

Our study is the first to investigate sarcopenia by pectoral muscle measurement on MRI in Turkish female patients with newly diagnosed breast cancer. In this study, we found that radiation-free breast MRI can be a good alternative in the evaluation of sarcopenia in patients with breast cancer. CT and DXA are generally preferred among imaging methods to evaluate sarcopenia. However, both methods involve radiation. Breast MRI is a radiation-free method that is frequently used in patients with breast cancer for indications such as determining the spread of the disease and planning treatment. Particularly in breast cancer patients, the use of conventional CT for staging purposes may not be possible with the wide spread use of PET-CT. The fact that breast MRI, which is already obtained in daily practice as part of the diagnostic algorithm, can healthily predict sarcopenia and provide data that will help the clinician in treatment planning. Among the factors affecting sarcopenia, race and gender are important variables. Our study included a relatively homogeneous series as it involved only the female Turkish population with breast cancer patients, and therefore its results are valuable.

The latest studies present a highly variable prevalence of sarcopenia among cancer patients. In the HEAL study, the prevalence of sarcopenia in breast cancer patients was 16% and sarcopenia was associated with an increased risk of overall mortality.<sup>5</sup> In a meta-analysis, the prevalence of sarcopenia in all stages of the disease before cancer treatment was found to range from 15% to 74%.<sup>17</sup> In this meta-analysis, the prevalence of sarcopenia before both chemotherapy and surgery was 39%, while the prevalence of sarcopenia before chemotherapy was 29%. In another meta-analysis, the prevalence of body composition measurement and sarcopenia was reported to be 11-74% using abdominal CT, while the prevalence of sarcopenia calculated using body composition measurement and functional assessment tools remained at 12-51%.<sup>15,17-20</sup> In Pamukdjian *et al.*'s review of 26 studies, sarcopenia was noted in 25% of men and 13.1% of women.<sup>21</sup> Although our study consisted only



of female patients with breast cancer, the prevalence of sarcopenia was 17% in line with the literature.

Sarcopenia is defined by the European Society of Parenteral and Enteral Nutrition (ESPEN) and the European Working Group on Sarcopenia in Older People (EWGSOP) as a progressive disease involving loss of muscle mass, muscle strength, and/or physical performance.<sup>6</sup> There is a study showing that muscle mass loss is the most important of the three factors in terms of postoperative complications.<sup>19</sup> In our study, we evaluated sarcopenia based on loss of muscle mass before treatment, which is important in determining the patients that may experience complications after treatment.

Sarcopenia is particularly common among cancer patients, as the incidence of cancer increases with age.<sup>22</sup> In addition, the sedentary lifestyle brought about by old age, chronic diseases, and some related drug treatments may exacerbate muscle wasting in elderly individuals diagnosed with cancer.<sup>23,24</sup> In our study, unlike some other studies, no correlation was found between age and sarcopenia.<sup>25</sup> However, as in most studies, low BMI appeared to be a factor negatively affecting sarcopenia.<sup>13,26</sup> Prevalence rates in patients with advanced disease in the literature have been reported to be higher than in patients with early-stage disease.<sup>13,17</sup> However, it was not found to be statistically significant. Also, Zang *et al.* have shown that sarcopenia is a risk factor for mortality among female early breast cancer patients.<sup>27</sup> In our study, sarcopenia was found significantly more frequently in patients with metastasis.

Our hospital is located in a predominantly Turkish region. We had Turkish females who were newly diagnosed with breast cancer as a relatively homogeneous patient group. The most important limitation of our study is the small size of our sample group and a single-center study. Since the measurements were made by consensus,

intraobserver difference analyses were not needed. Another limitation is that the cancerous group was not compared to a normal control group and the absence of a clinical test for sarcopenia. In addition, evaluating sarcopenia with only the pectoral muscle measurement is an important limitation. There is only one study in the literature that found a correlation between the psoas muscle and the pectoral muscle areas.<sup>10</sup> More studies are needed for this generalization.

## CONCLUSION

It has been shown that breast MRI with radiation-free examination can be used in the evaluation of sarcopenia in patients with breast cancer. This result is important for physicians to be able to predict and be prepared for possible complications before treatment.

## ETHICAL CONSIDERATIONS

The study was conducted in accordance with the principles of the Helsinki Declaration. As a routine procedure, written informed consent was obtained from each patient for all procedures and publication. Ethics committee approval was received for this study from the Clinical Trials Ethics Committee (ID:180 / April 2021).

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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