

Turkish Journal of Geriatrics DOI: 10.29400/tjgeri.2024.373

2024; 27(1):1-10

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Received : Dec 08, 2023 Accepted : Jan 04, 2024

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ORIGINAL ARTICLE

THE EFFECT OF FRAILTY AND SARCOPENIA ON PERIOPERATIVE COMPLICATIONS IN PATIENTS OVER 65 YEARS UNDERGOING ELECTIVE SURGERY, PROSPECTIVE-OBSERVATIONAL STUDY

Abstract

Introduction: With aging of population, frailty and sarcopenia have become very important issues. Therefore, we aimed to evaluate patients for frailty and sarcopenia preoperatively who aged 65≤ underwent elective surgical operation in university hospital and search complications intraoperatively and postoperatively.

Materials and Method: This prospective, cross-sectional study performed between November 2021 and May 2022 at university hospital and patients aged 65 years and older underwent elective surgery included. Patients scored with frailty index. Both thickness and cross-sectional area of rectus femoris muscle were measured by ultrasound for evaluating sarcopenia in all patients, preoperatively. Anesthetic management, surgical risks were determined. Intraoperative and postoperative complications recorded.

Results: Totally 1112 patients were assessed and 279 patients were included. According to the cross-sectional area 35.5%; according to rectus femoris thickness 32.2% and according to both of them 25.4% were detected as sarcopenia. While fragility was detected in 151(54.7%) patients which 112(74.2%) pre-frail, 39(25.8%) fragile. 176(63.8%) patients experienced intraoperative complications. Postoperative complications were detected in 115(41.7%). The sarcopenia, frailty, and higher surgical risk classifications are increased intraoperative and postoperative complications (4.7, 4.1, 4 and 3.7, 6.4, 3.9 fold, respectively). Length of stay hospital (6.5 and 5 days) and intensive care unit (21 and 19 days), intraoperative (91.4% and 100%) and postoperative complication (81.4% and 87.2%) was higher sarcopenia and frailty (p<0.001).

Conclusion: Intraoperative and postoperative complications were observed higher in frail and sarcopenic patients. Evaluation of frailty and sarcopenia in over 65 years at preoperative period can be helpful for prediction to risk of intraoperative and postoperative complications.

Keywords: Intraoperative Complications; Frailty; Mortality; Postoperative Complications; Sarcopenia.

INTRODUCTION

Due the aging of the population, the frequency of surgical interventions in the elderly population is increasing. People older than 65 years comprise the majority of healthcare expenditure, and more than 40% of all surgical procedures involve geriatric patients (1,2). The prevalence of frailty has been reported to be between 4% and 59% in elderly populations (3).

Fried et al. defined vulnerability as a clinical syndrome with a biological basis due to the depletion of physiological reserves of multiple organ systems with age (4,5). Frailty is commonly associated with physical inactivity, smoking, poverty, cardiovascular diseases, and cancer (4). Surgical procedures are a source of acute stress. Such stress can lead to complications in the elderly population. As a result, frail individuals have a high risk of perioperative complications and delayed recovery (4,6,7). Frailty can assess with Frailty index which is first described by Fried et al (5).

Sarcopenia, which may be the cause or result of frailty, refers to the progressive loss of muscle mass and strength. Frailty increases after the seventh decade due to inactivity and increased muscle mass loss, which is associated with the loss of functional independence in many cases. In addition to fragility, sarcopenia is associated with immobilization, trauma, decreased physical strength, a weakened immune system, postoperative morbidity, and an increased mortality risk (5, 8, 9). Sarcopenia can be diagnosed based on low muscle quality or quantity using a number of methods. These include a simple 5-item questionnaire (SARC-F) and grip strength, chair stand, and timed-up-andgo tests. Muscle quality and quantity can also be assessed using dual-energy X-ray absorptiometry, bioelectrical impedance analysis, ultrasound (USG), computer tomography, or magnetic resonance imaging (10). USG is a practical and non-invasive bedside technique for the assessment of muscle thickness, fascicle length, cross-sectional area, echogenicity, and pennation angle. A systematic review concluded that USG is a reliable method for assessing muscle size in elderly individuals and aids in the diagnosis of sarcopenia (11). The effect of sarcopenia on postoperative complications has presented as independent risk factor (11,12).

In this prospective observational study, we aimed to evaluate the association between fragility, sarcopenia and perioperative complications in an elderly population.

MATERIALS AND METHOD

Our study included patients aged \geq 65 years who underwent elective surgery at our university hospital between November 2021 and May 2022. Ethics Committee approval was obtained on (21 October 2021; No:156). Written informed consent was obtained from all the patients. The exclusion criteria were patients younger than 65 years, patients where local anesthesia was administered, and patients who underwent emergency surgery. The same anesthesia resident performed all the preoperative assessments of the patients included in this study at the preoperative care unit. Preoperative patient data were obtained from the hospital database. The demographic data (sex, age, weight, height, body mass index [BMI]) of all patients were recorded. The type of operation, diagnosis, concomitant diseases, previous operations, surgical risk class, and American Society of Anesthesiology Physical Risk Classification (ASA) were recorded in the preoperative care unit. Marital status, income level, education level, cognitive impairment, and household status such as living alone were recorded. All patients were evaluated using the Fried Frailty Index to diagnose frailty (5). If the Frailty index score was 1 or 2, it was defined as prefrail, and if it was 3 or above, it was defined as frail.

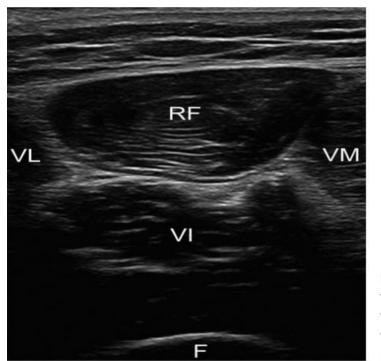
All patients underwent USG assessment (Esaote MyLabtmSix) in B mode for sarcopenia using a linear high-frequency probe, and rectus femoris muscle



measurements were made in the preoperative care unit. Rectus femoris muscle height and surface area were measured in all patients in the preoperative care unit. All measurements were performed by the same anesthesia resident to prevent interrater variation. Each measurement was performed three times and the average measurement was recorded. USG assessments and measurements were performed with the patient in a supine position, with both hips and knees in full extension, and at rest. The midpoint of the distance between the lateral epicondyle and trochanter major of the femur was determined as the reference point for measurements in all patients. A linear USG probe was placed in the transverse plane along the upper part of the thigh. A large amount of gel was applied to minimize muscle compression and avoid pressure on the muscle. Cross-sectional images of the rectus femoris muscle were obtained. After the

images were obtained, rectus femoris thickness and cross-sectional area measurements were performed (Figure 1).

To ensure that the preanesthetic assessment time was as short as possible, we did not assess muscle strength, and sarcopenia was defined based on low muscle mass, as determined using USG. To determine the cut-off value for the diagnosis of sarcopenia, rectus femoris muscle measurements with USG were obtained from 50 ASA I-II patients aged 20-40 years who were not recruited to the study population. Based on these measurements, we determined the cut-off values for defining sarcopenia. Which values below 3.36 cm^2 and 4.56 cm^2 for the rectus femoris cross-sectional area and, 11.11 mm and 11.9 mm for rectus femoris thickness in females and males, respectively, assumed as sarcopenia. This method was previously described by Kara et al (13).



RF: Rectus femoris
VL: Vastus lateralis
VI: Vastus intermedius
VM: Vastus medialis
F: Femur

Figure 1. Ultrasound Image of Rectus Femoris

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Flow Diagram

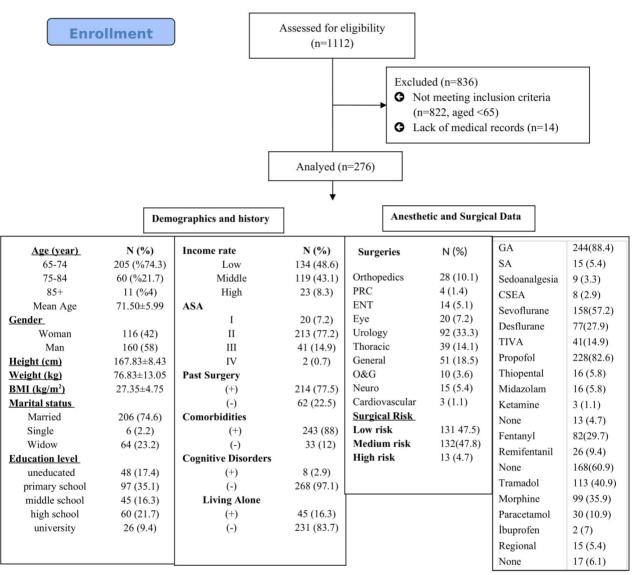


Figure 2. Flow diagram

Regarding the perioperative period, data on the type of anesthesia, duration of anesthesia, complications, and drugs were obtained from the anesthesia charts and the hospital's information record system. Patients' medical records during the postoperative period (postoperative care unit and/or 30th day of surgery) were searched, and complications (hypoxemia, hypotension,



hypertension, bradycardia, tachycardia, arrhythmias, reintubation, bleeding, etc.), discharge time, and intensive care unit admission were recorded.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS 23.0) program was used in the statistical analysis of the data. Categorical measurements are presented as numbers and percentages, and continuous measurements as mean and SD (median and minimum-maximum where appropriate). Chisquare and Fisher's exact tests were used to compare categorical data. The independent Student's t-test was used for normally distributed parameters and Mann-Whitney U test was used for non-normally distributed parameters. Logistic regression analysis was conducted to determine relationships between the variables.

RESULTS

A total of fourteen (1112) patients underwent surgery between November 2021 and May 2022 in our hospital, and 290 patients were aged \geq 65 years. A total of 290 patients were recruited for the study during the designated time period, but 14 patients were excluded because of a lack of medical records. A total of 276 patients aged \geq 65 years who underwent elective surgery were included in the study. The patient demographics, medical history, anesthetic and surgical data are shown in Flow diagram (Figure 2). A total of 176 patients (63.8%) experienced intraoperative complications, 115 patients (41.7%) experienced postoperative complications. Hypotension was the most common intraoperative complication (N=100, 38 %). Sarcopenia was detected in 98 (35.5%), 89 (32.2%), and 70 (25.4 %) patients according to the cross-sectional area, RF thickness, and both (crosssectional area and RF thickness), respectively. Frailty was detected in 151 patients (54.7%) [112 patients (74.2%) pre-frail and 39 patients (25.8%) frail. (Table 1). Relation between sarcopenia, frailty and complications are shown in Table 2. The hypotension (67.1 %), tachycardia (21.4%), arrhythmia (25.7%), hypoxia (22.9%), bleeding (31.4%) and ST changes (10%) risks are increased at intraoperative period and hypotension (22.9%), tachycardia (34.3%), arrhythmia (18.6%), hypoxia (40%), ST changes (18.6%) and exitus (10%) risks are increased during postoperative period in sarcopenic patients. Hypotension (74.4%) and arrhythmia (35.9%) risks increased during the intraoperative period and hypotension (38.9%), bradycardia (2.9%), arrhythmia (25.6%), hypoxia (53.8%), and ST changes (20.5%) increased during the postoperative period in Intraoperative complications frail patients.

	N (%)
Sarcopenia	
By cross-sectional area	98 (35.5)
By RF thickness	89 (32.2)
By both cross-sectional area and RF thickness	70 (25.4)
Frailty	151 (54.7)
Pre-frail	112 (74.2)
Frail	39 (25.8)

Table 1. Sarcopenia and Frailty

Table 2. Sarcopenia, Frailty and Complications

	Sarcopenia			Fr			
	(-) (n=206)	(+) (n=70)	Р	Pre-Frail (n=112)	Frail (n=39)	Р	
Intraoperative Complications	112 (54.4)	64 (91.4)	<0.001	87 (77.7)	39 (100)	0.001	
Intraoperative Complications							
Hypotension	58 (28.2)	47 (67.1)	<0.001	53 (47.3)	29 (74.4)	<0.001	
Hypertension	37 (18)	14 (20)	0.704	32 (28.6)	6 (15.4)	0.102	
Bradycardia	17 (8.3)	7 (10)	0.654	10 (8.9)	6 (15.4)	0.259	
Tachycardia	14 (6.8)	15 (21.4)	0.001	14 (12.5)	8 (20.5)	0.222	
Arrhythmia	15 (7.3)	18 (25.7)	<0.001	11 (9.8)	14 (35.9)	<0.001	
Нурохіа	24 (11.7)	16 (22.9)	0.021	23 (20.5)	13 (33.3)	0.106	
Bleeding	25 (12.1)	22 (31.4)	<0.001	24 (21.4)	14 (35.9)	0.073	
ST change	1 (0.5)	7 (10)	<0.001	4 (3.6)	4 (10.3)	0.108	
Postoperative Complications	58 (28.2)	57 (81.4)	<0.001	64 (57.1)	34 (87.2)	0.001	
Postoperative Complications							
Hypotension	9 (4.4)	16 (22.9)	<0.001	9 (8.0)	15 (38.9)	<0.001	
Hypertension	29 (14.1)	14 (20.0)	0.238	25 (22.3)	8 (20.5)	0.814	
Bradycardia	-	2 (2.9)	0.064	-	2 (2.9)	0.016	
Tachycardia	19 (9.2)	24 (34.3)	<0.001	26 (23.2)	13 (33.3)	0.214	
Arrhythmia	3 (1.5)	13 (18.6)	<0.001	6 (5.4)	10 (25.6)	<0.001	
Нурохіа	27 (13.1)	28 (40)	<0.001	29 (25.9)	21 (53.8)	0.001	
Bleeding	2 (1.0)	-	0,408	1 (0.9)	1 (2.6)	0.432	
ST change	1 (0.5)	13 (18.6)	<0.001	6 (5.4)	8 (20.5)	0.005	
Atelectasis	15 (7.3)	10 (14.3)	0.078	15 (13.4)	7 (17.9)	0.487	
Exitus	3 (1.5)	7 (10.0)	0.003	5 (4.5)	5 (12.8)	0.071	
Length of stay in hospital [Med (25-75)]	4 (2-6)	6,5 (3-14)	<0.001	3 (2-4)	5 (3-8)	<0.001	
Intensive Care Unit Admission	13 (6.3)	21 (30)	<0.001	15 (13.4)	19 (48.7)	<0.001	
	Others (n=239)	Both Sarcopenic and Frail (n=37)		р			
Intraoperative Complications	139 (58.2)	37	(100)	<0.001			
Postoperative Complications	82 (34.3)	33 (89.2)	<0.001			

Chi-square test and Fisher exact test were used

.



Complications											
	Intraoperative Complications						Postoperative Complications				
	β		Εχρ (β)	95% CI	95% CI EXP (β)	β	Sig	Εχρ (β)	95% CI EXP(β)		
		Sig		Upper	Lower				Upper	Lower	
Sarcopenia	1.552	0.001	4.719	1.958	11.375	1.312	0.000	3.712	1.814	7.596	
Frailty	1.418	0.000	4.130	2.197	7.761	1.858	0.000	6.408	3.252	12.627	
Age	-0.004	0.908	0.996	0.936	1.061	0.011	0.707	1.011	0.953	1.073	
Surgical risk	1.389	0.000	4.012	2.189	7.354	1.366	0.000	3.919	2.093	7.338	

Table 3.	Relation between Sarcopenia, Frailty, Age and Surgical Risk with Intraoperative and Postoperative
	Complications

were observed in all of both sarcopenic and frail patients (N=37), while postoperative complications were observed in 33 patients (89.2%) (p<0.001 and p<0.001, respectively) (Table 2), and there was a statistically significant relationship between sarcopenia, frailty, and surgical risk with intraoperative and postoperative complications in logistic regression analysis. In patients with sarcopenia, the risk of intraoperative complications is increased by 4.79 times, the risk of postoperative complications is increased by 3.71 times, in patients with frailty, the risk of intraoperative complications is increased by 4.13 times, the risk of postoperative complications is increased by 6.40 times, in patients with medium-high surgical risk, the risk of intraoperative complications is increased by 4.01 times, and the risk of postoperative complications is increased by 3.91 times (Table 3). The age did not affect to the intraoperative and postoperative complications in patients aged \geq 65 years.

DISCUSSION

In our study, we assessed patients aged \geq 65 years in the preoperative period in terms of sarcopenia and fragility and associated intra and postoperative complications. The results revealed that both frailty and sarcopenia were related to intraoperative and postoperative complications. When we assessed both rectus femoris muscle thickness and cross-sectional area, we found that 70 patients (25.4%) had sarcopenia. In a recent article on 160 cases, Yi et al. concluded that the measurement of rectus femoris thickness and echogenicity on USG was useful in demonstrating sarcopenia (14). In a study published in 2020, Kan et al. reported that the prevalence of sarcopenia among geriatric patients in Turkey was 26% (15). We found higher rates of sarcopenia in our study and detected sarcopenia in. All patients aged > 85 years were sarcopenic.

We determined that a low level of education, low-income level, presence of cognitive impairment, and living alone were significant risk factors for the development of sarcopenia. These risk factors are likely linked to poor nutritional status, resulting in sarcopenia. In our study, the rate of sarcopenia development was 21% and 26% in women and men, respectively. This result was consistent with the literature (16).

In a prospective study of 255 patients who underwent gastrointestinal surgery, Wang et al. assessed sarcopenia preoperatively based on various factors, such as lumbar skeletal muscle index, hand grip strength, and walking speed, and detected sarcopenia in 32 (12%) patients (17). They found a significant correlation between sarcopenia and low BMI, preoperative serum albumin, and hemoglobin levels in these patients. In their study, the postoperative complication rates, length of hospital stay, and hospital costs were higher in the patients with sarcopenia. In our study, the incidence of postoperative complications (hypotension, tachycardia, arrhythmia, and hypoxia) was significantly higher in patients with sarcopenia.

Previous research has been shown that sarcopenia is associated with a prolonged postoperative recovery period and hospital stay time, in addition to increased morbidity and mortality (18). Similarly, in our study, the postoperative mortality rate in patients with sarcopenia was significantly higher. In the present study, sarcopenia was detected more frequently in medium- or high-risk patients, according to the surgical risk classification.

Using Fried's frailty index, we detected frailty in 151 (54.7%) patients, with 112 (74.2%) patients classified as prefrail and 39 (25.8%) patients classified as frail. Hoover et al. reported frailty in 11– 25% of individuals older than 65 years and in 50% of individuals older than 85 years (19). Bandeen et al. conducted a comprehensive population survey of frailty in the U.S. population in 2011 that included over 7,000 individuals aged 65–90 years (20). In their study, 15.3% of the participants were frail, 45.5% were prefrail, and 39.2% were healthy. These results were consistent with the incidence of frailty observed in the present study.

Khandelwal et al. examined the relationship between frailty, mortality risk, and length of stay in hospitalized patients (N = 250) (21). They determined that 83 patients (33.2%) were frail and that the risk of mortality and prolonged hospitalization were higher among frail than nonfrail patients (21). In a meta-analysis consisting of 23 studies examining the relationship between frailty and postoperative outcomes, frailty was associated with increased postoperative complications, mortality, and prolonged hospitalization (13). In our study, the rate of intensive care hospitalization was higher in frail patients than prefrail patients. In addition, the frail group had a significantly higher mortality rate in the

postoperative period than the prefrail and nonfrail groups did.

In a study by Polidoro et al., atrial fibrillation was associated with frailty, independent of age, sex, and some common systemic diseases (22). In our study, arrhythmia in the postoperative period was higher in the frail group than in the prefrail and nonfrail groups. Thirty-three (89.2%) of 37 patients who were both sarcopenic and frail developed postoperative complications. Furthermore, sarcopenia, frailty, and higher surgical risk classifications increased intraoperative and postoperative complications.

LIMITATIONS

Our study has some limitations. First, this was a crosssectional study, and data were obtained only from patients undergoing elective surgeries. Therefore, the patient population was heterogeneous. A subsequent study could perhaps include patients undergoing emergency surgeries or specific surgical interventions. In addition, with the aim of shortening the preanesthetic evaluation time, we used only USG to evaluate sarcopenia. Clearly, a diagnosis of sarcopenia requires an assessment of muscle strength. To confirm the diagnosis of sarcopenia, other methods, such as dual-energy X-ray absorptiometry or magnetic resonance imaging, would have been needed. The diagnosis of sarcopenia based on muscle mass only using USG is a limitation of our study. However, USG is a practical, noninvasive method for the rapid prediction of sarcopenia in daily practice.

CONCLUSION

The assessment of sarcopenia with bedside USG is a very easy and useful method for daily practice. In this study, we assessed frailty and sarcopenia preoperatively in older patients and found that both sarcopenic and frail individuals were at risk for postoperative complications. We assumed that the detection of sarcopenia and frailty in



the preoperative period could provide better perioperative conditions and prevent complications in elderly patients undergoing surgical procedures.

REFERENCES

- Etzioni DA, Liu JH, Maggard MA, Ko CY. The aging population and its impact on the surgery workforce. Ann Surg 2003;238(2):170-7. (DOI: 10.1097/01. SLA.0000081085.98792.3d.).
- Zodet M. Characteristics of Persons with High Health Care Expenditures in the U.S. Civilian Noninstitutionalized Population, 2014. 2016 Oct. In: Statistical Brief (Medical Expenditure Panel Survey (US)) [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2001–. STATISTICAL BRIEF #496. PMID: 28422466. Available from <u>https://www.ncbi.nlm.nih.gov/books/NBK425790/pdf/Bookshelf_NBK425790.pdf</u> Accessed: 04.12.2023.
- Sabine Rohrmann. Epidemiology of Frailty in Older People. Adv Exp Med Biol 2020;1216:21-7. (DOI: 10.1007/978-3-030-33330-0_3).
- Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. J Surg Res 2013;183(1):104-10. (DOI: 10.1016/j.jss.2013.01.021).
- Fried LP, Tangen CM, Walston J et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56(3):146-56. (DOI: 10.1093/ gerona/56.3.m146).
- 6. Amrock LG, Deiner S. The implication of frailty on preoperative risk assessment. Curr Opin Anaesthesiol 2014;27(3):330-5. (DOI: 10.1097/ ACO.000000000000065).
- Birkelbach O, Mörgeli R, Spies C et al. Routine frailty assessment predicts postoperative complications in elderly patients across surgical disciplines–a retrospective observational study. BMC Anesthesiol 2019;19(1):204. (DOI: 10.1186/s12871-019-0880-x).
- Hubbard RE, Story DA. Patient frailty: the elephant in the operating room. Anaesthesia 2014;69(1):26-34. (DOI: 10.1111/anae.12490).
- Cruz-Jentoft AJ, Baeyens AJ, Bauer JM et al. European Working Group on Sarcopenia in Older People: Sarcopenia: European consensus on definition and diagnosis. Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39(4):412-23. (DOI: 10.1093/ageing/afq034).

- Zhuang CL, Huang DD, Pang WY et al. Sarcopenia is an independent predictor of severe postoperative complications and long-term survival after radical gastrectomy for gastric cancer: analysis from a largescale cohort. Medicine (Baltimore) 2016;95(13):e3164. (DOI: 10.1097/MD.00000000003164).
- Cruz-Jentoft AJ, Bahat G, Bauer J et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48(1):16–31. (DOI: 10.1093/ ageing/afy169).
- Endo T, Momoki C, Yamaoka M et al. Validation of skeletal muscle volume as a nutritional assessment in patients with gastric or colorectal cancer before radical surgery. J Clin Med Res 2017;9(10):844-59. (DOI: 10.14740/jocmr3129w).
- Kara M, Kaymak B, Ata AM et al. STAR—sonographic thigh adjustment ratio: a golden formula for the diagnosis of sarcopenia. Am J Phys Med Rehabil 2020;99(10):902-8. (DOI: 10.1097/ PHM.000000000001439).
- 14. Yi J, Shin Y, Hahn S, Lee YH. Deep learning based sarcopenia prediction from shear-wave ultrasonographic elastography and gray scale ultrasonography of rectus femoris muscle. Sci Rep 2022;12:3596. (DOI: 10.1038/s41598-022-07683-6).
- Kan Ü, Bulut EA, Soysal P, Işık AT. The effect of sarcopenia on balance and gait functions in older adults. Medical Journal of İzmir Hospital 2020;24(1):1-8. (in Turkish)
- Castillo EM, Goodman-Gruen D, Kritz-Silverstein D, Morton DJ, Wingard DL, Barrett-Connoret E. Sarcopenia in elderly men and women: the Rancho Bernardo study. Am J Prev Med 2003;25(3):226-31. (DOI: 10.1016/s0749-3797(03)00197-1).
- 17. Wang SL, Zhuang CL, Huang DD et al. Sarcopenia adversely impacts postoperative clinical outcomes following gastrectomy in patients with gastric cancer: a prospective study. Ann Surg Oncol 2016;23(2):556-64. (DOI: 10.1245/s10434-015-4887-3).
- Jones K, Gordon-Weeks A, Coleman C, Silva M. Radiologically determined sarcopenia predicts morbidity and mortality following abdominal surgery: a systematic review and meta-analysis. World J Surg 2017;41(9):2266-79. (DOI: 10.1007/s00268-017-3999-2).
- Hoover M, Rotermann M, Sanmartin C, Bernier J. Validation of an index to estimate the prevalence of frailty among community-dwelling seniors. Health Rep Sep 2013;24(9):10-7.

- Bandeen-Roche K, Seplaki CL, Huang J et al. Frailty in older adults: a nationally representative profile in the United States. J Gerontol A Biol Sci Med Sci 2015;70:1427-34. (DOI: 10.1093/gerona/glv133).
- Khandelwal D, Goel A, Kumar U, Gulati V, Narang R, Dey AB. Frailty is associated with longer hospital stay and increased mortality in hospitalized older patients. J Nutr Health Aging 2012;16(8):732-5. (DOI: 10.1007/s12603-012-0369-5).
- 22. Polidoro A, Stefanelli F, Ciacciarelli M, Pacelli A, Di Sanzo D, Alessandri C. Frailty in patients affected by atrial fibrillation. Arch Gerontol Geriatr 2013;57(3):325-7. (DOI: 10.1016/j.archger.2013.04.014).