SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Prevalence of sarcopenia and assessment of the Sarcopenia Quality of Life Questionnaire (SarQoL) among community-dwelling, outpatient, postmenopausal Hungarian women

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The Examination takes place at the Library of Laboratory Medicine Institute, IVD Center, University of Debrecen, 2024. 02. 09. 11:00.

Head of the **Defense Committee**:	Prof. Dr. József Balla, PhD, DSc, MHAS
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The PhD Defense takes place at the Lecture Hall of Building A, Department of Internal Medicine, University of Debrecen, 2024. 02. 09. 13:00.

INTRODUCTION

BACKGROUND

Ageing is a natural part of life. According to the World Health Organization (WHO), the percentage of people over 60 could increase by at least 1.5 times by 2050. This means we are living in an ageing population. As we age, different changes take place in a person's body. It is therefore important to take care of mental and physical health not only at a young age but also in old age. The best known changes are those involving loss of bone mass (osteoporosis) and changes affecting the musculoskeletal system. Age-related changes in musculoskeletal health are called sarcopenia. Rosenberg, in his study of the origin of the term sarcopenia, cited the Greek words sarx and penia, meaning flesh and loss, to reflect an age-related decline in lean body mass, manifested in changes in mobility, food intake and nutritional status, general independence and a decline in quality of life. Therefore, sarcopenia is a serious problem in the older age population. It is a worldwide known condition, with a prevalence of between 0.9% and 53.5% depending on the definition used in various studies. In China, the prevalence of sarcopenia in women and men aged over 60 years in the community is 12.5% and 8.5%, respectively. Ez az arány hasonlít más országokban talált adatokhoz, ahol 15-17% a kapott arány. This rate is similar to that found in other countries, where the rate is 15-17%. The prevalence rate of 21% for older people over 85 years also shows no significant increase. Sarcopenia is a musculoskeletal disorder with a poor prognosis and a steady worsening, with loss of muscle tone and quality, and a deterioration in strength and physical performance. Sarcopenia was originally described as age-related muscular atrophy in the elderly (primary sarcopenia). Today, muscle atrophy caused by various pathologies (secondary sarcopenia) also occurs at a younger age.

Sarcopenia has its own code in the International Classification of Diseases (ICD code: M62.84). The definition of sarcopenia has since evolved to focus on muscle function, defined

by muscle strength, physical performance, which is an effective predictor of relevant clinical outcome, rather than muscle mass. The prevalence of sarcopenia increases with age. Muscle mass and muscle strength, like bone density (up to the 30s), increase gradually in youth, reaching a peak in the 40s and then gradually decreasing after the age of 50. Muscle mass decreases by 0.5-2% and muscle strength by 1.5-5% each year; and this process accelerates after the age of 65, and after the age of 80 muscle mass reaches only 40% of its previous maximum.

PATHOPHYSIOLOGY

Skeletal muscle accounts for 30-40% of total body mass and 75% of protein. The striated muscles are composed of postmitotic multinucleated myofibrils of muscle cells. Satellite cells of the basal lamina play an important role in regeneration. These stem-like cells serve both for renewal and for further proliferation and differentiation. The number of muscle cells depends on the balance between the building and breakdown of muscle proteins, with increasing catabolism leading to a reduction in muscle mass with age. With ageing, the muscle's satellite cells are progressively depleted, resulting in impaired regeneration, increased insensitivity to stimuli to increase muscle mass, altered gene expression, reduced insulin sensitivity and impaired neuromuscular transmission.

THE IMPORTANCE OF SARCOPENIA

Maintaining the health and well-being of older people is a major challenge, and in this context, general changes in the musculoskeletal system play an important role. Sarcopenia is associated with a number of comorbidities that have a significant impact on public health. Consequences of sarcopenia include high mortality, increased risk of falls, prolonged hospitalisation, increased risk of fractures, reduced mobility and physical function, and poorer quality of life. The United Nations (UN) estimates that 985 million women worldwide were aged ≥50 years

in 2020, and this number is expected to rise to 1.65 billion by 2050. The consensus in Hungary in 2011 was that 2 179 606 women were aged ≥50 years (21.9% of the population). The latest data for 2022 puts this number at 2 189 456, representing 22.57% of the total population. This population can be considered postmenopausal, as menopause shows little variation in the onset date in human populations, being around the age of 50, and has remained fairly stable in developed societies over the last 100 years. Studies suggest that the decline in estrogen levels during menopause may play a role in the loss of lean body mass. Furthermore, postmenopausal women with sarcopenia also have a poorer quality of life in a recent study by Cevei and colleagues. For women, the increased number of falls due to sarcopenia, together with osteoporosis, which is also present in a high percentage, greatly increases the risk of fractures, including femoral neck fractures, and the serious consequences of which are increased mortality rates.

DIAGNOSIS OF SARCOPENIA

In the past, the diagnosis of sarcopenia was hampered by the lack of a widely accepted clinical definition. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) developed a definition to provide a framework for the diagnosis of sarcopenia. The definition was refined in 2019 and includes the assessment of muscle strength, muscle mass and physical performance within a well-defined algorithm. Although the EWGSOP2 consensus provides an exhaustive list of methods, the determination of handgrip strength is recommended for the assessment of muscle strength, dual-energy X-ray absorptiometry (DXA) for the determination of muscle mass, and gait speed for the determination of physical performance.

THE SARQOL QUESTIONNAIRE

Historically, mortality has been the primary indicator of public health. Modern medical innovations have significantly increased life expectancy, so medical science is more focused

on quality of life (QoL) and therefore there is a need to objectively assess it. Subsequently, the term QoL has gained increasing currency in healthcare. As a consequence, the focus has been on creating and testing tools to measure health-related QoL. The perception of health has undergone an intensive change, where the concept has been shifted from the traditionally favoured negative health risks and their consequences to a predominantly positive assessment of QoL.

The World Health Organization defines health-related quality of life as 'an individual's perception of his or her position in life as influenced by the culture, values, goals, expectations, patterns and relationships of his or her life-space. It is a broad concept, encompassing in complex ways an individual's physical health, psychological well-being, degree of independence, social relationships, personal beliefs and relationship to significant phenomena in the environment." It can be seen from the wording that an adequate quality of life is not merely the absence of illness or frailty, and that individuals with sarcopenia are likely to experience a decline in quality of life. Until the 2015 effort by Beaudart and colleagues, QoL of subjects with sarcopenia was assessed purely on the basis of generic questionnaires, which clearly fail to capture the ambiguous effects of the condition. Beaudart et al. formulated the concept of determining QoL in patients with sarcopenia (SarQoL) based on basic procedures for developing QoL questionnaires, expert recommendations and studies. SarQoL was developed and validated in French by Beaudart and colleagues. To date, the questionnaire has been translated into 30 languages and made available on the Internet at www.sarqol.org. In addition, its English, Romanian, Dutch, Polish, Hungarian, Lithuanian, Russian, Greek, Ukrainian, Serbian, Spanish, Korean, Chinese, Korean and Turkish versions have been validated and its psychometric properties evaluated.

The Hungarian translation of the original SarQoL questionnaire was completed by Hodinka and colleagues in 2018 and validated by Greenick and colleagues in 2022.

AIMS

Aware that there is a gap in our knowledge of the prevalence of sarcopenia in Hungary, one of the aims of the present study was to determine the prevalence of sarcopenia in a postmenopausal Hungarian cohort using the EWGSOP2 consensus recommendation. And since the study included the completion of the Hungarian version of the SarQoL questionnaire, we separately examined and evaluated the discriminative power, internal consistency and floor, ceiling effect of the questionnaire.

METHODS

POPULATION STUDIED

Women attending the Regional Osteoporosis Centre of the Department of Obstetrics and Gynaecology, Faculty of General Medicine, University of Debrecen for routine bone densitometry were eligible to participate in this cross-sectional study. A total of 100 women living in the community who met the inclusion criteria for postmenopausal status based on self-report, were ≥ 50 years of age, and gave written informed consent were recruited. Self-reported menopause was defined as continuous amenorrhea for at least 12 months after the last menstrual period. On arrival at the outpatient clinic, patients were verbally informed about the study initiation, given a brief summary of the importance of sarcopenia, and detailed information about the different study procedures. The study target of 100 patients was met in 3 months, between January and March 2019. None of the women refused to participate in the study. The SarQoL questionnaire was administered to the previously studied cohort of sarcopenia patients to examine its psychometric properties. The study was conducted in

accordance with the Declaration of Helsinki and approved by the Ethics Committee of the University of Debrecen (approval no. 5314-2019).

TEST PROCEDURES

The study started with a self-completed 5-item questionnaire (SARC-F), which included questions on strength, gait, standing up from a chair, stairs and falls, followed by assessments of muscle strength, muscle volume and physical performance.

SARC-F QUESTIONNAIRE

The SARC-F questionnaire is recommended by EWGSOP2 as a tool for the detection of sarcopenia, where patients answer questions about the suspicious signs of sarcopenia. The SARC-F questionnaire, consisting of 5 items, is a screening tool for the risk of sarcopenia, providing the patient's subjective assessment of his/her own fitness, ability to walk, stand up from a chair, climb stairs and answers about the presence or absence of falls that may have occurred in the past. Malmstrom et al. describe the SARC-F scale as having a maximum score of 10 (each of the 5 components can be scored from 0 to 2; and in total, 0 is the best and 10 is the worst), with a score of ≥4 being an indication for diagnostic testing to investigate sarcopenia. The strength is assessed by asking respondents how much difficulty they have lifting or carrying roughly 4.5 kg, or 10 pounds (0 = no difficulty, 1 = some difficulty, 2 = very much or unable). Walking ability is assessed by noting the difficulty the respondent has in walking across a room and the need for assistance or aids (0 = no difficulty, 1 = some difficulty, and 2 = great difficulty, use of aids, or need for personal assistance). Getting out of a chair refers to how difficult it is to get up from a chair or bed and whether they need help or aids to do so (0 = no difficulty, 1 = some difficulty, and 2 = very difficult, use of aids, or need help). Stair climbing is defined by asking how difficult it is for the respondent to climb 10 steps (0 = no difficulty, 1 = some difficulty, and 2 = great difficulty or unable to do so). For falls, a report

of a fall that occurred four or more times in the previous year is scored as 2, a fall that occurred 1-3 times a year is scored as 1, and if there were no falls, it is scored as 0.

ASSESSMENT OF MUSCLE STRENGTH

Muscle strength was measured using Hand Grip Strength (HGS), which was measured using a Jamar technologies hydraulic hand dynamometer (JLW Instruments, Chicago, IL, USA / Sammons Preston Rolyan, Bolingbrook, IL) as described by Roberts et al. Briefly, the patient is comfortably positioned in a chair with fixed legs and arms and backrest, with forearm resting on the armrest of the chair and wrist with thumb facing upwards over the end of the armrest of the chair. The use of the dynamometer is demonstrated and the importance of recording the best result in a tight grip is stressed. The instrument is held comfortably in the patient's right hand, with the thumb positioned around one side of the handle and the fingers around the other side. To counteract the effect of gravity, the examiner rests the palm of the hand on the base of the instrument, ensuring that the movement of the instrument is not restricted. A firm squeeze shall be applied until the needle is no longer elevated. The grip strength shall be read on the outer dial in kilograms. Repeat the measurement with the left hand, with two further measurements with both hands, and record the highest of the six readings and the dominant hand.

ASSESSMENT OF MUSCLE MASS

A whole-body dual-energy X-ray absorptiometry study was performed using a LUNAR Prodigy (GE-Lunar Corp., Madison, WI, USA) densitometer with the assistance of a trained DXA technician to assess fat mass, lean muscle mass, and bone mass in different regions. Limb skeletal muscle mass (ASM = limb lean body mass - limb bone mass) was calculated as the sum of lean muscle mass of the arms and legs (all four limbs), assuming that all non-fat and non-bone tissue is skeletal muscle. As the EWGSOP2 criteria do not make any

recommendation for adjustment of ASM by body size, height, ASM (<15 kg) alone was used to establish a diagnosis of sarcopenia. To determine the limb skeletal muscle mass index (ASMI), the muscle masses of the four limbs of the individual were summed, divided by the square of the height and converted to kg/m2. We then used a reference cut-off value (ASMI<5.5 kg/m2) to determine the presence of sarcopenia. In addition to this height-matched index, we can also use indices matched to body mass (skeletal muscle mass [kg]/body mass [kg]) or body mass index (skeletal muscle mass [kg]/body mass index (body mass [kg]/body height [m]2)).

ASSESSMENT OF PHYSICAL PERFORMANCE

Physical performance was assessed using the 4-Metre Gait Speed test (4MGS). Patients walked 4 metres on a straight, clearly marked track at their usual pace, using a walking stick or walker if used regularly, and the elapsed time was measured with a stopwatch. The speed was the distance covered divided by the time measured by the stopwatch. According to the 2019 definition of sarcopenia, patients with low muscle strength are diagnosed with probable sarcopenia, sarcopenia can be detected by further documentation of low muscle strength and low muscle volume, and sarcopenia is considered severe if the patient has low muscle strength, low muscle volume and low physical performance.

SARQOL

The SarQoL questionnaire consists of 22 questions, comprising a total of 55 individual items, which are rated on a 4-point Likert scale. The questionnaire is designed to give a maximum score of 100, with higher scores reflecting a better quality of life. The 55 items are grouped into seven separate domains, from domain 1 to domain 7. Each domain addresses the following separate characteristics: domain 1 - physical and mental health; domain 2 - physical activity; domain 3 - body composition; domain 4 - functionality; domain 5 - activities of daily living; domain 6 - leisure activities; domain 7 - fears. The questionnaire is a self-administered

questionnaire designed to be completed in 10 minutes. After registration, free personalised access is available and, once answers have been entered in the dedicated fields on the online platform, overall and domain-specific scores are calculated. All completed questionnaires and calculated scores are stored and can be retrieved on demand. The Hungarian version of the questionnaire was used in our cohort. The psychometric properties were checked by discriminative power analysis, internal consistency assessment, and floor and ceiling effect assessment. As suggested by Beaudart et al, the discriminative power analysis was performed on the entire study population (n=100), and the latter two analyses were performed only on those with a diagnosis of sarcopenia according to the EWGSOP2 definition (n=31). For the discriminative power analysis of the questionnaire, we assumed that the score obtained from the SarQoL questionnaire was higher for subjects without sarcopenia than for subjects with sarcopenia. Correlation analysis was performed between the overall and domain scores of the SarQoL questionnaire and the limb skeletal muscle mass of individuals with sarcopenia. The homogeneity of the SarQoL questionnaire, i.e. its internal consistency, was measured using the Cronbach's alpha coefficient. The lower and upper bounds for the overall and domain SarQoL scores were set when the subject scored the lowest or highest, respectively. Lower and upper bounds of more than 15% between the scores obtained by subjects were considered significant.

STATISTICAL METHODS

Descriptive statistics are given as median and range for all continuous variables. For correlation analysis, Spearman's correlation coefficient was calculated. Spearman ϱ values above 0.81, between 0.61 and 0.80, between 0.41 and 0.60, between 0.21 and 0.40 and below 0.20 were rated as excellent, very good, good, acceptable and unsatisfactory. Univariate and multiple regression analysis using the stepwise method was used to determine correlations and independent relationships between parameters. Limb skeletal muscle mass was the dependent variable and SARC-F, body weight, body height, body mass index, HGS and GS were the

independent variables. Standardized linear coefficients β were determined to measure the linear correlation between the two parameters. The independent correlation between the dependent and independent variables was indicated by the regression coefficient B (95%CI). Statistical significance was indicated by p-values < 0.05. The normality of the distribution was tested using the Kolmogorov-Smirnov test. The Mann-Whitney U test was performed to assess the difference in SarQoL total and domain scores between patients with and without sarcopenia. Odds ratios (95% CI) calculated by binary logistic regression were used to measure the association between SarQoL questionnaire overall and domain scores and the likelihood of sarcopenia. Cronbach's alpha coefficient was calculated to assess the internal consistency of the SarQoL questionnaire. A Cronbach's alpha coefficient value greater than 0.70 was considered as a high level of internal consistency. Statistically significant difference was considered as $p<0.05$. Analyses were performed using SPSS Statistics software versions 25.0 and 29.0 (IBM Corps., Armonk, NY, USA).

RESULTS

According to the EWGSOP2 definition, the distribution of probable sarcopenia (low muscle strength), sarcopenia (low muscle strength and low muscle volume) and severe sarcopenia (low muscle strength, muscle volume and low physical performance) among the study participants was 36%, 31% and 8% respectively. When comparing study participants with low (<15kg) and normal (≥15kg) ASM, significant differences were found in body weight (57 (41-71) kg versus 67.5 (47-95) kg; $p<0.001$), height (152.5 (141-170) cm versus 158 (146-169) cm; $p<0.001$), body mass index (24.2 (19.2-31. 3) kg/m2 versus 27.5 (18.8-36.5) kg/m2; $p<0.001$), SARC-F questionnaire score (6 (4-9) versus 2 (0-7); $p<0.001$), hand grip strength (12,. 6 (10.9-14.5) kg versus 21.2 (11.1-27.9) kg; $p < 0.001$) and gait speed (1.05 (0.39-1.61) m/s versus 1.11 (0.9-1.61) m/s; $p < 0.001$). All parameters used in the calculation of ASM, i.e. the fat-free mass of

the left upper limb, left lower limb, right upper limb and right lower limb, were statistically significantly lower in those with a limb skeletal muscle mass less than 15 kg. The BMI-adjusted ASM suggested by Cawthon et al. was also significantly lower in those with ASM < 15 kg.

Limb skeletal muscle mass showed a statistically significant correlation with height, body weight, body mass index, SARC-F questionnaire score, HGS and GS. In univariate analysis of the cohort data, participants with lower limb skeletal muscle mass had lower height, weight, body mass index, hand grip strength and gait speed, and higher SARC-F scores. Multiple linear regression analysis showed that height, body weight, HGS and GS were independent predictors of limb skeletal muscle mass.

All study participants (n=100) completed the SarQoL questionnaire. The overall and subdomain median (interquartile range - IQR) were calculated by entering the responses to the SarQoL questionnaire questions on the SarQoL website.

When comparing sarcopenic and non-sarcopenic individuals, the overall SarQoL score was statistically significantly lower (75.3 (62.1-86.3) vs. 83.7 (71.4-92.1); p=0.041) [median(IQR)]. Among the individual domains, D2 (72.2 (55.6-88.9) vs. 86.1 (69.4-97.2); p=0.008) for movement and D5 (78.3 (55.0-88.3) vs. 88.3 (75.8-94.1); p=0.012) for activities of daily living were the two domains out of a total of 7 domains in which statistically significant differences were found between sarcopenic and non-sarcopenic individuals. In addition, the likelihood of sarcopenia was statistically significantly predicted by the total score of the SarQoL questionnaire, the score of the D2 mobility domain of the SarQoL questionnaire and the score of the D5 activities of daily living domain of the SarQoL questionnaire with odds ratios (95% CI) of 0.967 (0.942-0.997), 0.970 (0.948-0.993) and 0.965 (0.940-0.990), respectively.

Sarcopenic patients showed a statistically significant correlation between the total SarQoL score (Spearman ϱ = 0.412) and the D2 domain-movement SarQoL questionnaire score

(Spearman ϱ = 0, 372), between the D3 domain - body composition SarQoL questionnaire score (Spearman ϱ = 0.439) and the D5 domain - activities of daily living SarQoL questionnaire score (Spearman ϱ = 0.372) and the mass of the limb skeletal muscle. The overall Cronbach's alpha of 0.937 indicated high internal consistency of the Hungarian version of the SarQoL questionnaire. The Cronbach's alpha ranged from 0.917 (with the deletion of domain 4 - functionality) to 0.945 (with the deletion of domain 6 - leisure activities). In addition, the scores of all domains showed a statistically significant correlation with the total score, with Spearman's ϱ ranging from 0.529 (domain 6 - leisure activities) to 0.949 (domain 5 - activities of daily living). No sarcopenic subject showed the lowest or highest total score on the SarQoL questionnaire. Consequently, there was neither a downscale nor an upscale attenuation effect. However, for each subdomain, when analysing floor and ceiling effects, there was a significant ceiling effect of 22.6% and 32.3% for domain 3 - body composition and domain 7 - fears, respectively.. A non-significant (<15%) ceiling effect was observed for domain 1 - physical and mental health (9.7%), domain 2 - physical activity (3.2%) and domain 5 - daily living activities (3.2%). No top scale attenuation effect was observed for domain 4 - functionality and domain 6 - leisure activities. No downscaling effect was observed for any of the domains.

DISCUSSION

Following the algorithm detailed by EWGSOP2, in our study 40 (40%) participants were diagnosed with possible sarcopenia based on the results of the SARC-F questionnaire, 36 were diagnosed with probable sarcopenia based on muscle strength, 31 were diagnosed with proven sarcopenia based on muscle mass, and 8 were diagnosed with severe sarcopenia after assessment of physical performance. Although the EWGSOP2 criteria do not explicitly define presarcopenia, those with a SARC-F score ≥4 and ASM <15kg may be classified as

presarcopenic and require close follow-up in the near future. In our study, the criteria for presarcopenia were confirmed in 5 individuals.

The prevalence of sarcopenia has been reported by quite a number of people from different parts of the world. Although the 2010 EWGSOP consensus sets out a system for assessing sarcopenia, it is permissive in that variables are measured using different techniques, which naturally leaves room for variation in the comparison of published prevalence data. Published data on the prevalence of sarcopenia range from 0.9% to 53.5%, the above may explain this large variation, but other factors such as the variable age of study participants and the inclusion or non-inclusion of both sexes in the study cohort may also contribute. It should be mentioned that in addition to the EWGSOP consensus recommendations, the recommendations of the International Working Group on Sarcopenia (IWGS) and the Asian Working Group on Sarcopenia (AWGS) are also used.

The likely limitations of our study are the relatively small number of participants and the non-inclusion of men. The study participants were women who were referred for routine bone densitometry and are therefore not representative of the general population per se. Selection bias arises as postmenopausal women who were reluctant to undergo routine testing may have been excluded from the study and those with musculoskeletal complaints may have been more likely to be included. The reliability of self-assessed menopausal status may be confounded by the subjective recall of the reporting individual, and perhaps an additional assessment of follicle-stimulating hormone levels could have further helped to document more accurately the menopausal status of the women studied. The sample size of the study population was limited to 100 participants. The main objective of the present study was to estimate the prevalence of sarcopenia in a community-based outpatient population in postmenopause. To calculate the sample size in a statistical study, it is necessary to know the expected rates and prevalences in the population, which are derived from previous studies or pilot projects. There are no

Hungarian data on the prevalence of sarcopenia, but since we know from previous studies abroad that in other populations the prevalence of sarcopenia in women in different age groups, although estimated between 0.9-43.1% according to different definitions of sarcopenia, the sample size chosen in the present study would be appropriate for a prevalence estimated at less than 7%. The findings of the present study are, at best, the results of a pilot study, with the limitations that this entails, and advocate the definition of a sample size based on the average population. Additional limitations of the results include the lack of data on potential confounders such as total body fat, physical activity, diet and ethnicity.

Most studies find no significant association between the prevalence of sarcopenia and gender. However, Landi and colleagues reported that men are more often affected than women, and Patel and colleagues reported a higher prevalence of sarcopenia in women than in men. The lack of consensus, as well as the variation in sarcopenia prevalence between men and women across studies, calls for further investigation into the effect of gender on sarcopenia prevalence. The decrease in oestrogen, especially after menopause, is one of the factors that play a role in the loss of muscle mass in women.

In our study, we used the EWGSOP2 recommendations published in 2019. Compared to the EWGSOP, the EWGSOP2 better delineated the recommended techniques for assessing muscle strength, muscle mass and physical performance. For the assessment of muscle mass, we used the DXA technique using limb skeletal muscle muscle mass. As recommended by the EWGSOP2 criteria, ASM was not adjusted for body size in our cohort. However, the use of unadjusted ASM to diagnose sarcopenia limits comparability with previous studies where ASM was adjusted for body height or body mass index.

In 2015, Beaudart and colleagues developed and validated the first sarcopenia-specific quality of life questionnaire for the scientific community. The results of studies validating the SarQoL questionnaires translated into different languages are summarised. It can be seen that cohorts

of different sizes were studied, with varying proportions of subjects with sarcopenia. It can also be seen that only 7 of these studies could meet the requirement of including at least 50 subjects with sarcopenia to assess the internal consistency of the questionnaire and the floor and ceiling effects. Furthermore, there is a lack of uniform application of the definition of sarcopenia across studies. We used the EWGSOP2 definition and applied dual-energy X-ray absorptiometry to determine lean muscle mass. It should perhaps be emphasized that the EWGSOP definition was used when the SarQoL questionnaire was created by Beaudart et al. The EWGSOP2 definition of sarcopenia was published in 2019, and all SarQoL studies conducted thereafter have chosen this updated definition to define sarcopenia in the populations studied, with the exception of Le et al, who used the AWGS 2019 definition.

Surveys would typically require power analysis, but the small number of subjects involved tends to diminish this statistical power, and as the prevalence of sarcopenia in different populations is now being mapped, this hampers the attempts to determine the samle size, the number of individuals to include in robust statistical analyses. A limitation of our study is that, to assess the internal consistency and the lower and upper bound effect of the SarQoL questionnaire, data from only 31 sarcopenia patients were available instead of the recommended 50 subjects.

A decrease in estrogen levels, especially during menopause, may cause a decrease in lean body mass. In light of this, the inclusion of both sexes in sarcopenia studies may dilute the interpretation of the different research questions, and cohorts where both sexes were included to draw conclusions may naturally hinder acceptable proof of the research hypothesis. In addition, the heterogeneity of the study protocols of the different studies published on this topic may hinder head-to-head comparisons.

Although the discriminant power of the overall score of the SarQoL questionnaire has been validated by most studies, the results obtained in each domain are heterogeneous. In the original

French SarQoL questionnaire, and later in the Dutch, Lithuanian, Russian, Greek and Turkish versions, scores for all 7 independent domains were significantly lower in patients with sarcopenia compared to patients without sarcopenia. In other validation studies, the English version scored D3, D6 and D7; the Romanian version scored D4 and D6; the Polish version scored D4, D6 and D7; the Ukrainian version scored D2 and D6; the Spanish study by Fabrega-Cuadros et al. scored D2; and the Chinese version scored D6; and in the Spanish study by Montero-Errasquin et al. scores in domains D2, D3, D6 and D7 were not significantly lower in subjects with sarcopenia. The study by Matijevic et al. using the Serbian version found no statistically significant difference in total and individual domain scores when comparing subjects with and without sarcopenia. The most likely reason for this non-significant difference is that 687 non-sarcopenic subjects were compared with only 12 sarcopenic subjects. In our study, the overall score of the SarQoL questionnaire was statistically significantly lower in sarcopenic than in non-sarcopenic individuals, however, the individual domains D1, D3, D4, D6 and D7 were not significantly lower in sarcopenic individuals. Although some studies found non-significantly but lower values in sarcopenic subjects on the different domains, the domain D6 - leisure activities - was a common denominator in all of them. The reason here may be, as previously suggested by Konstantynowicz and colleagues, cultural difference, and this is particularly noticeable in the area of leisure activities, on the one hand, and the lack of a robust sample size of the cohorts studied, on the other.

The internal consistency of the Hungarian version of the SarQoL questionnaire was high, and there was a statistically significant correlation between the total and individual domain scores. This is consistent with all previously published validation studies. In our study cohort, we observed a significant ceiling effect in the D3 and D7 domains. Previously, Dzhus et al. also reported a significant ceiling effect in the D7 domain in their Ukrainian cohort. A likely explanation may lie in the intercultural sensitivity of the questions in domains D3 and D7,

however, this idea is refuted by Greenick et al. when they validated the Hungarian version of the SarQoL on Hungarian native Romanian subjects and found neither floor nor ceiling effects. Although there were no sarcopenic subjects in the cohort recruited for the validation study.

To the best of our knowledge, the test-retest reliability of the Hungarian version of the SarQoL questionnaire is still pending.

Given the growing body of knowledge on the SarQoL questionnaire, it is conceivable that a change in its scoring might help to increase its effectiveness in future intervention studies. Nevertheless, the increasing knowledge of sarcopenia, the growing amount of data and the economic implications of the condition and its consequences for health care may spur us to greater efforts to detect and diagnose it early, and the SarQoL may provide a very good objective starting point for better understanding the day-to-day impact of the condition on patients' quality of life. Our results are likely to have public health implications and could accelerate the development of policies to promote healthy ageing.

CONCLUSION

The 31% prevalence of sarcopenia in the postmenopausal women studied highlights the need for proper assessment of this old-age condition. The total score of the Hungarian version of the SarQoL questionnaire has a significant discriminative ability to distinguish between patients with and without sarcopenia, has a high internal consistency and has no ceiling nor floor effect.

SUMMARY

According to the World Health Organization (WHO), the percentage of people over 60 could increase by at least 1.5 times by 2050. As we age, different changes take place in a person's body. The best known changes are osteoporosis, which is associated with a loss of bone mass,

and sarcopenia, which is associated with a loss of lean body mass, resulting in changes in mobility, food intake and nutritional status, general independence and a reduced quality of life. Aware that there is a gap in our knowledge about the prevalence of sarcopenia in Hungary, one of the aims of the present study was to determine the prevalence of sarcopenia in a postmenopausal Hungarian cohort using the EWGSOP2 consensus recommendation. And since the study included the completion of the Hungarian version of the SarQoL questionnaire, we separately examined and evaluated the discriminative power, internal consistency, and floor and ceiling effects of the questionnaire.

Following the algorithm detailed by EWGSOP2, in our study 40 (40%) individuals were diagnosed with sarcopenia based on the results of the SARC-F questionnaire, 36 individuals were assessed as having probable sarcopenia based on muscle strength, 31 were assessed as having proven sarcopenia based on muscle mass, and 8 were diagnosed with severe sarcopenia following assessment of physical performance. Presarcopenia criteria were confirmed in 5 individuals.

The internal consistency of the Hungarian version of the SarQoL questionnaire was high, and there was a statistically significant correlation between the total and individual domain scores.t.

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Registry number: DEENK/383/2023.PL
Subject: PhD Publication List

Candidate: Zoltán Domokos Pap
Doctoral School: Kálmán Laki Doctoral School

List of publications related to the dissertation

1. **Pap, Z. D.**, Kalabiska, I., Balogh, Á., Bhattoa, H. P.: Evaluation of the sarcopenia quality of life (SarQoL) questionnaire in community dwelling outpatient postmenopausal hungarian women.
BMC Musculoskelet. Disord. 24 (1), 1-7, 2023.
DOI: http://dx.doi.org/10.1186/s12891-023-06454-2
IF: 2.3 (2022)

2. **Pap, Z. D.**, Kalabiska, I., Balogh, Á., Bhattoa, H. P.: Prevalence of sarcopenia in community dwelling outpatient postmenopausal Hungarian women.
BMC Musculoskelet. Disord. 23 (1), 1-11, 2022.
DOI: http://dx.doi.org/10.1186/s12891-022-05167-2
IF: 2.3

List of other publications

3. Pethő, Z., Kalina, E., **Pap, Z. D.**, Hódosi, K., Falcsik, R., Balogh, Á., Szekanecz, Z., Bhattoa, H. P.: Characterization of bone metabolism in hungarian psoriatic arthritis patients: a case control study.
BMC Musculoskelet. Disord. 22 (1), 1-9, 2021.
DOI: http://dx.doi.org/10.1186/s12891-021-03952-z
IF: 2.562

4. Jakab, É., Kalina, E., Pethő, Z., **Pap, Z. D.**, Balogh, Á., Grant, W. B., Bhattoa, H. P.: Standardizing 25-hydroxyvitamin D data from the HunMen cohort.
Osteoporosis Int. 28 (5), 1653-1657, 2017.
DOI: http://dx.doi.org/10.1007/s00198-017-3924-4
IF: 3.856

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5. Jakab, É., Pethő, Z., **Pap, Z. D.**, Kalina, E., Földesi, R., Balogh, Á., Antal-Szalmás, P., Bhattoa, H. P.: Cystatin C as a potential predictor of osteoprotegerin levels in healthy men, a cross-sectional, observational study.
BMC Musculoskelet. Disord. 16 (277), 1-7, 2015.
DOI: http://dx.doi.org/10.1186/s12891-015-0684-1
IF: 1.684

Total IF of journals (all publications): 12,702
Total IF of journals (publications related to the dissertation): 4,6

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of the Journal Citation Report (Impact Factor) database.

18 August, 2023

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