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Regression model for the prediction of risk of sarcopenia among older adults

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SUMMARY

Background. Sarcopenia is a generalized loss of skeletal muscle mass and strength. Early identification is essential to minimize the adverse effects and consequences, which can help in the prevention and timely management of sarcopenia. Hence we developed a regression model for the prediction of sarcopenia.

Methods. This study adopted a case-control design. The dependent variable was skeletal mass index and independent variables assessed were age, body mass index (BMI), physical activity status, depression status, alcohol consumption, cigarette smoking, type 2 diabetes mellitus, grip strength, quadriceps strength, gait speed, physical performance measures, and SARC F questionnaire. Binary logistic regression was used to determine the odds ratio and to develop the model.

Results. One hundred and four older adults were included and analyzed in this study. Among the variables considered, age, BMI, physical activity, grip strength, quadriceps strength, balance, and SARC F showed a significant odds ratio ($r^2 = 0.724$; $p \leq 0.05$); thus they were considered for developing the regression model.

Conclusion. A regression model for the risk of sarcopenia was developed, which can help in early detection and of individuals with sarcopenia at the community level.

KEY WORDS

Aging; Low muscle mass; Muscle loss; Prediction; Risk factors

BACKGROUND

Sarcopenia is one of the most common problems affecting the elderly population, which increases the likelihood of functional disability, falls, loss of independence, decreased quality of life, increased cost of healthcare, and increased mortality (1,2). The European working group in sarcopenia in older adults (EWGSOA), 2010 defined the condition as "a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death" (3).

The muscle tissue is a power generator with functions such as storage of protein, glucose control, hormone production, and cellular processes; sarcopenia inflicting disequilibrium of these functions (4). The global prevalence of sarcopenia is 29% in community-dwelling older adults and 33% in institutionalized older adults, (5) whereas 21.8 % of men and 22.9 % of women aged 65 to 89 years have sarcopenia in Asia (6). Loss of muscle mass begins at the rate of 3 -5 percent at an early age and then begins to rise quickly after 60 (4).

The causes of this condition varies from genetic, physiological, and environmental factors (7). The risk factors of sarcopenia can be divided into modifiable and non-modifiable factors; the modifiable factors being alcohol consumption, cigarette smoking, nutritional factors, physical inactivity, BMI (underweight), depression, diabetes mellitus, social environment, osteoporosis and age, gender and genetics are the non-modifiable factors (6,7). Studies have shown an association between sarcopenia and limited mobility, disability in activities of daily living, disability in instrumental activities of daily living, and frailty; these health outcomes are the predictors of mortality (8,9). It is reported that bringing down the prevalence of sarcopenia by 10 percent in the US would reduce the health care cost by 1.1 billion dollars (10). In countries like India, where affordability is a major factor influencing health care, reducing the prevalence of sarcopenia would have a major health economic impact. Hence it

is important to identify sarcopenia early for minimizing the adverse effects and consequences and to help prevent and manage sarcopenia early (11).

Diagnosis requires the presence of low muscle mass plus low muscle strength or low physical performance (2). Muscle mass measurement for sarcopenia diagnosis is done using the Dual-energy X-ray absorptiometry (DEXA), Bioelectrical Impedance Analyzer (BIA), CT/MRI or ultrasound. DEXA is the gold standard for sarcopenia diagnosis, but has its limitations like cost factor, availability at health care centers, and utility at the community level. Hence BIA is commonly used as it is affordable and portable. It is challenging to regain muscle mass once the loss has occurred, a screening strategy at the community level that allows for early detection is essential.

Despite being a severe health problem, sarcopenia in older adults is still overlooked and underdiagnosed, especially in developing countries like India. Early identification is vital in reducing healthcare costs, minimizing the consequences, and thereby preventing disabilities. Screening using diagnostic tools is the ideal method for early identification. However, the feasibility of such a program is limited due to inadequate resource in countries like India. The feasible option would be to develop a risk prediction model using known risk factors and predictive factors. Hence this study aimed at developing a regression model for the early detection and prediction of sarcopenia among older adults using known risk factors and physical performance measures in the Indian population.

MATERIALS AND METHODS

The study utilized a case-control method and was conducted in institutions for elderly in Udupi taluk and camps conducted by Kasturba hospital, Manipal between August 2018 and January 2019. After obtaining permission from the Institutional Ethics Committee, Kasturba Hospital (IEC 107/2018), the trial was registered under Clinical Trials Registry of India (CTRI/2018/04/013341); this study meets the ethical standards of the journal (12). The exclusion criteria were participants with end-stage disease frail older adults and those with contraindications in performing any of the physical performance measures. Adults more than or equal to 55 years of age, Montreal Cognitive Assessment score more than or equal to 26 and participants ambulating without assistance, or assistive devices were included. The sample size was estimated to be 94 (47 among cases and 47 among controls) using the formula n=(2×PQ(Z1-∝/2+Z1-β)2)/(P1-P2) 2; where P1 is the probability of exposure among cases and P2 is the probability of exposure among controls at 80% power and 5% level of significance.

After obtaining written informed consent, the participants' demographic details were noted and were screened for the following risk factors of sarcopenia: history of smoking, history of alcoholism, physical inactivity using the Rapid Assessment of Physical Activity (RAPA) questionnaire (13), malnutrition using Short Nutritional Assessment Questionnaire (SNAQ) (14), history of depression using short Geriatric Depression Scale (GDS) (15) and history of diabetes mellitus type 2. Investigator conducted testing of grip strength using Jamar dynamometer (Patterson Medical, Illinois, US, 2002/ Jamar -5030J1), quadriceps strength using hand-held dynamometer (Chatillon, Ametek sensors, test and calibration 2012, MSE-100-M), gait speed using 6-meter walk test and Physical Performance using short physical performance battery (SPPB) (16) were performed. The short physical performance battery (SPPB) is a group of measures that combines the results of the gait speed, chair stand, and balance tests. It has been used as a predictive tool for possible disability and could aid in the monitoring of function in older people. The scores range from 0 (worst performance) to 12 (best performance). The SPPB has been shown to have predictive validity showing a gradient of risk for mortality, nursing home admission, and disability.

The grip and quadriceps strength were measured using the standard evaluation protocol (17, 18). For grip strength evaluation, the participants sat on an armless chair with the arm by the side of the body and elbow at 90 degrees, the handle of the dynamometer was adjusted according to the fist size of the participant. Each participant squeezed the handle of the dynamometer as hard as possible for five seconds. Mean of 3 trials was recorded in kilograms. Quadriceps strength was assessed using a hand-held dynamometer which has a precision accuracy of + 0.5% of full scale; the participants sat at the edge of a high chair or couch, the hand-held dynamometer was kept at two finger distance above the lateral malleolus. The subjects were asked to sit straight and place their arms across their chest and perform isometric knee extension, for 5 seconds, Three trials were done, and the mean of the 3 values was considered as the final score.

The investigator administered the SARC F questionnaire, which is a valid measure for identifying sarcopenic and it is a clinical symptom index which is based on individuals' difficulty in lifting, walking, transferring, climbing stairs and the number of falls. The percentage of skeletal muscle mass was measured using Bioelectrical Impedance Analyzer (Omron, Body Composition Monitor HBF-701) (BIA). This device has a weight measurement accuracy of ±400 g from 0.0 kg to 40.0 kg and ±1% from 40.1 kg to 135.0 kg. Also, it can measure 5 to 60% of skeletal mass with an increment of 0.1%. The participants stood on the BIA machine with

their back and legs straight. They held the arm piece of BIA machine with arms raised perpendicular (90°) to the body and parallel to the floor, and the elbows were extended. The percentage of skeletal mass was noted and converted to skeletal mass index (SMI) as given by Janssen et al. (19) Participants were categorized into cases and controls using the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) diagnostic criteria.

Statistical analysis

Data analysis was done by using SPSS version 16 software. The Independent t-test for continuous variables and the Chi-square test for categorical variables were used to compare the demographic variables and the exposed factors between cases and controls. Binary logistic regression was used to determine the odds ratio and to develop the model. The level of significance was set at $p \leq 0.05$.

RESULTS

Two hundred and twenty-three older adults were screened for eligibility, and after screening for the selection criteria, 119 subjects were excluded for various reasons like pain, history of cerebrovascular disease (CVA), open wounds and history of fractures. One hundred and four participants completed the assessment, and data was analyzed, as shown in **figure 1**. The results are explained under the following headings: demographic characteristics, unadjusted odds ratio, adjusted odds ratio, and regression model.

Demographic characteristics

Table I depicts the demographic characteristics of the participants in the case and control group. It can be seen that all the variables showed a statistically significant difference between the participants in cases and controls. The mean age and SARC F score among cases were 09.43 years and 1.97 points more, whereas mean BMI, grip strength, quadriceps strength, gait speed, physical performance measures and the percentage of skeletal mass were 03.82 kg/m², 06.31 kgs, 04.58 kgs, 0.11 m/s, 1.72 points, 0.87 points, 0.99 points, and 3.58 points less respectively when compared with controls. **Table I** also represents the percentage of participants exposed to the risk factors among case and control group. As reported, all the risk factors showed a statistically significant difference between cases and controls.

Unadjusted odds ratio

Table II represents the unadjusted odds ratio; after the univariate analysis, 12 variables showed a statistically signif-

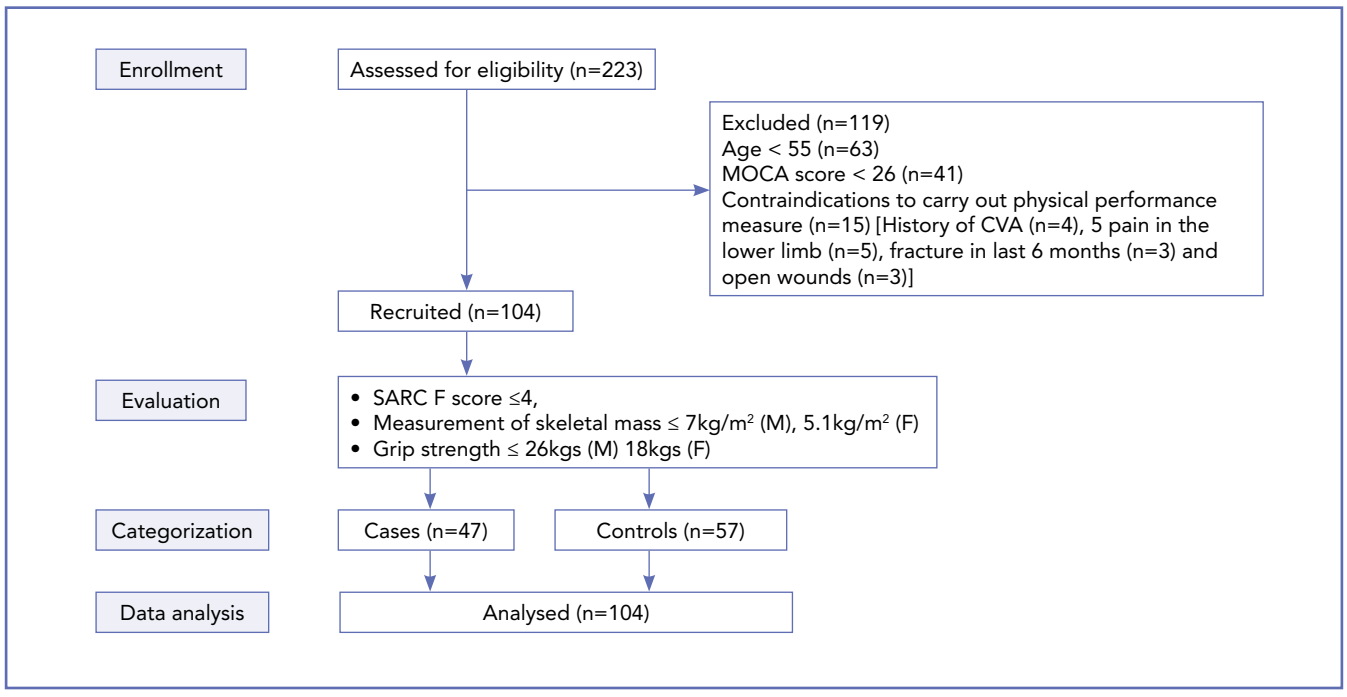

Figure 1. Flow of participants

Table I. Demographic characteristics and the exposed factors among cases and controls (n=104)

Variables	Cases (N=47)	Controls (N=57)	p-value
	Mean ± SD		
Age (years)	74.46 ± 9.92	65.03 ± 9.36	**<0.001**
BMI (Kg/m2)	21.94 ± 3.68	25.76 ± 4.52	**<0.001**
Grip strength (Kgs)	17.44 ± 4.14	23.75 ± 7.12	**<0.001**
Quadriceps strength(Kgs)	14.75 ± 5.19	19.33 ± 4.39	**<0.001**
Gait speed (m/s)	0.67 ± 0.12	0.78 ± 0.12	**<0.001**
Physical performance- balance	1.91 ± 1.57	3.63 ± 0.85	**<0.001**
Physical performance- gait speed	6.51 ± 1.45	7.38 ± 1.13	**<0.001**
Physical performance- chair stand	1.44 ± 1.33	2.43 ± 1.21	**<0.001**
Physical performance- total score	9.87 ± 3.78	13.45 ± 2.47	**<0.001**
SARC F	3.74 ± 2.19	1.77 ± 1.89	**<0.001**
Percentage of skeletal mass (%)	20.54 ± 3.99	23.17 ± 4.26	**<0.001**
	Number/Percentage		
Gender	16(34%) /31 (66%)	17(29%) /40 (70.2%)	**<0.001**
Depression (n=22)	18(81.8%)	4(18.1%)	**0.008**
Alcohol consumption (n=5)	3 (60%)	2(40%)	**<0.001**
Cigarette smoking(n=3)	1(33.3%)	2(66.6%)	**<0.001**
Type 2 DM(n=37)	12(32.4%)	15(40.5%)	**<0.001**
Physical Inactivity (n=54)	24 (44.4%)	30 (55.5%)	**<0.001**
Malnutrition	0	0	-

Table II. Unadjusted Odds Ratio (OR) with exposed factors

Variable	Unadjusted OR (95% CI	p value
Age(years)	1.099 (1.052, 1.148)	**<0.001**
BMI kg/m^2	0.786 (0.696, 0. 888)	**<0.001**
Physical activity status	0.847 (0. 653, 1. 097)	0.209
Depression status	1.346 (1.096 , 1.652)	**0.005**
Alcohol consumption	0.533 (0.085, 3.333)	0.501
Cigarette smoking	1.480 (0.147, 14.864)	0.739
Type 2 DM	1.042 (0.431, 2.516)	0.928
Grip strength(Kgs)	0.809(0.733, 0.892)	**<0.001**
Quadriceps strength (Kgs)	0.825(0.753, 0.904)	**<0.001**
Gait speed (m/s)	0.001 (0.000, 0.029)	**<0.001**
Physical performance- balance	0.377(0.257, 0.551)	**<0.001**
Physical performance- gait speed	0.590(0.423, 0824)	**0.002**
Physical performance- strength	0.908(0.849, 0.971)	**0.005**
Physical performance- total	0.790(0.610, 0.824)	**<0.001**
SARC F	1.555(1.264, 1.913)	**<0.001**
Percentage of skeletal mass	0.852(0.766, 0.947)	**0.003**

icant odds ratio which are age, BMI, depression status, grip strength, quadriceps strength, gait speed, physical performance (balance, gait speed, strength, total score), SARC F and percentage of skeletal mas

Adjusted odds ratio

Table III represents the adjusted odds ratio; after the multivariate analysis, 7 variables had significant odds ratio i.e. age, BMI, physical activity status, grip strength, quadriceps strength, physical performance (balance) and SARC F, hence were taken for developing the model.

Regression model

The regression model obtained for the risk of sarcopenia is Exp [-0.193+0.405 (age) -1.554 (BMI) +1.382 (physical activity) - 1.882 (grip strength) -0.482 (quadriceps strength) - 5.399 (SPPB balance) + 1.56 (SARC F score)]

DISCUSSION

This study aimed at developing a regression model for sarcopenia among older adults. Sixteen independent variables were considered for developing the model of which 5 were categorical, and 11 were continuous variables. After performing backward stepwise regression, only 7 variables, that showed a statistically significant relationship were considered for developing the regression equation.

In this study, age is shown to have a significant positive relationship with sarcopenia with an odds ratio of 0.667. A study done by Martinez BP et al. (2015) evaluated the frequency and factors associated with sarcopenia among Brazilian older adults reported older age to be a factor associated with sarcopenia with an odds ratio of 1.14 (95% CI: 1.06, 1.23). In the above study, the mean age of sarcopenics was 78.9 ± 9.5, and non-sarcopenics was 68.8 ± 6.8, which suggests that age influences sarcopenia (20). This could be attributed to the physiological and morphological changes among elderly characterized by skeletal muscle changes and a general decline in the size of the skeletal muscles and number of fibers of skeletal muscle, mainly the type 2 muscle fibers, and increased adiposity in the skeletal muscle (21).

The present study showed a negative relationship between BMI and sarcopenia with an odds ratio of 0.612. Senior HE et al., (2015) evaluated the factors associated with sarcopenia among older adults living in nursing homes. Multivariate analysis suggested low BMI as a significant factor for the prediction of risk of sarcopenia among older adults with an odds ratio of 0.80 (95% CI 0.65–0.97) (22). Studies done by Mesquita AF et al., (2017) and Yu R et al., (2014) suggested that elderly people with a low BMI have greater muscle reserve impairment while obesity is shown to be a protective factor in sarcopenia development. Although obesity is considered as a risk factor for many adverse health outcomes, it may be beneficial for the elderly population to be slightly overweight with muscle mass and hence becomes important for the elderly to maintain a healthy body weight (7,23).

Table III. Adjusted Odds Ratio (OR) with exposed factors

Variable	Adjusted OR (95% CI)	p value
Age	0.667 (0.464, 0.959)	**0.029**
BMI	0.612 (0.491, 0.761)	**<0.001**
Physical activity status	0.746 (0.598, 0.930)	**0.025**
Depression status	1.006 (0.732, 1.383)	0.976
Alcohol consumption	16. 548 (0.547, 500.762)	0.176
Type 2 DM	3.942(0.784, 19.827)	0.163
Grip strength	0.803 (0.694, 0.930)	**0.014**
Quadriceps strength	0.854(0.615, 0.947)	**0.012**
Gait speed	0.0149(0.000, 16.215)	0.320
Physical performance- balance	0.271(0.134, 0.548)	**0.002**
Physical performance- gait speed	0.271(0.134, 0.548)	0.865
Physical performance- strength	0.308(0.002, 4.287)	0.381
Physical performance- total	1.197(0.898, 1.597)	0.303
SARC F	4.795(1.059, 21.713)	**0.042**
Percentage of skeletal mass	1.127(0.852, 1.491)	0.483

We hypothesized a negative relationship of physical activity with sarcopenia, but the results of this study show a positive relationship with an odds ratio of 0.746. The current study incorporated a self-reported questionnaire i.e., Rapid Assessment of Physical Activity (RAPA), which is a subjective measure. The results could have been different if a quantitative measure was used. Steffl M et al. (2017) reported a protective effect of physical activity on sarcopenia (24) Mijnarends DM et al. (2016) suggested that the incidence of sarcopenia among highly active older adults was significantly lower when compared to the least active older adults (25). The present study identified that low handgrip strength is associated with sarcopenia. The mean grip strength (kgs) in this study was 26.96 ± 6.93 and 18.08 ± 4.37 for males and females respectively. Jun Yoo et al. (2017) and Alonso AC et al. (2018) found weak hand grip strength (HGS) to be predictive of sarcopenia (26, 27). Lower mean HGS, i.e, 26 kgs for men and 18 kgs for women is mandatory to diagnose sarcopenia. In a study done by Gray M (2016) the mean handgrip strength was 16.07 ± 1.24 and 26.82 ± 97 for sarcopenics and non-sarcopenics respectively whereas the mean HG for men and women were 39.29 ± 8.34 and 21.19 ± 5.16 respectively (28). The reasons for decreased strength in sarcopenia could be due to decreased protein uptake, the decreased capacity of muscle regeneration, changes in neural drive, tendinous changes and loss of force per cross-sectional area (29).

This study also identified an association between low quadriceps strength and sarcopenia with an odds ratio of 0.854. In a study done by Khongsri N et al. (2016), quadriceps strength was significantly related to sarcopenia with an odds ratio of 3.77 (95% CI: 1.70, 8.37) (30). The mean quadriceps strength was 18.42 ± 4.64 kg and 22.92 ± 3.02 kg among sarcopenic and non-sarcopenic men respectively whereas it was 12.85 ± 4.44 kg and 17.81 ± 3.99 kg among sarcopenic and non-sarcopenic women respectively. For quadriceps strength, the EWGSOP has recommended a cut off value of 18 kgs for men and 16 kgs for women (3).

This study identified a negative relationship between sarcopenia and static standing balance. Gadelha AB et al. (2018) reported that sarcopenia has a negative impact on balance and increases the fear of falling in women living in the community the reason for balance issues can be a reduction in the quadriceps strength (31).

The other models that exist for sarcopenia are developed by Gray M et al., 2016 and Stoever K et al., 2017 (28, 32). The model developed by Gray M et al., has age, gender, weight in kgs, height in cms, grip strength in kgs, speed of walking in seconds, muscular power for sit to stand as the variables. The model developed is Appendicular skeletal muscle mass = -17.441– 4.056(gender) +0.083(weight) –0.391(10-m walk) +0.161(age) + 0.084 (HG) + 0.108(height) –0.003 (muscular power). The model developed by Stoever K et al., is Skeletal Mass Index = 19.071 + 9.341(gait speed) + 0.155(grip strength) - 0.130(repeated chair stand).

Unanswered questions

We had hypothesized a positive relationship between Diabetes Mellitus type 2, however we could not confirm this finding. This could not be commented on as the details of the status of diabetes were not taken.

Strengths of the study

To the best of our knowledge, this is the first regression model developed for the Indian population using risk factors and the physical performance measures and was conducted at the community level.

Limitations

This study has a few limitations to address. Majority (70%) of the study participants were females, and hence generalization would be difficult. Secondly, this study has used questionnaires for assessing the nutritional status and physical activity; recall bias could have influenced the rating as it is common among older adults. Thirdly, hydration status, intake of caffeine, and water retention, which could affect the BIA readings were not controlled.

Future recommendations

This model could be validated with DEXA, which is the gold standard for evaluation of muscle mass.

An objective measure, like accelerometry or activity monitors could be used for the measurement of physical activity.

Significance of the study

The regression model developed may address the issues related to muscle mass assessment like high cost, lack of availability, and need for trained personnel. This would also help in the early detection of individuals with sarcopenia at the community level leading to the early management of sarcopenia.

CONCLUSION

A regression model for the risk of sarcopenia has been developed, and the variables in the model are age, BMI, physical activity, grip strength, quadriceps strength, balance, and SARC F.

Conflict of interest

No other relationships/conditions/circumstances that present potential conflict of interest.

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