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THE IMPACT OF SARCOPENIA ON A PHYSICAL ACTIVITY INTERVENTION: THE LIFESTYLE INTERVENTIONS AND INDEPENDENCE FOR ELDERS PILOT STUDY (LIFE-P)

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Abstract

Objective—To determine if sarcopenia modulates the response to a physical activity intervention in functionally limited older adults.

Design—Secondary analysis of a randomized controlled trial.

Setting—Three academic centers.

Participants—Elders aged 70 to 89 years at risk for mobility disability who underwent dual-energy x-ray absorptiometry (DXA) for body composition at enrollment and follow-up at twelve months (N = 177).

Intervention—Subjects participated in a physical activity program (PA) featuring aerobic, strength, balance, and flexibility training, or a successful aging (SA) educational program about healthy aging.

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Measurements—Sarcopenia as determined by measuring appendicular lean mass and adjusting for height and total body fat mass (residuals method), Short Physical Performance Battery score (SPPB), and gait speed determined on 400 meter course.

Results—At twelve months, sarcopenic and non-sarcopenic subjects in PA tended to have higher mean SPPB scores (8.7±0.5 and 8.7±0.2 points) compared to sarcopenic and non-sarcopenic subjects in SA (8.3±0.5 and 8.4±0.2 points, p = 0.24 and 0.10), although the differences were not statistically significant. At twelve months, faster mean gait speeds were observed in PA: 0.93±0.4 and 0.95±0.03 meters/second in sarcopenic and non-sarcopenic PA subjects, and 0.89±0.4 and 0.91±0.03 meters/second in sarcopenic and non-sarcopenic SA subjects (p = 0.98 and 0.26), although not statistically significant. There was no difference between the sarcopenic and non-sarcopenic groups in intervention adherence or number of adverse events.

Conclusion—These data suggest that older adults with sarcopenia, who represent a vulnerable segment of the elder population, are capable of improvements in physical performance after a physical activity intervention.

Keywords

Sarcopenia; physical activity; gait speed; short physical performance battery

Introduction

Aging is associated with muscle mass decline. By age 80, it is estimated that 40% of the muscle mass present at age 20 is lost (1). However, a subpopulation of older adults has muscle loss that is greater compared to others in their age group. Termed “sarcopenia,” this condition of extreme muscle loss has been associated with physical performance limitations and increased risk of disability. Cross-sectional data demonstrated the odds of functional limitations increased two- and three-fold in sarcopenic older men and women, respectively (2). The Cardiovascular Health Study (CHS) showed the risk of disability is 27% greater in sarcopenic elders (3).

Work has demonstrated that physical activity improves physical performance in functionally limited elders (4). Studies have found that nursing home residents and cancer patients demonstrate improvements after a physical activity program (5, 6). Although these studies suggest that physical activity will likely improve physical performance in sarcopenic elders, the evidence is indirect, as no studies have specifically focused on sarcopenic elders. The state of extreme muscle loss represented by sarcopenia may cause a treatment threshold, below which improvement is minimal.

Using data from the Lifestyle Interventions and Independence for Elders Pilot (LIFE-P) Study, we investigated whether sarcopenia modified the physical performance improvements observed after a physical activity intervention (PA). For comparison, we also examined the effect of sarcopenia on physical performance changes observed after a health education program regarding successful aging (SA). We hypothesized sarcopenic elders would have attenuated improvements in physical performance compared to their non-sarcopenic counterparts. Additionally, we examined if the presence of sarcopenia affected participation as well as the number of adverse events, given the greater co-morbidity burden associated with sarcopenia (7).

Methods

Study Design: The Lifestyle Interventions and Independence for Elders Pilot (LIFE-P) Study

This was a single-blind multi-center randomized controlled trial (Cooper Institute, Dallas, TX, Stanford University, Palo Alto, CA, University of Pittsburgh, Pittsburgh, PA and Wake Forest University, Winston-Salem, NC), comparing the efficacy of a physical activity intervention to a successful aging education program on the incidence of mobility disability in functionally limited elders (4). Institutional Review Boards of all sites gave approval and all subjects provided written informed consent.

Subjects—Eligibility criteria have been described elsewhere (8). Subjects were 70 to 89 years, able to walk 400 meters in ≤ 15 minutes (9), sedentary, scored < 10 on the Short Physical Performance Battery (SPPB), and were followed for 12 to 18 months. A total of 424 subjects were enrolled, and 247 subjects at the Cooper Institute, University of Pittsburgh, and Wake Forest University underwent dual-energy x-ray absorptiometry (DXA) imaging. Twenty-seven were excluded for poor quality and 43 for metal artifact. Results for 177 subjects were analyzed.

Demographics and Medical History—Height, weight, sex, and race were recorded. Body mass index (BMI) was calculated from height and weight. Serum glucose was measured during a fasting state. History of diabetes, hypertension, myocardial infarction, congestive heart failure, or lung disease was obtained.

Dual-energy x-ray absorptiometry (DXA)—Subjects underwent DXA at enrollment and at 12 months with a Hologic QDR 4500 densitometer (Hologic, Inc., Bedford, MA, version 9.03). Bone, fat and fat-free mass were quantified at Wake Forest University. Fat-free mass was assumed to represent lean muscle mass (10). Daily phantom scans were performed for quality control.

Interventions

Physical Activity—Subjects underwent a regimen of aerobic, strength, balance and flexibility exercises for twelve to eighteen months, with walking as the primary activity. During weeks 1 to 8, thrice weekly sessions were supervised at the field center. From weeks 9 to 24, supervised sessions were twice weekly and home-based exercises initiated. At 24 weeks, subjects transitioned to a home-based program with an optional weekly supervised session. After 24 weeks, subjects were contacted by phone periodically to encourage adherence (4). Subjects were instructed to perform activity at a moderate level per the Borg scale (11).

Successful Aging—Subjects participated in seminars on health topics, such as nutrition. For weeks 1 to 24, sessions were weekly. At week 25, the sessions became monthly. After a missed session, subjects were contacted to encourage attendance. At the conclusion of sessions, participants performed five to ten minutes of gentle upper extremity stretching (4).

Variables

Sarcopenia—Sarcopenia was defined using a multiple linear regression model (12), which assumes that the mean appendicular (arm and leg) lean muscle mass (ALM) is approximated by a combination of total body fat and height. For each subject, the measured amount of baseline body fat and height was input to obtain a model predicted value for appendicular lean mass. This was subtracted from the measured DXA value, resulting in a residual value. Subjects with residuals in the bottom quintile (20%) were classified as sarcopenic and the remaining nonsarcopenic (12). Due to different inclusion criteria between this study and the Health ABC study, the lowest quintile cutoff may not have been appropriate (12). Analyses were repeated using the lowest decile (10%) and tertile (30%) as the residual value of the residual cutoff. The strongest associations were found using the lowest 20% cutoff, which are reported herein.

As no current operational definition of sarcopenia exists (13), analysis was repeated using the appendicular lean muscle mass in kilograms/height in meters^2 (ALM/height^2) definition using published cutoffs of 7.26 kg/m^2 for men and 5.45 kg/m^2 for women (14).

Short Physical Performance Battery (SPPB)—The SPPB measures gait speed, repeated chair stand time, and balance. For each task, a subject is scored from zero to four, and the sum is the SPPB score with a maximum score of twelve (15). For gait speed, subjects walked four meters at their usual pace. Faster of the two trials was recorded in meters per second. Time required determined the score. For repeated chair stand time, subjects were asked to stand up from a seated position five times in a row without stopping or using arms. Time required determined the score. For subjects who could not complete a chair stand or utilized arms, their time was recorded as zero seconds. For balance, subjects attempted three standing positions: 1. feet side by side, 2. heel of foot beside toe of other foot, and 3. heel of foot in front of other foot. Time maintained in each position determined the score (15).

Gait speed using 400 meter walk test—Time required to walk 10 laps at usual pace on a 20 meter course was recorded. Rest for up to 60 seconds was permitted, but sitting or leaning against the wall was not. Canes were allowed, but not walkers or human assistance. Gait speed was calculated by dividing distance by time in seconds, including rest time. If the walk was not completed within 15 minutes, the walk was terminated. If the walk was stopped early, the total distance achieved and the amount of time was recorded (16). Gait speed was measured on a 400 meter course as opposed to a four meter course as it is thought to more closely simulate the activity of a community-dwelling older adult (17). Prior work has demonstrated that the Spearman correlation coefficient for gait speed measured on a 400 meter course and a 4 meter course is 0.93 (18).

Adherence—Sessions attended was compared to sessions available, excluding closings. The number of sessions differed between sites due to weather and holidays. For comparison of PA and SA groups, the total number of sessions for each group at each site for the study was used. Comparison of adherence by sarcopenia status was compared within each intervention group.

Adverse events—Any death, life-threatening event, inpatient hospitalizations, or clinically significant laboratory or diagnostic test abnormalities that required immediate medical attention during screening, randomization, or study duration was recorded. This information was collected during assessments, intervention sessions, or reminder calls. All events, whether study-related or not, were analyzed.

Covariates—Analyses were adjusted for age, field center, and baseline value of outcome. No adjustment was made for BMI due to collinearity with sarcopenia (Spearman's correlation coefficient ϱ=0.86).

Statistical Analysis

Analysis was performed using SAS (version 9.2, SAS Institute, Inc., Cary, NC). Baseline demographics and physical performance were compared using two sample t-tests and chi square tests. Adherence was compared using the Wilcoxon rank sum test, and the number of adverse events was compared using the chi square test.

Six and twelve month SPPB scores and gait speeds between intervention groups were compared using repeated measures analysis of covariance (ANCOVA). Interaction between sarcopenia and intervention was non-significant. Within each arm, SPPB scores and gait speeds of sarocpenic and non-sarcopenic subjects were compared with ANCOVA as well. The interaction of time and intervention was forced into the models. Data are expressed as least squares mean values with 95% confidence intervals.

Results

Baseline Characteristics and Physical Performance Measures by Sarcopenia Status

The mean age and proportion of females were similar. Mean BMI was lower in sarcopenic subjects (Table 1). Although not statistically significant, the frequencies of diabetes and lung disease were higher in the non-sarcopenic subjects, while sarcopenic subjects had a higher frequency of congestive heart failure. Fasting glucose did not differ between groups. Grip strength tended to be lower in sarcopenic subjects.

Adherence

Within PA, overall adherence was 74% for the sarcopenic subjects, and 71% for the non-sarcopenic subjects (p=0.59). During the final PA phase with optional sessions, sarcopenic subjects had 70% adherence, while non-sarcopenic subjects had 60% (p=0.14). For SA, during the latter half with monthly sessions, sarcopenic subjects had 85% adherence, compared to 79% for non-sarcopenic subjects (p=0.43).

Adverse events

When stratified by intervention, sarcopenic and non-sarcopenic participants did not differ in the number of life-threatening events, inpatient hospitalizations, or clinically significant abnormal laboratory or diagnostic tests (Table 2, all $p > 0.05$). No deaths occurred.

Analysis of SPPB

At six months, the adjusted mean follow-up SPPB for PA was 9.1 points (95% CI 8.7,9.5) and for SA 8.5 points (95% CI 8.1,8.8, p=0.01). At twelve months, scores decreased slightly to 8.7 points (95% CI 8.3,9.1) in PA and 8.4 points (95% CI 8.0, 8.8, p=0.28, p value for trend=0.05) in SA. The original LIFE-P results demonstrated a 0.7 point difference between PA and SA at six months, then a 0.6 point difference at twelve months (4).

At six months, both sarcopenic and non-sarcopenic subjects in PA had higher SPPB scores compared to SA subjects (p=0.12 and p=0.04, respectively, Table 3), with the non-sarcopenic group achieving statistical significance. These improvements were attenuated slightly at 12 months. Within the PA group, the adjusted least square mean twelve month SPPB scores for the sarcopenic and non-sarcopenic groups were both 8.7 points with overlapping 95% confidence intervals (95% CI 7.7,9.7 and 8.3, 9.2, respectively). Analyses using the ALM/height^2 definition demonstrated similar trends (data not shown).

Analysis of 400 meter gait speed

All participants completed the 400 meter walk at twelve months. At six months, gait speed was 0.96 m/s in PA subjects (95% CI 0.91,1.02) and 0.95 m/s (95% CI 0.90,1.00, p=0.77) in SA subjects. By twelve months, the gait speeds were 0.95 m/s (95% CI 0.90,1.00) and 0.91 m/s (95% CI 0.86, 0.96, p=0.21, p value for trend=0.30) in PA and SA, respectively.

Stratification by sarcopenia status demonstrated the six month changes in the mean gait speeds of sarcopenic subjects were not statistically different (p=0.32, Table 4) between PA and SA, with similar results found for non-sarcopenic subjects (p=0.54). At twelve months, both sarcopenic and non-sarcopenic subjects in PA had adjusted mean gait speeds faster than SA, although not statistically significant (PA: p=0.36, p value for trend=0.98 and SA: p=0.28, p value for trend=0.26). Results were similar using the ALM/height^2 definition (results not shown).

Change in sarcopenia status

In the PA group, three subjects went from sarcopenic at baseline to non-sarcopenic at follow-up, while ten subjects transitioned from non-sarcopenic to sarcopenic (p=0.20). For the SA group, four subjects became non-sarcopenic, while three became sarcopenic (p=0.85).

Discussion

In this secondary analysis of functionally limited older adults, the effectiveness of physical activity to improve SPPB scores does not appear to be attenuated by sarcopenia. Similar to the full study, these results demonstrate that physical activity is more effective in improving

SPPB scores, compared to a successful aging program. In addition, adherence to physical activity did not differ between sarcopenic and non-sarcopenic subjects. Finally, adverse events occurred with equivalent frequency in the sarcopenic and non-sarcopenic groups, whether they were randomized to PA or SA.

These results are consistent with prior work examining older adults with conditions predisposing to sarcopenia. In a study of nursing home residents by Fiatarone, ten weeks of resistance exercise increased strength (5). In prostate cancer patients, aerobic and resistance training improved strength and six meter walk time (6). Similar improvements were seen with older women with congestive heart failure who did resistance exercise (19). In mobility-limited elders, Reid found three months of resistance exercise improved knee strength (20).

Reid found there was no change in the leg muscle mass after a physical activity intervention (20), similar to our findings. In contrast, Fiatarone demonstrated an increase of the mid-thigh muscle area after their intervention (5). However, these results are not directly comparable as we examined total appendicular mass and Fiatarone was limited to cross-sectional area.

Like the main study, we demonstrated that the improvements in SPPB scores were greater at six months. A reason may have been the transition by PA subjects into a home-based program at this time. Similar findings were observed in a study of older women whose improvements in strength and maximal gait speed became attenuated after a transition to a home-based physical activity program (21). Studies of intermittent claudication patients have demonstrated that a home-based physical activity program resulted in smaller gains in treadmill walking time compared to a supervised program (22, 23).

Co-morbidities are greater in sarcopenic elders (7), presenting potential barriers for intervention adherence. We observed no differences in adherence between sarcopenic and non-sarcopenic subjects, consistent with work showing a compliance rate of 82% in homebound elders undertaking a physical activity program (24). In a study of older adults with osteoarthritis, adherence to an aerobic exercise program was 68% (25). Our work provides additional evidence for the feasibility of physical activity in functionally limited elders.

The increased co-morbidity burden is thought to increase the risk of adverse events in sarcopenic elders. Trials of physical activity in patients with prostate cancer (6), congestive heart failure (19), or in the nursing home (5) have shown that adverse events rates in these groups were limited, but these trials were less than six months. This trial was twelve months, so the lack of difference between groups is reassuring.

Although we defined sarcopenia by quantitative measure, recent studies have demonstrated that the functionality of the muscle mass may need to be included in the definition (26). A possible mechanism for these results is that physical activity may modify the neuromuscular signals generated in muscle activation. Studies have shown that these signals are depressed in older adults (27, 28). Interestingly, pilot work has demonstrated rates of neuromuscular activation in older adults increased after resistance exercise (29). While the study focused on the hand muscles, this suggests that physical activity is a potential intervention to modulate the neuromuscular response. Further research is needed to determine if physical activity has similar effects in lower extremity muscles.

Strengths of our study include the focus on functionally limited elders, as prior interventions examining physical activity have mainly focused on healthy elders. Second, our study is among only a few assessing muscle mass in the context of an intervention. In terms of limitations, our operational definition of sarcopenia was limited to only muscle mass. Working groups on sarcopenia have recommended that gait speed be included as criteria for sarcopenia to account for muscle quality (7, 13). Given the lack of precise criteria, we chose a priori to limit our definition to muscle mass only. Also we were limited by sample size, as this was a subset analysis.

In conclusion, our results provide preliminary evidence that sarcopenic older adults are capable of responding to a physical activity. Sarcopenia did not affect the safety profile or adherence of subjects to the intervention. Clinically, sarcopenic individuals represent a vulnerable segment of the older adult population. These results demonstrate they are capable of physical performance improvements in response to a physical activity. The presence of sarcopenia or conditions responsible for sarcopenia should not deter clinicians from encouraging physical activity in older patients.

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Table 1

Baseline Characteristics and Physical Performance of Sample by Sarcopenia Status (N=177)

	Sarcopenic (N=33)	Non-sarcopenic (N=144)	P value
Mean age in years ± S.D.	77.5 ± 4.2	76.5 ± 4.0	0.22
% women (no.)	75.8% (25)	70.1% (101)	0.52
% white (no.)	93.9% (31)	78.5% (113)	0.04
Mean body mass index in kilograms/meter^2 ± S.D.	26.9 ± 3.7	30.0 ± 5.4	<0.01
% diabetes mellitus (no.)	6.1% (2)	16.7% (24)	0.17
Mean fasting glucose in milligrams/deciliter ±S.D.	94±18	98± 19	0.19
% hypertension (no.)	60.6% (20)	64.6% (93)	0.67
% history of myocardial infarction (no.)	9.1% (3)	7.6% (11)	0.72
% congestive heart failure (no.)	9.1% (3)	4.2% (6)	0.40
% with lung disease (no.)	6.1% (2)	11.8% (17)	0.53
% in physical activity intervention	48% (16)	51% (73)	0.82
Hand grip strength[1] in kilograms ± S.D. (N=162)	21.8 ± 10.5	25.1 ± 8.9	0.85
SPPB[2] score in points ± S.D.	7.4 ± 1.3	7.8 ± 1.3	0.14
Gait speed[3] in meters/second ± S.D.	0.90 ± 0.17	0.89 ± 0.19	0.74

[1]Measured twice with each hand using a Jamar dynamometer, highest value recorded;

[2]Score range: 0 to 12, with 12 representing robust overall physical function;

[3]Measured on 400 meter course.

Table 2

Number of adverse events

Adverse event	Sarcopenic N = 33		Non -sarcopenic N=144		P value
	PA	SA	PA	SA	
Life-threatening event	0	0	2	1	>0.99
Inpatient hospitalization	2	9	15	18	0.16
Clinically significant abnormal laboratory or diagnostic test	1	0	5	4	>0.99

Abbreviations: PA: Physical activity intervention, SA: Successful aging intervention.

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Table 3

Least Square Means Short Physical Performance Battery[1] scores at baseline, six months and twelve months

	Sarcopenic				Non-sarcopenic			
	PA (95% CI) (N=16)	**SA (95% CI) (N=17)**	**P value**	**P value for trend**	**PA(95%CI)N=73)**	**SA (95%CI) (N=71)**	**P value**	**P value for trend**
Baseline	7.4 (6.9,7.9)	7.4 (6.9,7.9)		0.24	7.8 (7.6,8.0)	7.8 (7.6,8.0)		0.10
6 months	9.5 (8.3,10.6)	8.3 (7.2,9.4)	0.12		9.0 (8.6,9.4)	8.5 (8.1,8.9)	0.04	
12 months	8.7 (7.7,9.7)	8.3 (7.3,9.3)	0.54		8.7 (8.3,9.2)	8.4 (8.0,8.9)	0.31	

Abbreviations: PA: Physical activity intervention, SA: Successful aging intervention;

[1]Score range: 0 to 12, with 12 representing robust overall physical function

Table 4

Least Square Means gait speed[1] at baseline, six months and twelve months

	Sarcopenic				Non-sarcopenic			
	PA (95% CI) (N=16)	**SA (95% CI) (N=17)**	**P value**	**P value for trend**	**PA (95%CI) (N=73)**	**SA (95%CI) (N=71)**	**P value**	**P value for trend**
Baseline	0.90 (0.84,0.96)	0.90 (0.84,0.96)		0.98	0.89 (0.86,0.92)	0.89 (0.86,0.92)		0.26
6 months	0.92 (0.84, 1.00)	0.97 (0.89,1.04)	0.32		0.97 (0.91,1.03)	0.95 (0.88, 1.01)	0.54	
12 months	0.93 (0.85, 1.01)	0.89 (0.81,0.96)	0.36		0.95 (0.90,1.01)	0.91 (0.85,0.97)	0.28	

Abbreviations: PA: Physical activity intervention, SA: Successful aging intervention;

[1]Measured on 400 meter course.