International Journal of Gerontology 7 (2013) 17–21

Contents lists available at SciVerse ScienceDirect

International Journal of Gerontology

journal homepage: www.ijge-online.com

Original Article

Association Between Functional Measures and Mortality in Older Persons☆

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ARTICLE INFO

Article history:
Received 25 August 2011
Accepted 22 March 2012
Available online 15 June 2012

Keywords:
elderly,
mortality,
strength,
walking

SUMMARY

Background: Functional limitations may be a mortality risk among older people. The aim of this work is to determine if body composition and strength are risk factors related to mortality in older Chilean people.
Methods: In a retrospective study, 306 independent elderly Chileans (age: 61–91 years) were followed for a median of 7.2 years. Baseline information was obtained, including gender, living conditions, smoking and drinking habits, educational status, history of chronic diseases, cognitive function, and depression. Body composition was assessed using dual-energy X-ray absorptiometry (DXA). Functionality was assessed by determining isometric handgrip strength and 12-minute walking capacity. The associations between all of these parameters and mortality were assessed using univariate and multivariate models.
Results: During follow-up, 23 (30.7%) male and 34 (14.7%) female participants died ($p < 0.01$). Univariate analysis showed that left handgrip strength, total lean mass, and solitary living have significant associations with mortality in men, whereas 12-minute walking capacity is associated with mortality in women. According to the Weibull multivariate analysis, walking capacity was significantly associated with mortality in women, while only age and total lean mass were predictors of mortality in men. The mortality hazard ratio for women allocated to the first quartile of walking capacity was 2.72 (95% CI: 1.33–5.54), and the mortality hazard ratio for men allocated to the first quartile of total lean mass was 3.28 (95% CI: 1.43–7.54).
Conclusion: Low muscle mass and reduced walking capacity are associated with a higher risk of mortality in older men and women, respectively.

1. Introduction

In order to promote preventive and effective public health interventions among older people, we need simple markers that can be used to predict functional decline and mortality. Among these, weight loss[1] and a history of chronic and debilitating diseases and frequent falls[2] are well-recognized risk factors of mortality. Nutritional parameters and functional status could also be used as risk factors of mortality. The relative importance of these last two factors is a matter of controversy.

Among older people, a moderately high body mass index (BMI) is not a risk factor of mortality; however, it is associated with a higher risk of disability[3]. Changes in body composition, which can be accurately measured using double energy X-ray absorption (DEXA) in order to determine the one's composition of lean muscle and fat, could also be used to determine the risk factors for mortality among older people. Recently, we reported that the loss of appendicular lean body mass, as measured using DEXA, is a significant predictor of mortality among apparently healthy older Chilean people[4].

There is an association between the loss of muscle mass and decline in functional status among the elderly[5]. On the other hand, muscle strength and cardiorespiratory fitness, which are the key determinants of functional status, demonstrate a good relationship with mortality in the elderly[6–9].

Handgrip strength, when assessed using dynamometers, is simple, objective, inexpensive, and has been validated as an indicator of functional limitations in Chilean older people[10]. Cardiorespiratory fitness is commonly assessed through the maximal treadmill exercise test. However, this requires an instrument that is

☆ Disclosure of conflicts of interest: None of the authors have any financial interests to declare related to the materials of this manuscript. They certify that all of the affiliations or financial involvement, within the past 5 years and foreseeable future, with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript are completely disclosed (e.g., employment, consultancies, honoraria, stock ownership or options, expert testimony, grants, patents received or pending, royalties).

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1873-9598/$ – see front matter
doi:10.1016/j.ijge.2012.05.005

not always available, especially in field studies, but an alternative simpler method is to measure walking capacity. The 12-minute walking capacity test was first used to measure the physical fitness of male United States Air Force officers. The advantage of this test is that it can be used to evaluate large groups, does not require expensive equipment, and has a high correlation with maximal oxygen consumption, which is also measured using the maximum treadmill test[11]. It has also been used to evaluate patients with respiratory diseases, showing a good correlation with maximal oxygen consumption that is measured using a cycle ergometer[12]. Some studies have used the 6-minute walking test instead[13]. This is a simpler variant that can be used to assess functional limitations in cardiopulmonary patients. We are not aware of any studies that have reported associations between the results of the 12-minute walking test and mortality in older people. Thus, it is worth exploring if handgrip strength and the 12-minute walking test are predictors of mortality in healthy older people.

Although body composition and functional measures are both predictors of mortality, it is worth comparing both parameters in order to determine which is a better predictor. This will help design future studies that could be used in the field. Therefore, the purpose of this study was to evaluate if functional parameters, such as handgrip strength and 12-minute walking capacity, are better predictors of all-cause mortality in older independent Chilean people than body composition parameters.

2. Materials and methods

We analyzed a database that was generated from longitudinal studies published by the Instituto de Nutrición y Tecnología de Alimentos (INTA) of the University of Chile. All of the studies were approved by the ethics committee, and all of the participants signed an informed consent form authorizing the use of the information in the database. We included 231 women (75.5%) and 75 men (24.5%), aged 61–91 years, who were evaluated between 1999–2005. All of the participants came from middle- and low-income communities. All of the participants were recruited from community centers for older people that normally function as an adjunct to public primary care clinics. As inclusion criteria, the study participants had to be living independently, be able to reach the clinic by themselves, and have no limiting or acute diseases[5]. Smokers, problem drinkers, and patients with stable chronic diseases (e.g., hypertension and diabetes) were included. Patients who died during the follow-up period, which lasted through August 2008, were identified using the mortality records of the Servicio de Registro Civil e Identificación del Ministerio de Justicia del Gobierno de Chile using the patient's unique national ID number. Participants who died in the first 6 months after the baseline evaluation were excluded from further analysis.

3. Measures

3.1. Independent variables

BMI was determined as weight (kg) divided by height (m^2). Body composition was measured using DEXA (Lunar Prodigy instrument; General Electric Medical System, Madison, WI, USA). Data on total fat mass, total lean mass, appendicular fat mass, and appendicular lean mass were also obtained.

Isometric handgrip strength was measured in the right and left hands using a hand-held dynamometer (model 78010; Lafayette Instrument Co, IN, USA), and the results are expressed in kilograms. The instrument could be adapted to the size of the hand of the participant in order to ensure an efficient measurement of grip. The participant was encouraged to apply the highest pressure possible, and the best of three trials was used for each hand. The 12-minute walking capacity was assessed by a physical education teacher at a flat field measuring 20 $\times$ 40 m. The participants were asked to walk in groups of four or five for as fast as they could for 10 minutes without becoming exhausted. A professional registered the number of laps that each patient walked, including the partial distance covered during the last lap, in order to calculate the total distance covered. All of these measurements were performed by the same professional when measuring each participant.

Cognitive function was evaluated by a general practitioner using a modified version of Mini-Mental State Examination (MMSE), and participants with a score < 22 were considered to have cognitive impairment[14]. Depression was assessed using the short Yesavage depression scale[15]. Subjects with ≥ 4 points on this scale were considered to be depressed. Problem drinkers were defined as those with one or more affirmative answers on the CAGE (Acronym for Cut, Annoyed, Guilty and Eye opener) questionnaire[16].

3.2. Covariates

The possible effects of living conditions (living alone or with somebody), smoking (current smoker or nonsmoker), educational status, and history of chronic diseases such as diabetes and hypertension, depression, and alcoholism on mortality were also evaluated.

3.3. Statistical analysis

Stata/SE 10 (Statacorp, Texas USA) was used to analyze all data. We used the Shapiro-Wilk test to determine if the variables had a normal distribution. The clinical, demographic, and educational features of the participants are expressed as frequencies and percentages. The characteristics and measurements of the variables with normal distributions are expressed as the mean $\pm$ standard deviation (SD), and the variables with nonnormal distributions are expressed as the median (range). The Chi-square test was used to evaluate differences in proportions.The *t* test was used to the compare variables with normal distributions, and the Kruskal-Wallis test was used to evaluate variables with nonnormal distributions. The Pearson correlation coefficient was used to determine the correlation between independent variables. To account for the effect of height on the body composition data, total and appendicular lean mass and total and appendicular fat mass were divided by height. Logical variables were converted into dummies. For educational status, we used four levels: 1, basic incomplete; 2, high school incomplete; 3, high school and technical; 4, college. Other logical variables were categorized as yes (1) or no (0). The Weibull survival function was used to evaluate the effects of these variables on mortality. Univariate analysis was used to determine which independent variable or covariate had a significant effect on overall survival. Variables identified as significant were selected for multivariate analysis. Because sex is a well-known risk factor, all models were run separately for men and women. Age was considered as an independent variable because of its significant effect on mortality. When two variables were highly correlated, they were not included in the same multivariate model. The follow-up period of this study was closed in August 2008. There was no further contact with participants after the baseline evaluation.

4. Results

Data from the 306 elderly patients were analyzed. The clinical, demographic, and educational features of the study participants are shown in Table 1. No significant differences in terms of age, educational level, or diabetes status were observed to be associated

Table 1
Clinical, demographic, and educational features of the study participants by sex.

	Females (n = 231)		Males (n = 75)		p
	No.	%	No.	%	
Age (y)	75.5	(69–90)	74.9	(61–91)	NS
Deceased	34	14.7	23	30.7	<0.01
Smoker	8	3.5	15	20.0	<0.01
Drinker	2	0.87	6	8.0	<0.01
Diabetes	17	7.4	2	2.7	NS
Hypertension	117	50.7	25	33.3	<0.01
Living alone	54	23.4	6	8	<0.01
Educational status					
Basic incomplete	29	12.6	10	13.3	NS
High school incomplete	156	67.5	51	68.0	NS
High school/technical	44	19.1	13	17.3	NS
College	2	0.9	1	1.3	NS

with sex. During the observational period, which lasted a median of 7.2 years (range: 0.8–9.3 years), 23 of 75 males and 34 of 231 women died ($p < 0.01$) after a median period of 4.2 (range: 0.8–8.3 years) and 4.9 years (range: 1–9 years), respectively. Body composition, functional status measurements, and the characteristics of the participants in this study are shown in Table 2. No significant differences in the mini-mental scores were observed to be associated with sex. Women demonstrated higher BMI, fat mass, and rate of depression and lower lean mass, strength, and 12-minute walking distance compared with men. No participant had clinically significant peripheral or coronary artery disease.

The correlation matrix between the independent variables is shown in Table 3. There was a high correlation between left and right handgrip strength (r = 0.89), total fat mass and appendicular fat mass (r = 0.94), total lean mass and appendicular lean mass (r = 0.95), and BMI and total (r = 0.88) and appendicular fat mass (r = 0.82). There were moderate although significant correlations between lean body mass and hand grip strength among men. No association between lean body mass and walking capacity was observed in either sex.

The results of the univariate analysis demonstrate that left handgrip strength, total lean mass, and living alone have significant effects on mortality in men and 12-minute walking capacity is associated with women's mortality (Table 4). No statistically significant effect was observed between the other variables and mortality. Specifically, a history of diabetes mellitus or hypertension had no effect on mortality.

Multivariate analysis using the Weibull survival function, which included age, left handgrip strength, 12-minute walking capacity, and total lean mass divided by height, showed that only walking capacity was a significant indicator of mortality in women, while age and total lean mass were significant indictors in men (Table 5). To analyze the difference between walking capacity in women and total lean mass in men, separate models were constructed for walking capacity quartiles and total lean mass quartiles. The mortality hazard ratio for women allocated to the first quartile for walking capacity (lower performance, with a cutoff point < 680 meters), in comparison with the three other quartiles, was 2.72 (95% confidence intervals [CI]: 1.34–5.55). Likewise, the hazard ratio of the patients located in the fourth quartile (higher performance, with a cutoff point > 864 meters) was 0.26 (95% CI: 0.09–0.75). In terms of total lean mass, the mortality hazard ratio for men allocated to the first quartile (lower muscle mass, with a cutoff point < 275 g/cm) compared with the three other quartiles was 3.28 (95% CI: 1.43–7.54). The other independent variables were not significant predictors of mortality.

5. Discussion

This study shows that simple functional measures, such as walking capacity, can have prognostic value for predicting mortality among older women but not older men.

The study participants correspond to healthy low- and middle-income older persons living in metropolitan Santiago, Chile. The high proportion of women is due to their higher level of involvement in the social activities of community centers, which is where the participants were recruited from, and because women are generally more cooperative to participate in these types of studies[4]. The proportion of diabetic patients in this study is lower than the prevalence of diabetes among older patients in the general Chilean population[17], and this may represent a selection bias toward healthier patients. In fact, the selected patients had to be devoid of physical limitations and be able to reach the clinic using their own means.

Separate analyses were performed for men and women because sex differences in terms of body composition, hand grip strength, and walking capacity are important. Therefore, even if we tried to adjust the multivariate models according to sex, the distortion of the results would have been significant. Performing separate analyses for men and women reduced the statistical strength of the results but reduced the chance of obtaining flawed conclusions.

The Weibull survival function was used instead of the Cox model because the former renders models with a better correlation coefficient. In this particular situation, the Weibull survival function was preferred over Cox regression because it is a parametric model that is especially suited for situations where most of the variables are parametric. When observing the Weibull function survival presented here, we noticed that the 12-minute walking distance was always accepted as a variable with a significant prognostic value for women. Age was accepted in the univariate analysis, but

Table 2
Body composition, functional status measurements, and mini-mental examination and depression scores of the study participants according to sex.

	Females (n = 231)		Males (n = 75)		p
	Mean or median	SD or range	Mean or median	SD or range	
Weight (kg)	60.8	±10.8	67.9	±11.6	<0.01
Height (cm)	146.9	±6.4	162.4	±6.5	<0.01
Body mass index (kg/m^2)	28.1	±4.6	25.7	±4.1	<0.01
Lean mass (g)/height (cm)	235.8	±23.0	294.8	±30.6	<0.01
Fat mass (g)/height (cm)	168.9	±49.6	112.8	±42.6	<0.01
Appendicular lean mass (g)/height (cm)	97.5	±12.0	129.2	±18.2	<0.01
Appendicular fat mass (g)/height (cm)	70.5	(10.4–178.4)	39.2	(10.2–96.8)	<0.01
Right handgrip strength (kg)	20.0	±3.9	32.3	±7.0	<0.01
Left handgrip strength (kg)	18.9	±4.1	31.0	(10 - 46)	<0.01
12-minute walking test (m)	758.3	±165.8	964.0	(480–1440)	<0.01
Mini-mental score (modified version)	26.0	(13–30)	26.0	(19–30)	NS
Yesavage depression score (GDS-15)	4.0	(0–13)	3.0	(0–10)	0.04

Table 3
Correlation matrix of the independent variables included in the survival models.

		Lean body mass[b]	Fat body mass	Appendicular lean body mass	Appendicular fat mass	Right hand grip strength	Left hand grip strength
Fat body mass[b]	Females	0.5 ($p < 0.01$)[a]					
	Males	0.5 ($p < 0.01$)					
Appendicular lean body mass[b]	Females	0.88 ($p < 0.01$)	0.47 ($p < 0.01$)				
	Males	0.93 ($p < 0.01$)	0.61 ($p < 0.01$)				
Appendicular fat mass[b]	Females	0.47 ($p < 0.01$)	0.93 ($p < 0.01$)	0.52 ($p < 0.01$)			
	Males	0.46 ($p < 0.01$)	0.95 ($p < 0.01$)	0.59 ($p < 0.01$)			
Right hand grip strength	Females	0.1 (NS)	0.06 (NS)	0.14 ($p = 0.04$)	0.06 (NS)		
	Males	0.42 ($p < 0.01$)	0.28 ($p = 0.01$)	0.42 ($p < 0.01$)	0.17 (NS)		
Left hand grip strength	Females	0.09 (NS)	0.06 (NS)	0.13 ($p = 0.05$)	0.07 (NS)	0.7 ($p < 0.01$)	
	Males	0.33 ($p = 0.03$)	0.15 (NS)	0.33 ($p < 0.01$)	0.04 (NS)	0.82 ($p < 0.01$)	
12-minute walk	Females	0.03 (NS)	0.02 (NS)	0.08 (NS)	0.02 (NS)	0.18 ($p < 0.01$)	0.21 ($p < 0.01$)
	Males	0.12 (NS)	0.05 (NS)	0.11 (NS)	0.02 (NS)	0.33 ($p < 0.01$)	0.38 ($p < 0 .01$)

[a] Results are expressed as a correlation coefficient (level of significance).
[b] All of these values have been corrected for height (g/cm).

not in the multivariate analysis, as a significant factor in women. For men, only total lean mass and age were accepted in all models. Left handgrip strength, which was significant in the univariate analysis, was not significant in the multivariate analysis. Living alone was not included despite being significant because this result could have been biased by the small number of men (8%) included in this category. Age was not included in the model, probably because of its correlation with functional parameters.

Fat mass and BMI were not found to be significant predictors of mortality. This is not surprising, especially considering the fact that large epidemiological studies have not shown an association between fat mass and mortality in the elderly[3], unlike young people.

Two functional indicators—handgrip strength and walking capacity—were chosen to assess their potential prognostic capacities for indicating mortality. Handgrip strength has been extensively used to assess older people[18,19] and is closely related to functional limitations and mobility[20]. Additionally, numerous reports have reported its association with mortality[20,21]. However, other reports do not confirm the power of handgrip strength as a predictor of mortality in women[22,23]. A meta-analysis showed a weaker association between handgrip strength and mortality in studies with a follow-up period < 5 years or > 20 years and for patients < 60 years[24]. In the present analysis, handgrip strength was never accepted for women and was only included for men in the univariate analysis, not the multivariate analysis. The discrepancies between our results and those mentioned above could be due to the fact that when handgrip strength was evaluated by other authors, they did not include an evaluation of walking capacity and most of them assessed physical activity level through a questionnaire or self-report, not through an actual physical test. As shown in Table 3, there is a weak correlation between walking capacity and handgrip; therefore, it is not surprising that one of these variables was discarded by the multivariate analysis. Another possibility is a type II error, in which the small number of participants reduced the power to detect the influence of handgrip strength on mortality. It is also worth mentioning that handgrip has been extensively used to assess hospitalized patients as a prognostic factor, and walking capacity is mainly used to assess ambulatory patients[25].

The predictive value of walking capacity was significant only for women. The risk of mortality of those women who were allocated to the first quartile (i.e., walking < 680 meters) was almost three times higher than for that of women allocated to the three upper quartiles. Some studies have shown that cardiorespiratory fitness, when evaluated using an exercise stress test, is an important predictor as well[26–28]. Few studies have used walking capacity to predict mortality, and it is used less frequently to assess older adults. One of the advantages of this test is that walking is something that everybody does in daily activities and is usually performed by independent older adults. The measurement of this parameter is much easier than a laboratory test, such as a treadmill test, and has been used to assess patients with chronic bronchitis and cardiac failure[29,30]. The results of similar tests, such as the 6-minute walking test, long distance corridor walking assessment, and walking speed assessment, are good prognostic indicators of disability, mobility limitations, and death in older people[13,31]. A recent meta-analysis of nine studies that measured gait speed over a distance of 6 m showed that this parameter is associated with 5-year survival in older patients[32]. It must be emphasized, however, that tests that assess walking capacity over a short distance do not assess aerobic capacity or physical fitness level, unlike the treadmill test and the 12-minute walking test[33].

It remains to be demonstrated that improving cardiorespiratory fitness and skeletal muscle function enhances life expectancy. Other simple measures of functional capacity, such as the timed up-and-go test and short physical performance battery, have been

Table 4
Univariate analysis of the Weibull survival function for all-cause mortality.

	Females			Males		
	RR	95% CI	p	RR	95% CI	p
Age	1.09	(1.02–1.15)	<0.01	1.13	(1.05–1.22)	<0.01
Living alone	1.35	(0.65– 2.83)	0.42	17.13	(5.49– 53.4)	<0.01
Left handgrip strength	0.94	(0.86–1.02)	0.14	0.92	(0.86–0.98)	0.01
Right handgrip strength	0.98	(0.90 - 1.06)	0.58	0.97	(0.91–1.02)	0.24
Walking capacity	0.99	(0.995–0.998)	<0.01	0.99	(0.99–1.00)	0.38
Total lean mass[a]	0.99	(0.983–1.013)	0.80	0.980	(0.96–0.99)	0.01
Body mass index	0.93	(0.84–1.02)	0.41	1.17	(0.99–1.37)	0.07
Diabetes mellitus	2.25	(0.48–10.51)	0.301	0.0	(0)	0.99
Hypertension	1.26	(0.62–2.58)	0.52	0.58	(0.23–1.47)	0.256

[a] Values have been corrected for height (g/cm).

Table 5
Multivariate analysis of the Weibull survival function for all-cause mortality.

	Females			Males		
	RR[a]	95% CI	p	RR	95% CI	p
Age	1.06	(0.99–1.13)	0.06	1.11	(1.03–1.19)	0.004
Walking capacity	0.99	(0.995–0.998)	<0.01			
Total lean mass [b]				0.98	(0.96–0.99)	0.026

[a] RR = relative risk.
[b] Values have been corrected for height (g/cm).

proposed for use in older patients. These parameters improve significantly after exercise training[34] and can also be used to predict mortality[35], functional limitations, and disabilities[33]. However, it was impossible to measure these parameters in the participants in this study. No reports were found comparing the results of the 12-minute walking test and these measures as prognostic parameters in older patients.

As we previously reported, the decline in lean mass demonstrates a prognostic value associated with mortality, but functional measures were not assessed in that paper[4] as it was here. Therefore, these new results complement and provide a better perspective of the measures that are relevant to predicting mortality in free living and relatively healthy older people. In the present study, a prognostic value was found for the total lean mass in men but not women. To analyze how lean mass is related to mortality, we separated its values into quartiles. Those in the first quartile of lean mass (<275.32 g/cm) were at 3.2 times more risk when compared with patients in the other quartiles. The loss of lean mass is an important parameter that must be taken into account in primary care settings because it can be prevented by proper exercise. Resistance exercise training is one of the most effective ways to increase muscular power, maintain muscle quality, and increase lean mass in older adults[36].

This study has three weaknesses. First, the sample is rather small and many associations, especially those between body composition and mortality, could have been missed. Second, lower limb strength, which is related to walking capacity and associated with mortality in older subjects, was not measured[20]. Third, it was impossible to record the causes of mortality in our cohort. Nevertheless, survival analysis of the overall mortality was performed because the high occurrence of inaccurate death certificates is a well-recognized problem[21]. Therefore, it is probably best to work only with overall mortality in order to avoid biasing the results. Death registry is very accurate in Chile because it is mandatory to obtain a burial permit. Therefore, practically all deaths are recorded.

In conclusion, 12-minute walking capacity and appendicular lean body mass are prognostic indicators of mortality in older women and men, respectively. It remains to be demonstrated if improving these parameters with training is associated with a reduction in the mortality of older people.

Financing

This work was financed by grant # 1110035 from the Chilean National Research Funding Institution FONDECYT.

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