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The Impact of Weight Change and Measures of Physical Functioning on Mortality

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Abstract

Introduction—Lower grip strength and measures of physical functioning are associated with all-cause mortality. Relationships amongst long-term weight loss, physical functioning and mortality in older women are understudied.

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Methods—Participants were 5,039 women who were part of the Long Life Study (LLS) ancillary study to the Woman's Health Initiative (WHI). Average age was 78.76 ± 6.92. We de fined long-term weight loss or gain as a decrease or increase of 5% or more of baseline body weight. Our primary outcome was all-cause mortality and our secondary outcomes were vascular death, and coronary heart disease (CHD). The mean follow-up time was 5.4 years. Cox regression modeling was performed for each outcome of interest. Variables of interest were weight change, grip strength, and functional status as measured by the Short Physical Performance Battery (SPPB) controlling for multiple potential confounders.

Results—Weight loss of 5% or more percent body weight was associated with a hazard ratio of 1.66 (1.37–2.01) for all-cause mortality. Weight gain was not related to mortality or cardiovascular outcomes. Those in the highest grip strength quartile had a hazard ratio of 0.51 (0.39–0.66) for all-cause mortality. For the SPPB the hazard ratio was 0.29 (0.21–0.40), adjusting for changes in weight, race, smoking, history CHD, smoking, and diabetes. Higher grip strength and SPPB were associated with lower risks for vascular death, and CHD, independently of weight change.

Conclusions: Weight loss was associated with increased mortality. Stronger grip strength and higher SPPB scores were associated with lower mortality risk independent of weight change.

Keywords

Weight change; obesity; mortality

Introduction

Grip strength and Short Physical Performance Battery (SPPB) are measures of physical functioning[1]. Grip strength assesses strength of grip alone, whereas SPPB is a cumulative score considering 3 components: balance test, timed walk, and chair stands. Balance testes involve a side-to-side stand, tandem, and semi-tandem stands for 10 seconds. Timed walk looks at gait speed, and chair stands asks the subject demonstrate standing without arms. Studies demonstrate associations between increased grip strength and lower all-cause mortality[2]. SPPB considers timed walk, balance test, and chair stands, and is associated with CVD risk in older women[3].

Effects of SPPB and grip strength have been mixed, with some studies showing weight loss improves these parameters, but it is also known that weight loss is associated with frailty which leads to increased mortality[1], and weight loss itself is a predictor of mortality[4]. The results are mixed for studies assessing weight loss and physical functioning[5,6].

This study explores the relationship of weight changes and functional status to mortality and cardiovascular events.

METHODS

Population:

The study population included 7,875 older women enrolled in the Long Life Study (LLS) of the Women's Health Initiative (WHI). Participants in LLS were women who had been in one of the hormone clinical trials in the WHI and women in the WHI Observational Study (OS) who self-identified as Hispanic or African American. To be eligible for LLS, women had to be at least 63 years old by January 1, 2012, provide informed consent and not be living in an institution. LLS participants had an in-person home visit in 2012–2013 during which there was a clinical assessment, blood draw and an assessment of physical status, including hand grip strength, timed walk, chair stands and balance tests. For the present study, we excluded women with a history of cancer at WHI baseline or incident cancer between baseline and LLS. We also excluded participants on anti-depressants, steroids, or anti-cancer drugs, all of which are associated with weight change. Our analytic cohort consisted of 5,039 women.

Exposure variables:

Weight change: Long term weight change was measured as weight at LLS visit minus the WHI baseline weight. The period between these 2 points was between 14 and 18 years. Weight change was defined as loss if there was a loss of greater than or equal to 5% of the body weight. It was defined as gain if there was a gain of greater than or equal to 5% of the body weight and stable if there was a less than 5% change in either direction.

Handgrip: Hand grip strength was measured using a calibrated Jamar hand-grip dynamometer, with two measurements in both arms (if appropriate, recorded to the nearest kilogram). In our analyses we used the maximum grip strength recorded, and the scores were divided into quartiles.

Short Physical Performance Battery (SPPB): The SPPB score consisted of measurements of gait speed by a timed walk, balance test, and chair stands. Scoring was from the Established Populations for the Epidemiologic Studies of the Elderly E) Short Physical Performance Battery (SPPB). The SPPB Score is the sum of 3 individual scores: the Total Balance Score, the Chair Stand Score, and the Gait Speed Score, and yields a continuous score ranging from 0 to 12. Details are described elsewhere[7]. SPPB scores were divided into quartiles.

Covariates: The following covariates were measured at LLS baseline, except for race/ethnicity and education which were obtained at WHI baseline. Metabolic Syndrome (MetS) we used was defined as 2 or more of the following: triglycerides >=150 mg/dL, HDLC <50 mg/dL, glucose >100, hypertension defined as DBP >=140 or DBP >=90 or on medications for hypertension. This modified score was used because history of diabetes and weight were already entered in the model as separate variables.

Outcomes:

Our primary outcome was total all-cause mortality and secondary outcomes were vascular death, coronary heart disease (CHD), which included fatal and non-fatal myocardial infarction, and stroke, which included fatal and non-fatal stroke. Outcomes were adjudicated as previously described[8]. Mean follow-up time from LLS baseline was 5.38 years, s.d = 1.21.

Statistical methods

We compared functional status among those who were weight losers, maintained stable weight or were weight gainers (as defined above), by analyses of covariance. Cox proportional hazards regression models were used to examine associations of weight change, grip strength and SPPB with CHD and mortality. Multiple models were created successively adding covariates. The first model was adjusted for age and weight change; the second additionally adjusted for race/ethnicity, smoking, and education; and finally the third model further adjusted for history of CHD, stroke, and diabetes prior to the LLS baseline visit. A fourth model was created which was further adjusted for blood biomarkers of LDLC, HDLC, and HOMA-IR and baseline systolic and diastolic blood pressures. Since results were essentially unchanged with these additional adjustments, and to avoid overfitting, we decided not to report his model. To determine if there was a significant trend across quartiles we considered quartiles of grip strength and SPPB as ordinal variables from 1 to 4 and determined the significance of the beta coefficients for the continuous variables of grip strength and SPPB. To determine if the effects of grip strength and SPPB on death were mediated by weight change, we calculated Cox models including and excluding weight change as a covariate.

RESULTS

Table 1 shows baseline characteristics by weight change.

Overall, subjects with lower grip strength were more likely to be white, older, and smokers (see table 1).

Weight and weight change

The mean weight change for the entire cohort was −8.7 pounds, sd= 24.8 pounds. This represented a mean weight loss of 4.4% of baseline weight, s.d. = 12.1%. Mean weight at LLS visit was 157.7 pounds.

Mortality outcome adjusting for covariates

Weight: Weight loss was associated with a higher risk of mortality (HR=1.61, 95%CI: 1.34–1.93), controlling for age, race/ethnicity, education, smoking and history of CHD, stroke and diabetes and grip strength. The results were similar when weight change was adjusted for SPPB rather than grip strength, with weight loss being associated with higher risk of mortality (HR = 1.66, 95%CI: 1.37–2.01). There was no association of weight gain on mortality (Table 2). We also did Cox regression analyses using a 5-pound change in weight rather than a percentage change. The results were similar: for all-cause mortality a 5 lb. weight loss had a hazard ratio of 1.64 (95%CI: 1.33– 2.01) compared to stable weight (a change of −5 ls to + 5lbs.), controlling for age, self-reported race, education, smoking, and history of diabetes, CHD or stroke. We present results for weight change of 5% as this takes into account weight loss proportional to baseline weight and because it was used in prior studies looking at weight change and outcomes[9,10].

The correlations of weight parameters indicated that weight was significantly, though modestly, correlated with grip strength whereas it was inversely correlated with SPPB (r=0.2, p<0.001 and r=−0.11 p<0.001, respectively). Change in weight was also positively correlated with grip strength (i.e. gain in weight is associated with higher grip strength), and with higher SPPB scores. Grip strength and SPPB measure different capabilities; the correlation between them was r=0.27, which, while statistically significant, indicate that only 7% of the variants in one measure is explained by the other.

In stratified analyses of those with a history of diabetes or metabolic syndrome (MetS) at LLS baseline, weight loss, compared to stable weight, were associated with a 102% higher mortality (HR= 2.02, 95%CI: 1.54–2.65), after controlling for age, race, education, smoking, history of CHD or stroke, SBP, and DBP. Weight gain was not associated with mortality in these groups. In contrast, among those with no history of diabetes or metabolic syndrome, weight loss was associated with a 54% increase in risk of mortality (HR=1.54, 95%CI: 1.17–2.03) in a fully adjusted model, while weight gain was associated with a 40% *reduced* risk (HR=0.60, 95%CI: 0.37–0.96). Excluding deaths in the first 6 months of follow-up did not change these findings.

Grip strength and physical functioning: Higher grip strength was associated with reduced mortality. After controlling for weight change and other covariates; the highest quartile compared to the lowest quartile of grip strength had HR= 0.51 (95%CI: 0.39 – 0.66), with a dose-response relationship (p for trend <.001), (Table 3). Controlling for weight at time of grip strength measurement (rather than percent change in weight) yielded similar results (HR=0.49, 95%CI:0.38–0.63). In models treating quartiles as an ordinal variable the HR of death was 20% lower per higher quartile of grip strength (HR=0.80, 95%CI: 0.74–0.86, p <.0001). Neither weight at time of grip strength measurement nor weight change between WHI baseline and LLS modified these relationships.

The relationship of SPPB to mortality was stronger than for grip strength; there was a 71% lower mortality risk in the highest quartile of SPPB compared to the lowest (HR=0.29, 95% CI: 0.21–0.40), independent of weight change. Similar results were obtained when controlling for weight at the time of SPPB measurement (rather than change in weight), (HR= 0.27, 95%CI: 0.20–0.38). Sensitivity analysis excluding participants who died within 6 months of start of follow-up showed similar results (data not shown). Hazard ratios were unchanged when not including weight or change in weight in the models.

Effect of age, race and history of diabetes and CVD: In analyses stratified by age group, the relationship between grip strength and death was more pronounced among women aged 75 or older (highest versus lowest quartile HR =0.49, 95%CI: 0.37–0.65) than in those younger than 75 years, (HR =0.80, 95%CI: 0.33–1.96). The effect of grip strength was similar in Black women (HR=0.59, 95%CI: 0.36–0.97) and in White women (HR=0.46, 95%CI:0.33–0.64), in diabetic (HR= 0.56, 95%CI: 0.33–0.94) and non-diabetic women (HR=0.49, 95%CI: 0.36–0.66) as well as in those with a history of CVD (HR=0.50, 95%CI: 0.31–0.82) and those without a history of CVD (HR= 0.52, 95%CI 0.38–0.71) (see Table 4).

The relationship of physical functioning (SPPB) to all-cause mortality, controlling for weight change, and other covariates, comparing the highest quartile to the lowest, was similar for those younger than 75 years (HR= 0.33, 95%CI: 0.13–0.87) and those 75 years or older (HR=0.29, 95%CI: 0.21–0.41), for Black (HR=0.18, 95%CI: 0.6–0.50) and white participants (HR=0.29, 95%CI: 0.20–0.42), for those with diabetes (HR= 0.31, 95%CI: 0.14–0.68) and without diabetes (HR=0.29,95%CI: 0.21–0.41), and for those with a history of CVD (HR=0.14, 95%CI: 0.6–0.35) and without a history of CVD (HR=0.33, 95%CI: 0.24–0.48) (see Table 4)

Vascular Death, CHD and Stroke

Higher grip strength was associated with lower risk of vascular mortality (HR=0.69, 95% CI: 0.48–1.00, p for trend = .015) as well as with lower risk of CHD (HR= 0.56, 95%CI: 0.35–0.89, p for trend =.017), but not with stroke. The associations with vascular mortality, CHD and stroke were stronger for SPPB than for grip strength (Table 5), with HRs comparing quartile 4 to quartile 1 for vascular death = 0.17, (95%CI: 0.10–0.30, p for trend <.001); HR for CHD = 0.46, (95%CI: 0.27–0.77, p for trend <.01) and HR for stroke = 0.61, (95%CI: 0.38–0.99, p for trend <.05).

DISCUSSION

In this prospective study of over 7,000 older women followed for an average of 5.4 years, we found that long-term weight loss of 5 or more percent of body weight over the prior 14 years was associated with a 60% higher risk of all-cause mortality and that higher grip strength was associated with lower all-cause mortality, vascular death and CHD, independently of weight change. Physical functioning reflecting gait speed, balance and chair stands had even stronger inverse associations with mortality, vascular death, CHD and stroke. These associations were similar for women over 75 years old as for younger women, for Black and for White women, and for those with and without history of diabetes or cardiovascular disease. There were no significant associations between weight gain and any of the outcomes.

Studies of the effects of weight loss on grip strength which evaluated participants before and after weight loss interventions have shown inconsistent results. Siervo et al included 23 obese women greater than or equal to 60 years of age, andnoted improvement in grip strength with weight loss[6]. In contrast, Shaver et al looked at grip strength in 96 seniors with obesity and noted no statistical difference in grip strength with dietary intervention[5]. In our study, there was an average weight loss of 8.7 pounds with ageing, but those in the lowest quartile of grip strength had the most weight loss (−12 pounds) compared to those in the highest quartile, who lost an average of 5 pounds.

A study by Newman et al evaluated 4,714 adults 65 and older and noted an association between weight loss and mortality as well as an association between weight loss and lower grip strength. Sirola et al looked at a Finnish cohort of 587 individuals and noted no changes in grip strength between participants who lost or gained weight in their cohort[8]. Importantly, the difference between intentional weight loss and weight loss which may be related to aging, illness or comorbidities should be considered.

Several studies have evaluated associations of grip strength with mortality and cardiovascular disease, with some controlling for weight or BMI. A longitudinal analysis of 919 older women ages 65–101 with a 5-year follow up in the Women's Health and Aging Cohort found a relative risk of cardiovascular disease of 3.21 in the lowest quartile of grip strength when adjusted for age, race, height, and weight, with a CVD mortality risk of 2.17. Risk estimates were not meaningfully changed with adjustment for other variables, and results were similar for all-cause mortality[11]. The UK biobank study of 37–73 year-olds (a total of 356,721 participants) noted a lower risk of mortality with baseline higher grip strength. No associations of height, weight, fat-free mass, BMI, or fat-free mass index with mortality were observed. The English Longitudinal Study of Aging by Hamer et all of 6,864 men and women with mean age of 66 years found that in lower grip strength was associated with higher all-cause mortality within each BMI category. Looking at the hazard ratios in the lowest handgrip groups for this cohort for mortality, there was no statistical difference between participants with normal BMI, overweight, or obesity, but for those who lost weight there was higher mortality and also higher mortality if grip strength decreased[10]. A study of 10,088 females and 8,616 males from 12 countries by Wang et al (follow up of 9.4 years) showed that obesity and physical inactivity were related to decline in grip strength. Overall, while the results of our study of associations between weight loss and decreased grip strength and mortality were consistent with the findings of these prior studies, we extended these findings to considerably older women 63 years of age and above. We also showed that physical functioning, measured by gait speed, balance and chair stands, has even stronger relationships to mortality and cardiovascular outcomes than does grip strength alone. However, for clinical applications it would be more challenging to use the SPPB score as an indicator of risk, especially in patients who may have difficulty in ambulating, while grip strength was more easily measured.

Studies have looked at the Short Physical Performance Battery score with regards to various health outcomes. The score has been found to be associated with falls in older persons[14]. In addition, the SPPB score has been found be associated with MI, stroke, or CVD risk in older women[3]. The dichotomized score in older hospitalized patients has also been associated with readmission and mortality[15].

A limitation of our study is that it is unknown when the weight loss occurred during the extended the follow-up period in relation to the functional measurements, which could include multiple increases and decreases in weight. The trajectory of the weight loss is unknown-i.e. the weight loss could have occurred at any time in the 14 years or so preceding the physical function measures and start of follow-up for outcomes. While we cannot establish causality in this observational study, we did take measures to diminish the risk of reverse causality. We did control for some chronic conditions (diabetes, history of CHD, history of stroke). We also ran models additionally controlling for cholesterol, LDL-C, HDL-C, and HOMA-R, but this did not change our results (data not shown). In addition, we did sensitivity analyses excluding participants who died within 6 months of start of follow-up; these showed similar results.

Nevertheless, we cannot exclude the possibility that the weight loss occurred concomitantly with declines in grip strength and physical functioning and both are an indication of impending cardiovascular and mortality events. Strengths of our study included the long-term follow-up of a large, multi-ethnic cohort of older women with well-characterized phenotypes. Also, our study included women with varying weights, whereas previous intervention studies focused on obese participants and was large with more than 5,000 participants. In addition, we looked at two different measures of physical functioning, grip strength as well as a composite score of balance, gait speed and chair stands, that reflect different capabilities.

In conclusion, the results of this study indicated that long-term weight loss in this older population of women was associated with higher mortality and cardiovascular events. Furthermore, both higher physical functioning and higher grip strength were associated with lower mortality and lower risk of cardiovascular events independent of weight change. Although the present study could not determine causality since it is an observational design, these findings support efforts to improve mobility and muscle strength in older women and suggest that focusing on weight loss in older women needs to be re-considered.

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Key Points

- Increased mortality was seen with weight loss
- Higher grip strength was associated with lower mortality independent of weight change
- Higher SPPB scores are associated with lower mortality independent of weight change.

Why does this matter?

Efforts should be made to improve mobility and muscle strength in older women rather than weight loss.

Table 1:

Selected Demographic Variables, Grip Strength and Functional Status by Weight Change

Variable	Weight Loss	Weight Stable	Weight Gain
Total n	2522	1796	1005
Demographics			
Age, mean (SD)	80.6 (6.6)	77.75 (6.7)	75.98 (6.8)
Black%	28.1%	35.0%	40.7%
Hispanic%	14.4%	18.0%	21.0%
White%	57.5%	47%	38.3%
Smoking			
Never Smoked	57.7%	57.1%	52.7%
Past Smoker	37.0%	37.9%	37.7%
Current Smoker	5.3%	5.0%	9.6%
Drinks per Week	2.2 (4.7)	2.1 (4.6)	1.9 (5.0)
Disease History			
History Stroke (%yes)	3.7%	3.5%	3.0%
History CHD (%yes)	6.6%	4.9%	4.3%
History CVD (%yes)	21.9%	19.1%	19.7%
Blood Pressure			
Systolic BP	125.4(15.0)	126.1(14.4)	125.8 (13.7)
Diastolic BP	71.7(9.0)	73.3(8.7)	73.5(8.6)
History Diabetes (%yes)	22.0%	18.0%	16.4%
Body Mass Index (kg/m2)			
BMI	26.5 (5.4)	28.7 +/− 5.6	31.0 +/− 5.9
Change weight[a]	−25.3 (24.7)	−0.8 (4.7)	18.9 (11.2)
WC[b] (inches)	34.4 ± 5.4	35.8 ± 5.4	37.4 ± 5.1
Physical Function Measures			
SPPB[c]	4.3 ± 3.4	8.4 ± 2.6	8.3 ± 2.5
Grip strength[d]	17.0 ± 7.1	18.5 ± 7.1	19.5± 7.4

[a.] Represents change from baseline value to time of grip strength measurement

[b.] Waist circumference

[c.] Considers total balance score, chair stand score, and gait speed score

[d.] Represents maximal grip strength measure.

Table 2

Hazard Ratio of Weight Change and Mortality

Whole Cohort	N/n	Stable Weight	Weight Loss	Weight Gain
Model 1[a]	4999/692	1	1.66 (1.39–1.99)	0.99 (0.75–1.32)
Model 2[b]	4910/679	1	1.61 (1.34–1.93)	1.00 (0.76–1.33)
Model 3[c]	4714/640	1	1.66 (1.37–2.01)	0.97 (0.72–1.30)

[a] adjusted for age and weight change

[b] adjusted for age, weight change, grip strength, race/ethnicity, smoking, education

[c] adjusted for age, weight change, SPPB, race/ethnicity, smoking, education, history of CHD, stroke and diabetes

Table 3:

Hazard Ratio for Mortality and Grip Strength and SPPB

Parameters	N/n	Q1	Q2	Q3	Q4
GRIP STRENGTH[a]	4910/679	1	0.72 (0.59–0.87)	0.68 (0.55–0.83)	0.51 (0.39–0.66)
SPPB[a]	4714/640	1	0.65 (0.53–0.79)	0.42 (0.33–0.53)	0.29 (0.21–0.40)

a. Controlling for age, weight change, race, smoking, history of CHD, stroke, diabetes

Table 4

Hazard ratios of death in highest quartile of grip strength compared to lowest quartile, in subgroups

	Subgroup	N	Events	HR	95%CI
Age					
	<75	1555	49	0.80	(0.33–1.96)
	>= 75	3355	630	0.49	(0.37–0.65)
Self-reported race					
	Black	1624	125	0.59	(0.36–0.97)
	White	2473	506	0.46	(0.33–0.64)
Diabetes *					
	Yes	950	173	0.56	(0.33–0.94)
	No	3960	508	0.49	(0.36–0.66)
History of CVD **					
	Yes	988	220	0.5	(0.31–0.82)
	No	3922	459	0.52	(0.38–0.71)

* Defined as self-report of diabetes or being on treatment for diabetes with insulin or pills before grip strength measurmenrts

** History of CVD defined as myocardial infarction or stroke or TIA or revascularization before grip strength measurements

Table 5:

Hazard Radio for Vascular Disease and Grip Strength and SPPB

Parameter	N/n	Q1	Q2	Q3	Q4
Grip Strength [a]					
Vascular Death	4833/310	1	0.90 (0.68–1.19)	0.72 (0.52–0.99)	0.69 (0.48–1.00)
CHD	4910/188	1	0.58–1.22	0.78 (0.53–1.15)	0.56 (0.35–0.89)
Stroke	4910/189	1	1.04 (0.70–1.53)	0.98 (0.65–1.46)	0.89 (0.58–1.38)
SPPB [a]					
Vascular Death	4640/292	1	0.62 (0.47–0.81)	0.40 (0.29–0.56)	0.17(0.10–0.30)
CHD	4714/183	1	0.75 (0.52–1.09)	0.68 (0.46–1.10)	0.46 (0.27–0.77)
Stroke	4714/184	1	0.78 (0.53–1.14)	0.78 (0.53–1.15)	0.61 (0.38–0.99)

[a.] Controlling for age, weight change, race, smoking, history of CHD, Stroke, diabetes