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Special Article

Physical Functioning Among Women Aged 80 Years and Older With Previous Fracture

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Abstract

Background. The oldest old are the fastest growing segment of the elderly population. Little is known regarding the associations of fracture history with physical functioning assessed after age 80.

Methods. Among 33,386 women surviving to age 80 years (mean ± *SD* years 84.6 ± 3.4), we examined the relationship between history of incident fracture after entry into the Women's Health Initiative (follow-up 15.2 ± 1.3 years) and their physical functioning assessed using the RAND-36 instrument most proximal to 2012 end of follow-up.

Results. Baseline mean (±*SD*) physical function score was 82 (±18). After adjustment for demographic and medical characteristics, fracture at each site, including hip, upper limb, lower limb, and central body, was associated with significantly lower subsequent physical functioning (all $p < .001$). Hip, upper leg, spine, and pelvis fractures were particularly related with lower physical functioning scores, 11.7 (95% CI: 10.3, 13.1), 10.5 (8.8, 12.3), 9.8 (8.9, 10.8), and 8.7 (7.2, 10.2) units lower, respectively, compared with women without fracture (each $p < .0001$). Compared with women without central site fracture, women with central site fractures also had lower physical functioning scores (10.0 [9.3, 10.8] units lower]; $p < .0001$). In case-only analysis of fractures, older age, less than 1 year since fracture, one or more additional sites fractured, history of cardiovascular disease or cancer, higher body mass index, and no alcohol intake in the past 3 months also were independent predictors of lower physical functioning score (all $p < .05$).

Conclusions. Among women surviving to 80 years and older, prior fracture is associated with lower current physical functioning, regardless of anatomical site of fracture, independent of other major predictors of disability.

Key Words: Frailty—Fracture—Physical function

Osteoporosis is a major public health problem that is associated with a high morbidity and mortality (1,2). Presently, osteoporosis and low bone mass at the femoral neck or lumbar spine affects 53.6 million U.S. adults aged 50 years and older (3). Fracture is a major clinical manifestation of osteoporosis that predisposes to prolonged functional disability. Among adults aged 50 and older who are hospitalized for hip fracture, only about one-third regain their prior level of function 6 months post-fracture (4). Vertebral fractures are also associated with decreased physical function among women older than 50 years of age (5,6). Over half of persons who have had wrist fracture report only fair to poor physical functioning 6 months post-fracture (7). In the United States, 7% of survivors of all types of fracture have some degree of permanent disability, and 8% require nursing home care (7,8). It is estimated that a 50-year-old White American woman has a 13% chance of having decline in physical functioning after any fracture (7,9).

Virtually, all nations in the world are experiencing growth in the number of resident's aged 65 years and older. However, an important feature of population aging is that the older population is getting older. In developed countries, the oldest old (≥80 years of age) accounted for 26% of those aged 65 years in 2008. The percentage of the world's population that is older than 85 years of age will increase by 300% from 2005 to 2040 (10). Physical functioning limitations and associated reductions in functional independence and quality of life among the oldest old who have previously experienced fractures will be an increasing public health burden. Although one study has estimated fracture incidence by anatomical location in U.S. women aged 80 years and older (11), studies have not focused on how physical functioning may be impacted by fractures at different anatomical locations among U.S. women aged 80 years and older. In this increasingly common age group where physical functioning is important for independence, quality of life, and health care costs, little is known about the effect on physical functioning of fractures in general as well as effects of site-specific fractures.

We used data from the subset of participants of the Women's Health Initiative (WHI) Study who survived to 80 years or older. In these women, we assessed whether incident fracture occurring since enrollment during WHI follow-up to 2012 was associated with physical functioning score assessed most proximal to 2012. We tested the hypothesis that those who experienced incident fracture since study entry would have lower physical functioning than those who had not experienced fracture, and that this association would be evident for hip fracture and each of the other fracture sites evaluated. Using a case-only analysis, to identify other potentially relevant factors related with physical functioning subsequent to fracture, we also examined associations between selected cohort characteristics and physical functioning within subsets of site-specific fracture cases.

Methods

Participants

The WHI study is a multicenter study of women aged 50–79 years at baseline and is composed of several clinical trials and a large observational study (12,13). Eligible participants, recruited between 1993 and 1998, were aged 50–79 years, postmenopausal, and free from serious medical conditions (eg, severe chronic heart, liver, kidney, or lung disease) (12,14). The WHI Clinical Trials (WHI-CT) consisted of randomized controlled evaluation of three distinct interventions: a low-fat eating pattern, menopausal hormone therapy, and calcium and vitamin D supplementation (13). For the WHI Hormone Therapy Trials, women with intact uterus were randomized to receive placebo or conjugated equine estrogen with medroxyprogesterone acetate, and women with a prior hysterectomy were randomized to receive placebo or conjugated equine estrogen alone. Women were initially enrolled in the Hormone Trials and/or Dietary Modification Trial at baseline. One year later, women were asked to join the Calcium/Vitamin D Trial. The WHI Observational study (WHI-OS) was designed to explore the predictors and natural history of important causes of morbidity and mortality in postmenopausal women and enrolled 93,676 women representing diverse ethnicities to reflect the minority representation of the U.S. population (14).

At baseline entry into the WHI studies, self-administered questionnaires were used to collect the following information: race/ethnicity, education, history of fracture prior to WHI enrollment, and parental history of hip fracture. Height, weight, and waist circumference were directly measured at baseline using standardized protocols (15). Body mass index (BMI; kg/m^2) was calculated using height measured at baseline and weight. At baseline and annually thereafter, questions were asked regarding: smoking history, alcohol use during the past 3 months, menopausal hormone therapy use during the past year, usual recreational physical activity, social support, living alone, self-rated general health, fall frequency during the past year, and history of diagnosed cardiovascular disease (CVD), cancer, and treated diabetes mellitus (15). Each institution obtained human subjects committee approval, and participants provided written informed consent for all study activities.

For the current study, we analyzed data through the WHI data release cutoff of September 17, 2012 from all active WHI-OS and WHI-CT participants who achieved the age of 80 and for whom at least one measure of the physical functioning subscale of the RAND 36-Item Health Survey (SF-36) was collected after age 80. The analytic sample for this study consisted of 33,386 women who survived to 80 years of age and older, had at least one assessment for incident fractures between WHI baseline and 2012, and had at least one physical functioning assessment after age 80 (subsequent to the fracture, in participants who experienced fracture).

Fracture Assessment

Fracture was a predesignated key outcome of both WHI-OS and WHI-CT. Information regarding the self-reported fracture "exposure" variables for this analysis was collected on health update questionnaires administered at least annually. Fractures were assessed using the question "Since last reporting date, has a doctor told you that you had a broken, fractured, or crushed bone?" If the respondent responded affirmatively to this question, she was asked to identify which bones were broken, selecting all responses that apply. The response choices were: hip, upper leg (not hip), pelvis, knee (patella), lower leg or ankle, foot (not toe), tailbone (coccyx), spine or back (vertebra), lower arm or wrist, hand (not finger), elbow, upper arm or shoulder, or other (specify) (16).

Medical records were obtained for adjudication of all hip fractures among WHI-CT and WHI-OS participants during the main study through 2005. A subset of these women continued to have hip fracture adjudication through 2012. The agreement between self-report and medical-record-confirmed fractures among WHI participants has been previously examined. Agreements for single-site fractures and medical records were high for hip (78%) and forearm/wrist (81%) but relatively lower for clinical spine fractures (51%) (16). The average duration of follow-up for fractures was 15.2 years (*SD* 1.3 years). For these analyses, self-reported fractures occurring between baseline enrollment into WHI through 2012 and before the date of last physical functioning assessment were included.

Physical Functioning

The physical functioning subscale of the RAND 36-item health survey (SF-36) (17) was our main outcome measure. This subscale asks respondents to rate their degree of limitation in doing the following activities: (i) vigorous activities such as running, lifting heavy objects, or participating in strenuous sports; (ii) moderate activities such as moving a table, pushing a vacuum cleaner, bowling, or playing golf; (iii) lifting or carrying groceries; (iv) climbing several flights of stairs; (v) climbing one flight of stairs; (vi) bending, kneeling, or stooping; (vii) walking more than a mile; (viii) walking several blocks; (ix) walking 1 block; and (x) bathing or dressing yourself. Values on this subscale range from 0 to 100; higher scores indicate better functioning. The SF-36 physical functioning score was assessed annually. For statistical analyses, we used the data from the last SF-36 available (closest to September, 2012).

Statistical Analyses

Women were categorized with respect to presence versus absence of fracture occurring since WHI baseline enrollment. These were initially considered by anatomical site of fracture. A variable for site-specific fracture was created for each of the following fracture types: hip, pelvis, spine, elbow, hand, lower arm, upper arm, foot, knee, upper leg, and lower leg. Combined fracture categories were created for the following three anatomical regions: incident upper limb fracture (one or more of elbow, hand, lower arm, and upper arm fracture), lower limb fracture (one or more of foot, knee, upper leg, and lower leg fracture), and central body fracture (one or more of hip, pelvis, and spine fracture).

WHI screening (baseline) and current (post-baseline) measures were summarized by quintiles of physical functioning score and by incident hip fracture status (yes, no) using counts and percentages, or using medians, interquartile ranges, means and *SD*s. Incident fracture categories also were summarized by quintiles of physical functioning by the same approach.

For comparison, the referent group for each analysis on fracture site was defined as all women who did not experience the fracture at that anatomical site or region. For example, for pelvis fracture, the comparison group was women with no pelvis fracture, but nonpelvic fractures were included in the reference group. Differences between anatomical sites or regions were tested using chi-square tests or analysis of variance. Effects of incident fracture site/region on physical functioning were assessed in both unadjusted and adjusted analyses using linear regression models. Adjusted models included the following covariates: race/ethnicity, current age, current age^2, current BMI, current BMI^2, current history of CVD or treated diabetes, education level, baseline SF-36 physical function score, history of stroke, an indicator of participation in WHI Clinical Trial or Observational Study, and indicators of participation and treatment arm in the WHI Hormone Trials. Covariate selection was guided by observed relationships with physical functioning and fracture and by published findings of other studies. When a covariate had multiple assessments available in WHI, we used the value closest in time to the current physical functioning measure. Results are presented as absolute physical function score differences with associated 95% CIs for unadjusted and adjusted linear regression models. Also, mean SF-36 physical functioning scores and 95% CIs for each fracture site, and for no fracture and no hip fracture, were calculated and presented graphically.

In case-only analysis, using multiple linear regression models, we assessed within categories of hip fracture, central fracture, upper limb fracture, and lower limb fracture, the independent associations of personal characteristics including age, time since fracture (<1 year, 1–<5 years, 5–<10 years, ≥10 years), the occurrence of multiple fractures in a given participant, U.S. region, race/ethnicity, baseline SF-36 physical function score, history of treated diabetes, history of CVD, history of cancer, education level, BMI, smoking status, and alcohol intake with physical functioning score. Physical functioning score differences and 95% CIs are presented. The results of analyses according to each individual fracture site are presented in a Supplementary Table.

For hypothesis tests, p less than or equal to .05 (two-sided) was considered statistically significant and was not adjusted for multiple comparisons; some results could reach significance by chance alone. Analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

Participant Characteristics

Participant characteristics for the subcohort of WHI women 80 years and older according to quintiles of physical functioning score and hip fracture during WHI follow-up are described in Table 1. Among these women, the mean (±*SD*) time in the WHI since enrollment was 15.2 (±1.3) years with a range of 8–18 years. History of any fracture and hip fracture at age 55 or older at WHI enrollment were reported by 22% and 0.91% of women, respectively. At baseline, the mean (±*SD*) physical function score was 82 (±18). At the time of physical functioning assessment used in these analyses, mean age was 84.6 (±3.4) years and mean physical functioning score was 57 (±28). Based on assessments closest to the time of their physical functioning assessment, the majority of these women reported never smoking, while 44% and 1% reported being former and current smokers, respectively. Nearly 50% of women reported living alone, 58% were overweight or obese, 22% had a history of diagnosed CVD, 22% had a history of diagnosed cancer, 13% reported being treated for diabetes, and 8% reported using menopausal hormone therapy in the past year.

Several factors assessed nearest to the time of physical functioning assessment were related to the physical functioning score. Older age, higher BMI, history of CVD, history of cancer, history of treated diabetes, weight loss more than 10 pounds in past year, and history of recent falls were inversely related to physical functioning score ($p < .0001$). Alcohol intake, menopausal hormone use in past year, and recreational physical activity level were positively related to physical functioning ($p < .0001$). At the time of physical functioning assessment, participants who experienced a hip fracture after WHI enrollment were more likely to be White, older, normal or underweight, to have a history of CVD, recent falls, parental history of hip fracture, history of no menopausal hormone use in the past year, and to have lower self-rated health, lower recreational physical activity, and lower physical functioning than those not reporting hip fracture ($p < .01$).

Physical Functioning Score According to Fractures During WHI Follow-up

At least one fracture was reported by 34% of women in the subcohort 80 years and older after WHI enrollment and during follow-up. Table 2 shows the distribution of fractures occurring after WHI enrollment overall and according to quintiles of physical functioning score. Overall, the most common reported fracture site was lower arm (9.6%), followed by the spine (7.3%), lower leg (5.5%), upper arm (5.2%), and foot (5.1%), respectively. Hip fracture was reported in 3.4% of women. For anatomical region, corresponding percentages were seen for central body (12%), upper (16%), and lower (14%) limbs. Significant ($p < .05$) inverse associations with

Table 1. Characteristics of the Subgroup of WHI Study Participants Achieving the Age of 80 or Older According to Tertiles of SF-36 Physical Functioning Score and According to Hip Fracture Status*

	All (n = 33,386)	Physical Functioning SF-36 Score†				Incident Hip Fracture		
		Tertile 1 (n = 10,729)	Tertile 2 (n = 10,771)	Tertile 3 (n = 11,886)	Overall p‡	No (n = 32,247)	Yes (n = 1,139)	Overall p§
Physical Functioning Score at age 80 y or older at the last (most recent) assessment, median (IQR)	60 (35, 80)	25 (15,35)	60 (50, 65)	85 (80, 95)		60 (35, 80)	40 (20,65)	<.0001
Mean ± *SD*	57 ± 28	24 ± 12	58 ± 8.5	86 ± 8.0		58 ± 27	43 ± 28	
Min., max.	0, 100	0, 44.4	45.0, 72.2	75.0, 100		0, 100	0, 100	
Time in the WHI (y)	15 (14,16)	15 (14,16)	15 (14,16)	15 (14,16)	.040	15 (14,16)	15 (14,16)	.35
Mean ± *SD*	15 ± 1.3	15 ± 1.3	15 ± 1.3	15 ± 1.3		15 ± 1.3	15 ± 1.4	
Min., max.	7.8, 18	7.8, 18	8.0, 18	8.8, 18		7.8, 18	9.9, 18	
Enrolled in OS	19,358 (58)	6,175 (58)	6,219 (58)	6,964 (59)	.24	18,721 (58)	637 (56)	.15
Hormone therapy trial					<.0001			.042
CEE + MPA trial	3,662 (11)	1,054 (9.8)	1,188 (11)	1,420 (12)		3,511 (11)	151 (13)	
CEE-alone trial	2,194 (6.6)	837 (7.8)	678 (6.3)	679 (5.7)		2,122 (6.6)	72 (6.3)	
Dietary modification	9,745 (29)	3,182 (30)	3,200 (30)	3,363 (28)	.028	9,401 (29)	344 (30)	.44
Calcium + vitamin D	7,906 (24)	2,509 (23)	2,573 (24)	2,824 (24)	.67	7,637 (24)	269 (24)	.96
Measures at WHI baseline enrollment								
Race/ethnicity					<.0001			<.0001
White	30,297 (91)	9,783 (91)	9,772 (91)	10,742 (90)		29,202 (91)	1,095 (96)	
Black	1,484 (4.4)	514 (4.8)	488 (4.5)	482 (4.1)		1,467 (4.6)	17 (1.5)	
Hispanic	534 (1.6)	149 (1.4)	170 (1.6)	215 (1.8)		526 (1.6)	8 (0.70)	
Asian/Pacific Islander	589 (1.8)	135 (1.3)	190 (1.8)	264 (2.2)		582 (1.8)	7 (0.61)	
Other/unknown	482 (1.4)	148 (1.4)	151 (1.4)	183 (1.5)		470 (1.5)	12 (1.1)	
Age, mean ± *SD* (y)	69 ± 3.6	70 ± 3.8	69 ± 3.5	68 ± 3.2	<.0001	69 ± 3.5	70 ± 3.8	<.0001
Age group (y)					<.0001			<.0001
<65	2,778 (8.3)	616 (5.7)	885 (8.2)	1,277 (11)		2,724 (8.5)	54 (4.7)	
65–69	17,541 (53)	4,877 (45)	5,653 (52)	7,011 (59)		17,104 (53)	437 (38)	
70–74	10,238 (31)	3,818 (36)	3,378 (31)	3,042 (26)		9,788 (30)	450 (40)	
≥75	2,829 (8.5)	1,418 (13)	855 (7.9)	556 (4.7)		2,631 (8.2)	198 (17)	
BMI (kg/m^2)	26 (24,30)	28 (25,32)	26 (24,30)	25 (23,28)	<.0001	26 (24,30)	26 (23,29)	<.0001
BMI group					<.0001			<.0001
<25	12,637 (38)	2,750 (26)	3,898 (37)	5,989 (51)		12,127 (38)	510 (45)	
25–<30	12,320 (37)	3,878 (36)	4,254 (40)	4,188 (36)		11,913 (37)	407 (36)	
≥30	8,145 (25)	4,012 (38)	2,525 (24)	1,608 (14)		7,929 (25)	216 (19)	
Waist circumference (cm)	84 (76, 93)	89 (80, 98)	84 (77, 92)	80 (74, 88)	<.0001	84 (76, 93)	84 (75,93)	.19
Ever treated for diabetes	880 (2.6)	493 (4.6)	223 (2.1)	164 (1.4)	<.0001	840 (2.6)	40 (3.5)	.061
History of CVD	2,952 (9.0)	1,309 (12)	956 (9.0)	687 (5.9)	<.0001	2,824 (8.9)	128 (11)	.0038
History of stroke	969 (2.9)	438 (4.1)	291 (2.7)	240 (2.0)	<.0001	923 (2.9)	46 (4.1)	.020
History of cancer	3,235 (9.8)	1,183 (11)	1,043 (9.8)	1,009 (8.6)	<.0001	3,115 (9.8)	120 (11)	.33
Fracture at age ≥55 y	6,527 (22)	2,315 (25)	2,071 (22)	2,141 (21)	<.0001	6,205 (22)	322 (34)	<.0001
Hip fracture at age ≥55 y	262 (0.91)	112 (1.2)	80 (0.86)	70 (0.68)	.0003	243 (0.88)	19 (2.1)	.0001
Parental hip fracture	5,070 (19)	1,588 (19)	1,628 (19)	1,854 (19)	.48	4,825 (19)	245 (27)	<.0001
Education > HS or GED	26,299 (79)	8,139 (76)	8,541 (80)	9,619 (81)	<.0001	25,387 (79)	912 (80)	.27

Table 1. *Continued*

	All (n = 33,386)	Physical Functioning SF-36 Score†				Incident Hip Fracture		
		Tertile 1 (n = 10,729)	Tertile 2 (n = 10,771)	Tertile 3 (n = 11,886)	Overall p‡	No (n = 32,247)	Yes (n = 1,139)	Overall p§
Physical Functioning Score	90 (75, 95)	75 (60, 90)	85 (75, 95)	95 (85, 100)	<.0001	90 (75, 95)	85 (70, 95)	<.0001
Mean ± *SD*	82 ± 18	72 ± 21	83 ± 15	91 ± 11		82 ± 18	80 ± 18	
Min., max.	0, 100	0, 100	0, 100	0, 100		0, 100	0, 100	
Measures closest to the most recent SF-36 assessment								
Age, mean ± *SD* (y)	85 ± 3.4	85 ± 3.6	85 ± 3.3	84 ± 3.0	<.0001	85 ± 3.3	86 ± 3.7	<.0001
Age group (y)					<.0001			<.0001
80–84	19,915 (60)	5,285 (49)	6,434 (60)	8,196 (69)		19,441 (60)	474 (42)	
85–89	10,634 (32)	4,001 (37)	3,484 (32)	3,149 (26)		10,170 (32)	464 (41)	
≥90	2,837 (8.5)	1,443 (13)	853 (7.9)	541 (4.6)		2,636 (8.2)	201 (18)	
BMI (kg/m^2)	26 (23,29)	28 (24,32)	26 (23,29)	24 (22,27)	<.0001	26 (23,29)	24 (22,28)	<.0001
BMI group					<.0001			<.0001
<25	14,011 (42)	3,175 (30)	4,294 (40)	6,542 (55)		13,402 (42)	609 (54)	
25–<30	11,903 (36)	3,834 (36)	4,129 (39)	3,940 (33)		11,555 (36)	348 (31)	
≥30	7,266 (22)	3,652 (34)	2,280 (21)	1,334 (11)		7,089 (22)	177 (16)	
Smoking					.028			.18
Never	18,214 (55)	5,793 (54)	5,834 (54)	6,587 (56)		17,570 (55)	644 (57)	
Past	14,556 (44)	4,717 (44)	4,754 (44)	5,085 (43)		14,084 (44)	472 (42)	
Current	405 (1.2)	152 (1.4)	123 (1.2)	130 (1.1)		387 (1.2)	18 (1.6)	
Alcohol past 3 months					<.0001			.085
Never	9,872 (36)	4,032 (47)	3,028 (34)	2,812 (29)		9,534 (36)	338 (40)	
<1 time/wk	8,560 (31)	2,627 (31)	2,895 (32)	3,038 (31)		8,316 (31)	244 (29)	
1–2 times/wk	2,906 (11)	680 (7.9)	1,021 (11)	1,205 (12)		2,821 (11)	85 (10)	
3–4 times/wk	1,839 (6.7)	379 (4.4)	624 (7.0)	836 (8.5)		1,790 (6.8)	49 (5.8)	
5–6 times/wk	1,813 (6.6)	373 (4.3)	585 (6.6)	855 (8.7)		1,768 (6.7)	45 (5.4)	
Every day	2,358 (8.6)	506 (5.9)	784 (8.8)	1,068 (11)		2,278 (8.6)	80 (9.5)	
Used hormones past year	2,307 (8.2)	619 (7.0)	777 (8.4)	911 (9.0)	<.0001	2,254 (8.2)	53 (5.9)	.046
Treatment for diabetes	4,241 (13)	1,881 (18)	1,320 (12)	1,040 (8.8)	<.0001	4,103 (13)	138 (12)	.54
History of CVD	7,366 (22)	3,342 (32)	2,337 (22)	1,687 (14)	<.0001	7,057 (22)	309 (27)	<.0001
History of cancer	7,457 (22)	2,694 (25)	2,429 (23)	2,334 (20)	<.0001	7,178 (22)	279 (25)	.075
Lost ≥10 pounds in past year	5,501 (20)	2,367 (28)	1,735 (19)	1,399 (14)	<.0001	5,314 (20)	187 (22)	.13
Falls since last update					<.0001			<.0001
None	20,282 (61)	5,537 (52)	6,494 (61)	8,251 (70)		19,659 (62)	623 (56)	
1	7,355 (22)	2,456 (23)	2,529 (24)	2,370 (20)		7,106 (22)	249 (22)	
2	3,383 (10)	1,446 (14)	1,110 (10)	827 (7.0)		3,250 (10)	133 (12)	
≥3	2,006 (6.1)	1,163 (11)	521 (4.9)	322 (2.7)		1,891 (5.9)	115 (10)	
Total recreational physical activity (min/wk)	75 (0, 210)	0 (0, 75)	75 (10, 180)	175 (75, 300)	<.0001	75 (0, 210)	37 (0,150)	<.0001
Self-rated health					<.0001			<.0001
Excellent/very good	14,546 (44)	1,956 (18)	4,312 (40)	8,278 (70)		14,176 (44)	370 (32)	
Good	13,906 (42)	5,214 (49)	5,411 (50)	3,281 (28)		13,379 (41)	527 (46)	

Table 1. *Continued*

	All (n = 33,386)	Physical Functioning SF-36 Score†				Incident Hip Fracture		
		Tertile 1 (n = 10,729)	Tertile 2 (n = 10,771)	Tertile 3 (n = 11,886)	Overall p‡	No (n = 32,247)	Yes (n = 1,139)	Overall p§
Fair/poor	4,931 (15)	3,558 (33)	1,048 (9.7)	325 (2.7)		4,689 (15)	242 (21)	
Living alone	16,410 (49)	5,160 (48)	5,362 (50)	5,888 (50)	.029	15,856 (49)	554 (49)	.76
MOS social support	38 (32,43)	37 (31,43)	38 (32,43)	39 (33,44)	<.0001	38 (32,43)	38 (32,43)	.65

Notes: BMI = body mass index; CEE = conjugated equine estrogen; CVD = cardiovascular disease; GED = general equivalency diploma; HS = higher secondary; IQR = interquartile range; MOS = Medical Outcomes Study; MPA = medroxyprogesterone acetate; OS = observational study; WHI = Women's Health Initiative Study.

*Count (column %) or median (IQR) unless otherwise noted.

†Physical functioning groups were divided based on tertiles; ties were assigned to the higher of the two groups.

‡Overall p for association between the characteristic and physical functioning as calculated by chi-squared test (discrete characteristics) or analysis of variance (continuous characteristics).

§Overall p for comparison of the characteristic between women with and without incident hip fracture as calculated by chi-squared test (discrete characteristics) or two-sample t-test (continuous characteristics).

incidence of each fracture were seen across incremental quintiles of subsequent physical functioning score for each individual site as well as each anatomical region, except for elbow (p value .07). Particularly, steep inverse gradients were seen for fracture at the spine, upper arm, pelvis and hip, and the combined central body region (p < .0001, each).

Unadjusted and Adjusted Differences in Physical Function Score According to History of Fracture

To further explore these relationships, we calculated the difference in physical functioning scores for each fracture site and anatomical region in unadjusted and adjusted models (Table 3). Covariates included in adjusted models were age, race/ethnicity, BMI, and history of CVD, treated diabetes, indicator of participant in WHI Clinical Trial or Observational Study, baseline SF-36 score, education level, and history of stroke. For hip fracture (compared with no hip fracture), there was a difference of 11.7 (95% CI: 10.3, 13.1) units in SF-36 score. Except for the hand, each fracture site was associated with a poorer physical function score with the greatest differences seen for the upper leg (−10.5), spine (−9.8), pelvis (−8.7), and combined central body sites (−10.0) in adjusted models as compared with women without fracture at that site (p < .0001, each).

Associations Between Selected Participant Characteristics and Physical Function Score Among Participants Who Experienced Fracture During WHI Follow-up

In order to begin understanding factors that further contribute to physical functioning status in women who have experienced fracture, we examined relationships between physical functioning scores and selected participant characteristics in a case-only analysis for fractures of the hip, lower limb, upper limb, and combined central body (Table 4). Among women who experienced a hip fracture, following simultaneous adjustment for the other covariates, older age, history of CVD and cancer, higher BMI, and residence in the Southeast region were related with significantly ($p \le .01$) lower physical functioning scores. Alcohol intake one or more times/wk was associated with significantly (p < .05) higher physical functioning scores. Among women with a hip fracture, there was an 8.6 (95% CI: 6.5, 10.7) unit lower physical functioning score for each 5 year increase in age. Additionally, score differences in women with hip fracture were 5.5, 4.8, 5.4, and 6.1 units lower for those with history of CVD, cancer, higher BMI (per 5 kg/m^2), and living in the Southeast, respectively. Women drinking at least one time per week had physical functioning scores that were 8.5–13.9 units higher compared with never drinkers (p < .05). Similar associations were seen for the central, upper limb, and lower limb sites. Longer time since fracture was associated with modestly better physical functioning scores in women who had experienced fractures of the upper and lower limb sites and central body sites. Multiple fractures in a given participant was associated with worse physical functioning scores. Current and past smoking was associated with lower physical function scores among women who had experienced fractures of the upper and lower limbs, but not hip or central sites. Women who drank alcohol, compared with those who did not, had better physical functioning scores for central, upper limb, and lower limb sites. Physical functioning scores did not differ by race/ethnicity for any of the fracture sites. History of CVD and cancer were

Table 2. Distribution of Fractures Occurring During WHI Follow-up Among the Subset of Women Achieving 80 y or Older According to Tertiles of Physical Functioning Score*

Incident Fracture	All (n = 33,386)	SF-36 Physical Functioning Score at 80 y or older†			Overall p‡
		Tertile 1, range: 0–44.4 (n = 10,729)	Tertile 2, 45.0–72.2 (n = 10,771)	Tertile 3, 75.0–100 (n = 11,886)	
Hip fracture	1,139 (3.4)	604 (5.6)	322 (3.0)	213 (1.8)	<.0001
Other fracture					
Pelvis	998 (3.0)	452 (4.2)	287 (2.7)	259 (2.2)	<.0001
Spine	2,440 (7.3)	1,209 (11)	730 (6.8)	501 (4.2)	<.0001
Elbow	611 (1.8)	221 (2.1)	194 (1.8)	196 (1.7)	.068
Hand	555 (1.7)	204 (1.9)	173 (1.6)	178 (1.5)	.052
Lower arm	3,187 (9.6)	1,103 (10)	1,016 (9.4)	1,068 (9.0)	.0037
Upper arm	1,719 (5.2)	687 (6.4)	566 (5.3)	466 (3.9)	<.0001
Foot	1,707 (5.1)	624 (5.8)	534 (5.0)	549 (4.6)	.0002
Knee	943 (2.8)	349 (3.3)	321 (3.0)	273 (2.3)	<.0001
Upper leg	670 (2.0)	342 (3.2)	200 (1.9)	128 (1.1)	<.0001
Lower leg	1,829 (5.5)	670 (6.2)	599 (5.6)	560 (4.7)	<.0001
Any fracture§					
Central body	4,148 (12)	1,998 (19)	1,235 (11)	915 (7.7)	<.0001
Upper limb	5,328 (16)	1,900 (18)	1,720 (16)	1,708 (14)	<.0001
Lower limb	4,610 (14)	1,751 (16)	1,484 (14)	1,375 (12)	<.0001
None¶	22,173 (66)	6,405 (60)	7,197 (67)	8,571 (72)	<.0001

Notes: WHI = Women's Health Initiative Study.

*Count (column %).

†Physical functioning groups were divided based on tertiles; ties were assigned to the higher of the two groups.

‡Overall p for comparison of physical functioning between women with and without the incident fracture as calculated by chi-squared test.

§Central body fracture is one or more of hip, pelvis, and spine fracture; upper limb fracture is one or more of elbow, hand, lower arm, and upper arm fracture; and lower limb fracture is one or more of foot, knee, upper leg, and lower leg fracture.

¶Absence of a fracture is defined as no fracture of the hip, pelvis, spine, elbow, hand, lower arm, upper arm, foot, knee, upper leg, or lower leg during time in the WHI.

Table 3. Difference in SF-36 Physical Functioning Score According History of Fracture During WHI Follow-up in the Subset of Participants Achieving 80 y or Older*

	Unadjusted		Adjusted†	
Effect	Score Difference (95% CI)	p Value	Score Difference (95% CI)	p Value
Hip fracture	−15.1 (−16.7, −13.5)	<.0001	−11.7 (−13.1, −10.3)	<.0001
Other fracture				
Pelvis	−9.08 (−10.8, −7.35)	<.0001	−8.69 (−10.2, −7.21)	<.0001
Spine	−12.9 (−14.0, −11.7)	<.0001	−9.81 (−10.8, −8.85)	<.0001
Elbow	−2.57 (−4.78, −0.366)	.022	−2.41 (−4.29, −0.535)	.012
Hand	−3.17 (−5.48, −0.861)	.0072	−0.985 (−2.98, 1.01)	.33
Lower arm	−1.90 (−2.91, −0.896)	.0002	−2.12 (−2.98, −1.26)	<.0001
Upper arm	−6.63 (−7.97, −5.30)	<.0001	−4.04 (−5.18, −2.89)	<.0001
Foot	−2.99 (−4.33, −1.65)	<.0001	−2.12 (−3.26, −0.969)	.0003
Knee	−3.90 (−5.68, −2.12)	<.0001	−3.20 (−4.73, −1.67)	<.0001
Upper leg	−14.1 (−16.2, −12.0)	<.0001	−10.5 (−12.3, −8.76)	<.0001
Lower leg	−3.83 (−5.13, −2.53)	<.0001	−1.92 (−3.03, −0.809)	.0007
Any fracture§				
Central body	−12.5 (−13.4, −11.6)	<.0001	−10.0 (−10.8, −9.28)	<.0001
Upper limb	−3.17 (−3.98, −2.36)	<.0001	−2.51 (−3.20, −1.82)	<.0001
Lower limb	−4.90 (−5.75, −4.04)	<.0001	−3.30 (−4.04, −2.57)	<.0001

Notes: WHI = Women's Health Initiative Study.

*Score differences were derived using the coefficient for history of fracture from separate multiple linear regression models for each fracture site. Reference group is no history of fracture at that site during WHI follow-up.

†In adjusted models, the covariates include: race/ethnicity, education level, baseline physical functioning, indicator of participation in the WHI observational study, indicators of participation and trial arm in the WHI Hormone Therapy Clinical Trials, current age, current age^2, current body mass index (BMI), current BMI^2, history of stroke, current history of cardiovascular disease, and current receipt of treatment for diabetes. Sample size is n = 32,027 (<33,386) due to missing covariate values.

§Central body fracture is one or more of hip, pelvis, and spine fracture; upper limb fracture is one or more of elbow, hand, lower arm, and upper arm fracture; and lower limb fracture is one or more of foot, knee, upper leg, and lower leg fracture.

Table 4. Case-Only Analysis: Differences in SF-36 Physical Functioning Scores According to Personal Factors Within Case-Only Subsets of Hip Fracture and Fracture Site Groups in the Subset of WHI 80 y or Older*

Factor	Score Difference (95% CI) and Significance Tests*			
	Hip Fracture (n = 1,095)	Hip or Other Central Body Fracture (n = 3,970)	Upper Limb Fracture (n = 5,086)	Lower Limb Fracture (n = 4,401)
Age, y (differences are for a 5-y Δ in age)	−6.87 (−8.88, −4.87)¶	−6.45 (−7.53, −5.38)¶	−7.62 (−8.58, −6.66)¶	−6.55 (−7.59, −5.52)¶
Time since fracture, y		†	‡	¶
<1 y	Ref.	Ref.	Ref.	Ref.
1–< 5 y	11.3 (−1.98, 24.6)	1.60 (−0.684, 3.89)	1.79 (−0.346, 3.92)	3.97 (1.71, 6.23)§
5–< 10 y	12.1 (−1.18, 25.5)	2.83 (0.504, 5.16)†	2.93 (0.857, 5.01)‡	5.47 (3.26, 7.67)¶
≥10 y	12.6 (−1.04, 26.2)	4.07 (1.32, 6.82)‡	3.64 (1.54, 5.75)§	4.87 (2.65, 7.10)¶
Multiple fracture sites	−5.12 (−8.13, −2.11)§	−3.37 (−4.89, −1.86)¶	−6.16 (−7.47, −4.85)¶	−5.76 (−7.16, −4.36)¶
Region in United States				
Northeast	Ref.	Ref.	Ref.	Ref.
South	−4.00 (−8.32, 0.333)	−1.67 (−3.92, 0.585)	−0.946 (−2.85, 0.957)	−2.42 (−4.44, −0.403)
Midwest	0.564 (−3.59, 4.72)	0.986 (−1.18, 3.16)	−1.52 (−3.34, 0.290)	−2.21 (−4.18, −0.241)
West	−0.678 (−4.66, 3.30)	−0.214 (−2.27, 1.85)	−0.155 (−1.88, 1.57)	−1.15 (−3.03, 0.723)
Race/ethnicity				
White	Ref.	Ref.	Ref.	Ref.
Black	−2.81 (−15.0, 9.42)	4.03 (−2.94, 11.0)	3.87 (−0.839, 8.58)	3.91 (−0.221, 8.05)
Hispanic	3.96 (−14.3, 22.2)	2.57 (−5.73, 10.9)	−0.0344 (−5.40, 5.33)	4.97 (−2.21, 12.1)
Asian/Pacific Islander	−0.604 (−20.3, 19.1)	−2.50 (−10.2, 5.25)	−2.29 (−7.97, 3.40)	4.49 (−1.71, 10.7)
Other/unknown	2.76 (−11.2, 16.8)	3.28 (−3.35, 9.90)	2.99 (−2.41, 8.40)	0.623 (−5.51, 6.76)
Baseline physical functioning score (differences are for a 5-unit Δ in score)	2.60 (2.18, 3.02)¶	2.64 (2.42, 2.86)¶	2.65 (2.45, 2.84)¶	2.89 (2.69, 3.10)¶
Receiving treatment for diabetes	−2.80 (−7.37, 1.78)	−1.57 (−4.01, 0.874)	−3.47 (−5.50, −1.45)§	−1.91 (−3.96, 0.146)
History of CVD	−4.57 (−7.89, −1.24)‡	−5.76 (−7.50, −4.02)¶	−5.16 (−6.69, −3.62)¶	−6.62 (−8.23, −5.00)¶
History of cancer	−3.74 (−7.14, −0.335)†	−1.70 (−3.42, 0.0145)	−2.61 (−4.14, −1.09)§	−2.67 (−4.28, −1.06)‡
Education > HS or GED	1.82 (−1.91, 5.55)	1.51 (−0.455, 3.48)	0.801 (−0.830, 2.43)	−0.0430 (−1.81, 1.72)
BMI, kg/m² (differences are for a 5-unit Δ in BMI)	−2.86 (−4.53, −1.20)§	−3.19 (−4.03, −2.35)¶	−4.39 (−5.09, −3.70)¶	−3.64 (−4.37, −2.92)¶
Smoking			¶	§
Never	Ref.	Ref.	Ref.	Ref.
Past	−2.91 (−5.93, 0.107)	−1.63 (−3.19, −0.0775)	−2.58 (−3.92, −1.25)§	−2.65 (−4.08, −1.22)§
Current	−0.933 (−12.8, 11.0)	−2.11 (−9.44, 5.23)	−7.71 (−13.6, −1.81)†	−4.35 (−11.0, 2.26)
Alcohol past 3 months	†	¶	¶	¶
Never	Ref.	Ref.	Ref.	Ref.
< 1 time/wk	1.91 (−2.23, 6.06)	4.08 (2.01, 6.15)¶	6.02 (4.25, 7.79)¶	4.11 (2.22, 6.00)¶
1–2 times/wk	7.38 (1.35, 13.4)†	8.41 (5.45, 11.4)¶	8.84 (6.31, 11.4)¶	7.22 (4.54, 9.91)¶
3–4 times/wk	6.44 (−1.01, 13.9)	9.05 (5.30, 12.8)¶	9.84 (6.83, 12.9)¶	9.58 (6.35, 12.8)¶
5–6 times/wk	10.6 (2.83, 18.4)‡	10.4 (6.59, 14.2)¶	11.8 (8.85, 14.8)¶	6.01 (2.83, 9.18)§
Every day	6.79 (0.635, 12.9)†	5.60 (2.32, 8.88)§	8.58 (5.81, 11.4)¶	8.31 (5.35, 11.3)¶

Notes: BMI = body mass index; CVD = cardiovascular disease; GED = general equivalency diploma; HS = high school.

*Score differences were derived using the coefficients from separate multiple linear regression models for hip fracture and the fracture groups. Score differences, confidence intervals, and p values were calculated with simultaneous adjustment for all factors in the table. For each factor with more than two levels, an overall p value for comparison across the levels is reported, as are all p values for pairwise comparison to the reference level (ref.) when $p < .05$ overall. For levels of alcohol intake in the past 3 months, missing responses were combined to define an additional level (results not shown). The indicator for multiple fracture sites was determined based on number of sites among: hip, pelvis, spine, elbow, hand, lower arm, upper arm, foot, knee, upper leg, lower leg. Central body fracture is one or more of hip, pelvis, and spine fracture; upper limb fracture is one or more of elbow, hand, lower arm, and upper arm fracture; and lower limb fracture is one or more of foot, knee, upper leg, and lower leg fracture.

†$p < .05$.

‡$p < .01$.

§$p < .001$.

¶$p < .0001$.

associated with poorer physical functioning at each fracture site. Also, a history of CVD was associated with a 4.1–9.9 unit lower physical functioning score for all individual fracture sites (see Supplementary Table). Interestingly, history of treated diabetes was associated with significantly lower scores for fracture at the upper and lower limb. This was particularly apparent in the foot and lower arm sites. Additional information on individual fracture sites is displayed in the Supplementary Table.

Discussion

Functional impairment and physical disability are major public health concerns in an aging population (18). Declines in physical functioning among older women occur, in part, because of associations with reduced skeletal muscle mass and strength (19), greater sedentary behavior (20), presence of comorbidity (21), and menopause (22). Postmenopausal reductions in bone mineral density are associated with accelerated frequency of fractures at older ages (10). The extent to which postmenopausal fractures affect physical functioning at older ages has not been systematically studied. We examined this relationship in a large well-characterized cohort of postmenopausal women in whom a physical functioning assessment was obtained using the SF-36 instrument at age 80 or older and incident site-specific fractures since enrollment in the WHI were recorded through 2012. For every fracture site we examined, incidence since enrollment was significantly and inversely related with physical functioning scores at age 80 or older, with particularly strong relationships observed for hip, spine, upper leg, and pelvis fractures. After adjusting for relevant confounding factors, at every anatomical site we examined, significantly lower physical functioning scores were seen in women with fracture compared with women with no fracture, again with large effects seen at the hip, spine, upper leg, and pelvis. Analysis restricted to subsets of site-specific fracture cases revealed that older age, increasing BMI, and history of chronic diseases such as CVD, diabetes, and cancer were further associated with significantly lower physical functioning scores. To our knowledge, this is one of the largest and most comprehensive observational studies to evaluate the relationship between history of incident fracture and physical functioning after age 80.

The health consequences of fractures are enormous and they vary according to the different anatomic fracture sites. Following a hip fracture, 40% do not regain their ability to walk independently and 60% have limitations in activities of daily living (23). Women with hip fractures and very low vitamin D levels have reduced lower extremity physical performance measures 1 year post-fracture (24). Recovery of functional limitations varies following fractures (25). Spine fractures are associated with kyphosis, pain and discomfort, postural changes, functional impairments, and reduced quality of life (26,27). Pelvic fractures also cause pain, limitations in activities of daily living, and quality of life. Wrist fractures, in turn, can compromise activities of daily living, but in general are less incapacitating than hip or spine fractures (28). A recent multinational, 1-year prospective study in the Global Longitudinal study of Osteoporosis (GLOW; including North America) showed that spine, hip, and non-hip and non-spine fractures have effects on quality of life measures. Among 50,461 postmenopausal women including 1,822 fractures, in whom health-related quality of life was assessed using the EuroQol EQ-5D and SF-36, the greatest reductions in function and health status were following hip and spine fractures. Reductions in SF-36 physical functioning were identified for spine fractures and were borderline significant for fractures involving the pelvis/leg and shoulder/arm; spine fractures were most strongly negatively associated with EQ-5D score, followed by pelvis/leg and shoulder/arm and hip fractures. Thus, while decreases in function and health status were greatest for spine or hip fractures, other fractures also have detrimental effects on health-related, quality of life (29). In our current study, with 15 years of follow-up, incident fractures at the hip, upper leg, spine, and then pelvis were associated with markedly lower subsequent physical functioning scores, even though fracture may have occurred several years prior to age 80 when physical functioning was assessed.

The multiracial and ethnic cohort used in the present analysis is relevant since there are significant racial/ethnic differences in fracture rates (30). The impact of prior fractures on subsequent physical functioning in women 80 years and older is less clear with respect to potential racial/ethnic differences. Interestingly, we observed the significant association between fracture and subsequently lower physical function in all women in spite of the known lower fracture rates in U.S. minority populations in comparison to non-Hispanic Whites. A smaller number of hip fractures in minority groups, a limitation of this study, may have reduced our ability to detect the influence of race/ethnicity on physical functioning subsequent to prior fracture. Nevertheless, the consistency in the results across different fracture sites suggests that fracture prevention is important regardless of race/ethnicity because the functional consequences from fractures are seen for women from different racial/ethnic groups in the WHI. Further research is needed to clarify possible race/ethnic differences in fracture-related functional outcomes at advanced ages.

Our findings of lower physical functioning with higher BMI among women aged 80 years and older who have previously experienced fracture are consistent with the few existing studies. Although not focused on the oldest old, previous studies have linked greater degrees of weight loss with slower walking speed and weaker grip strength in the first year after hip fracture (31); associations are reported between greater BMI and longer recovery times after hip fracture (32).

It is plausible that pre-fracture conditions predisposed women to both fracture and CVD-related disability. In this scenario, fracture would be only a marker for risk of heart disease. A Swedish twins study suggests there are common genetically controlled risk factors for fracture and CVD (33). A cardiovascular event in one monozygotic sib predisposed, the unaffected one to a fracture. Heart failure, stroke, and peripheral arthrosclerosis all showed a greater relative risk of fracture than in dizygotic twins. A recent large U.S. cohort study found a high incidence of comorbidities in women with osteoporosis (34).

In this cohort of women aged 80 years and older, among women who reported prior fractures, higher alcohol use at study baseline was associated with higher subsequent physical function scores. To our knowledge, the associations between alcohol intake and physical function subsequent to fracture among women in this age group are unknown. One study of patients in an acute inpatient rehabilitation hospital (half of participants aged 80 years and older) reported that alcohol intake did not predict physical function after hip fracture (35). The effect of alcohol intake on fracture is complex and controversial (36,37). Some studies have found that low or moderate levels of alcohol intake are associated with higher bone mineral density levels (38,39), while higher levels of alcohol intake are associated with increased risk of fractures (39). Moreover, it is possible that alcohol intake earlier in life influences bone health after age 80 years. The WHI did not collect information regarding alcohol intake earlier in life. Aside from a direct effect of alcohol intake on bone metabolism, it is also possible that modest alcohol intake may be a surrogate indicator of better health, in part because there are fewer requests to avoid intake due to potential interactions with various conditions or medications. Low to moderate alcohol intake is associated with lower mortality (40), suggesting that alcohol intake may be a marker of better health. In the current study, baseline reported alcohol intake rates were very modest; only a small proportion of participants consumed more than one alcohol drink per day.

Strengths of this study include the large race/ethnically diverse cohort of women 80 years and older with a mean of 15 years follow-up, sufficient number of incident fractures at several sites for analysis, assessment of physical function with a standardized instrument used frequently in epidemiologic studies, and availability of information on various demographic and health factors for consideration as possible confounders. The low absolute number of non-White participants warrants caution in generalization of results among non-White women and in interpretation of findings specific to racial/ethnic groups. Additional limitations of this study are the generally healthy status of participants at study initiation with a higher socioeconomic status than the general population of women. Thus, we may not have been able to reliably examine fracture patterns and post-fracture sequelae at the lower range of socioeconomic status. Our study sample may not be representative of all U.S. women over age 80. Also, we could not rule out residual confounding due to the observational design of the WHI-OS. Finally, we did not capture recurrent fractures that occurred at the same anatomical site.

In conclusion, as the older U.S. population continues to grow, including those aged 80 years and older, there will be increases in the population burden of fractures and functional disability. Some of the reasons for this are well known, including decreased bone density and strength and increased rates of falling, with its attendant causes. Results of the present study suggest that prior fractures in women surviving to age 80 are associated with higher levels of functional disability. This association appears to be independent of other major chronic illnesses and general disease risk factors that are also associated with disablement in this age group. If this association is causal, it follows that programs that promote earlier fracture prevention, such as through falls prevention interventions, management of osteopenia and osteoporosis, nutritional enhancements and even controlling elder mistreatment might have an important long-term benefit on physical functioning in this age group. There may be also research directions of interest based on this report's findings. For example, are fractures managed optimally and with optimal physiological and mobility outcomes? Do the methods of long-term fracture treatment have adverse functional effects, such as from various joint prostheses or mobility devices? The observations here should hopefully promote more research into natural history, unintended iatrogenic influences and adverse clinical outcomes of what might appear to be benign and treatable fracture occurrences.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

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