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ORIGINAL ARTICLE

Physical function trajectory after wrist or lower arm fracture in postmenopausal women: results from the Women's Health Initiative Study

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Abstract

Summary Long-term physical functioning trajectories following distal forearm fracture are unknown. We found that women with versus those without distal forearm fracture were more likely to experience a 5-year decline in physical functioning, independent of initial physical functioning level. This association was most evident among women 80 years and older.

Introduction Physical functioning trajectory following lower arm or wrist fracture is not well understood.

Purpose This study is to evaluate physical functioning trajectory before vs. after lower arm or wrist fracture, stratified by age.

Methods We performed a nested case–control study of prospective data from the Women's Health Initiative Study ($n = 2097$ cases with lower arm or wrist fracture, 20,970 controls). Self-reported fractures and the physical functioning subscale of the RAND 36-item Short-Form Health Survey were assessed annually. We examined three physical functioning trajectory groups: stable, improving, and declining.

Results Mean (SD) number of physical functioning measurements was 5.2 (1.5) for cases and 5.0 (1.4) for controls. Declining physical functioning was observed among 20.4% of cases and 16.0% of controls. Compared to women without lower arm or wrist fracture, women with lower arm or wrist fracture were 33% more likely to experience declining physical functioning (adjusted odds ratio [aOR] 1.33 95% confidence interval [CI] 1.19–1.49, reference group stable or improving physical functioning trajectory). Associations varied by age: age ≥ 80 years aOR 1.56 (95% CI 1.29–1.88); age 70–79 years aOR 1.29 (95% CI 1.09–1.52); age < 70 years aOR 1.15 (95% CI 0.86–1.53) ($p_{interaction} = 0.06$). Associations between lower arm or wrist fracture and odds of declining physical functioning did not vary by baseline physical functioning or physical activity level.

Conclusions Women with lower arm or wrist fracture, particularly those aged 80 and older, were more likely to experience declines in physical functioning than women without such fractures, independent of baseline physical functioning level.

Keywords Forearm fracture · Osteoporosis · Physical function · Wrist fracture

Introduction

Fractures of the lower arm (distal radius and/or ulna) or carpal bones, collectively called "wrist fractures," are a type of major osteoporotic fracture. Most lower arm and wrist fractures occur in women; the age-adjusted female to male ratio is 4:1 [1]. The mean age of wrist fracture is 60 years, in contrast to 81 years for proximal femur fracture [2]. The age-related incidence of wrist fractures varies notably from those of vertebral and hip fractures [1]. The incidence of forearm fractures in women rises rapidly after the menopause transition and then reaches a plateau after approximately age 65 years [1]. Wrist fractures are the most common type of clinical fracture among younger postmenopausal women [2]. Wrist fractures often occur among relatively healthy older people [1]. For example, compared with persons who have hip fracture, persons with wrist fracture are less likely to have impaired walking ability and more likely to go outdoors frequently [3]. Compared to women without fracture, women with wrist fractures are more likely to walk at a brisk pace [4]. Wrist fractures often occur as a result of a fall in women who are relatively healthy and active and have good neuromuscular function [5]. In aggregate, data suggest that wrist fractures most commonly result from a fall sustained while walking when the individual is still able to mount a protective response such as stretching out the hand or arm.

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Most previous studies examining physical functioning after fracture have focused on hip fracture (after which only 40% of patient fully regain their pre-fracture level of independence [6]), whereas little attention has been paid to the trajectories of physical functioning after upper extremity fracture. If wrist and lower arm fractures are associated with declines in physical function trajectories, this finding has implications for clinical practice. For example, patients at high risk of decline in physical functioning after wrist or lower arm fracture should be targeted for interventions, including referral to physical therapy and occupational therapy to prevent or slow the rate of decline. Previous studies reported impaired physical functioning in several domains of activities of daily living following wrist fracture, including impairments in descending stairs, cooking meals, and shopping, and loss of grip strength [7–10]. To yield better insights into the effects of lower arm and wrist fractures on physical functioning, studies should include long-term follow-up and a non-fracture control group. Three longer term studies with a control (non-fracture comparison) groups have been performed [11–13], but only one of them compared results by age (younger women aged 50–64 years versus older women aged 65–99 years) [12]. Overall, associations of lower arm or wrist fractures with long-term physical functioning trajectories among postmenopausal women with a broad age range are not well-characterized.

The goal of this study was to evaluate change in physical functioning before versus after lower arm or wrist fracture during approximately 5 years of follow-up and determine whether these 5-year trajectories after fracture differed by age. In this nested case–control study, our research question was as follows: In postmenopausal women, what is the trajectory of physical functioning before versus after lower arm or wrist fracture, and does this trajectory of physical functioning differ by age? We hypothesize that lower arm or wrist fracture would be associated with declining trajectory of physical functioning several years after fracture and that the declines in physical functioning following lower arm or wrist fracture would be more pronounced among older compared with younger subgroups of postmenopausal women.

Methods.

Women's Health Initiative Study Design

We performed a nested case–control using the Women's Health Initiative Study data. This study included data from the WHI Observational Study and the WHI Clinical Trials. The Women's Health Initiative Study (WHI) was carried out at 40 clinical centers in the U.S. Details of the WHI Study design has been described in detail previously [14–21]. The WHI Observational Study and Clinical Trials enrolled postmenopausal aged between 50 and 79 years who were free of serious medical conditions at baseline. The WHI Extension studies followed all consenting participants from the observational study and clinical trials. WHI Extension Study 1 occurred between 2005 and 2010; WHI extension study 2 is ongoing (2010–2027).

Assessment of physical functioning level

During Extension Study 1 and Extension Study 2, physical functioning was assessed annually using the physical functioning subscale (10 items) of the RAND 36-item Short-Form Health Survey [22]. The 10 items assessed limitations in "vigorous activities (e.g., running, lifting heavy objects, or strenuous sports)," "moderate activities (e.g., moving a table, vacuuming, bowling, or golfing)," "lifting or carrying groceries," "climbing several flights of stairs," "climbing one flight of stairs," "bending, kneeling, stooping," "walking more than a mile," "walking several blocks," "walking one block," and "bathing or dressing yourself." Each of the 10 items had three response choices: limited a lot (score 0), limited a little (score 50), and not limited at all (score 100) (Supplemental Table 1). The well-validated SF-36 physical function score has been widely used to assess physical functioning limitations. The SF-36 physical function score is associated with objective performance-based measures of physical functioning [23, 24], adverse health outcomes, and mortality [25].

Scores for the 10 items were averaged to obtain the overall physical functioning score for each participant. The total physical functioning score ranged from 0 to 100 with a higher score indicating better physical functioning. For each participant, up to six data points within 6 years of the initial matched physical functioning time point were used.

Case definition

The algorithm for selection of cases and controls is displayed in Fig. 1. Cases were all participants with self-reported incident lower arm or wrist fracture during WHI Extension Study 1 or WHI Extension Study 2, during which physical functioning assessment was performed yearly by WHI. Of the 115,407 participants of the Extension Studies, information was available regarding model covariates (age, body mass index [BMI], smoking, alcohol intake, physical activity, myocardial infarction, stroke, treated diabetes, and cancer) for 113,056 participants.

Selection of cases and controls

The algorithm for selection of cases and controls is displayed in Fig. 1. For cases, from the pool of 7571 participants with an incident lower arm or wrist fracture during WHI

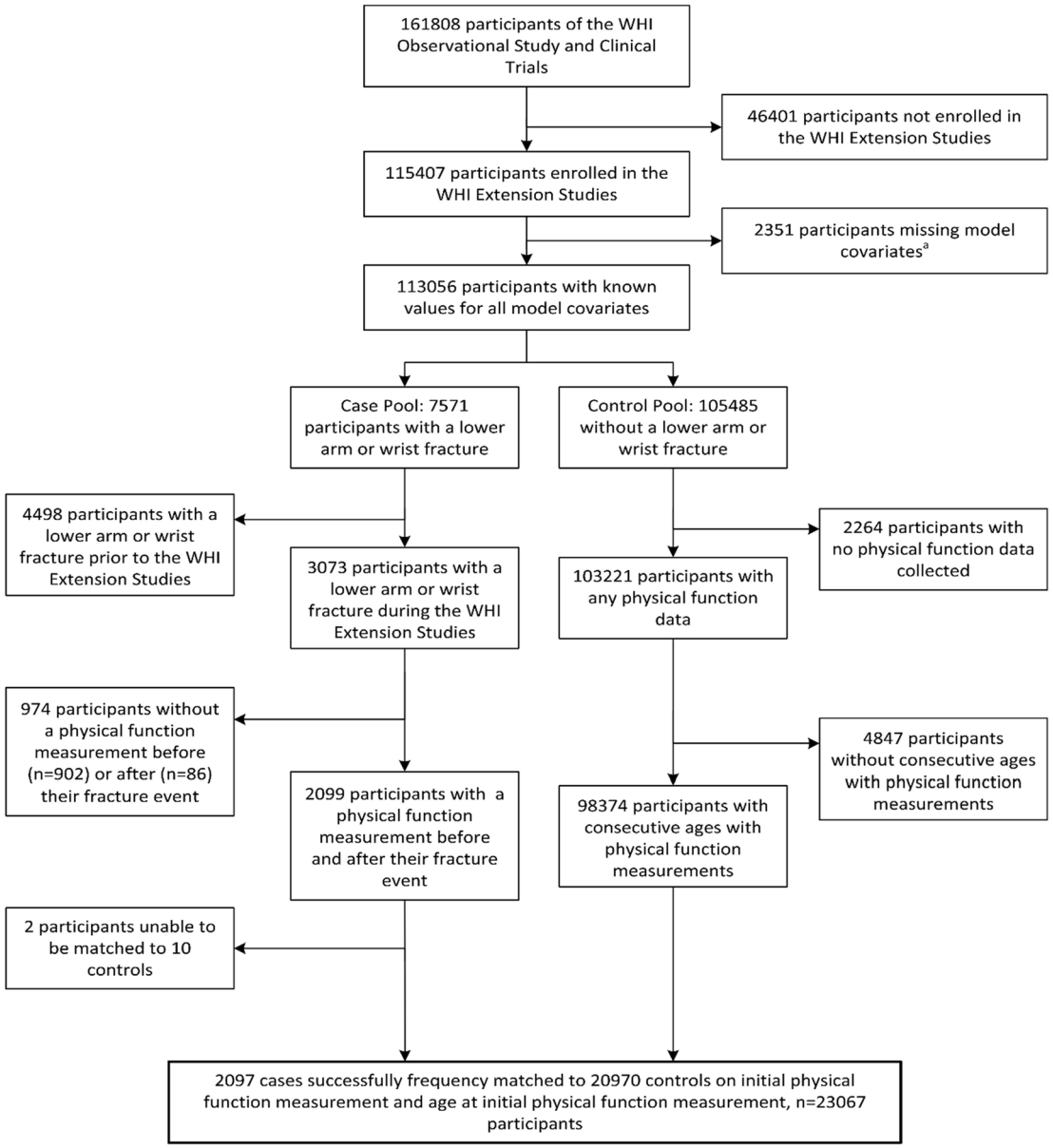


Fig. 1 STROBE analytic flow diagram

Extension Study 1 or WHI Extension Study 2, we excluded cases who had a lower arm or wrist fracture prior to the WHI Extension Studies ($n = 4{,}498$). This exclusion was necessary because there was no yearly assessment of physical function during the main WHI study; physical functioning assessments began during WHI Extension 1. We also excluded data from participants who did not provide information regarding physical functioning at the most recent visit before the lower arm or wrist fracture ($n = 902$) and at least one measure of physical functioning after the fracture ($n = 86$), resulting in 2099 cases. For controls, from the pool of 105,485 participants without a lower arm or wrist fracture, we excluded data from those who did not provide information regarding two consecutive physical functioning measures, resulting in a pool of 98,374 controls eligible for matching with cases.

We used frequency matching to match each participant who reported a lower arm or wrist fracture with 10 control

group participants without lower arm or wrist fracture, by age at initial physical functioning measurement and initial physical functioning level (0 to 100), ensuring balance on these two predictors of physical function trajectory. The initial (pre-fracture) physical functioning level and age of the case became the matched control's "baseline" time point at which we matched the corresponding control's age and physical functioning level to that of the case. Once a given control group participant was matched, the participant was removed from the control pool to avoid duplicate selection. Ultimately, 2097 of 2099 cases were successfully matched to 10 controls each. The final analytic sample consisted of 2097 cases and 20,970 controls. Mean (SD) of total physical functioning measurements was 5.2 (1.5) in cases and 5.0 (1.4) in controls. Cases and controls were balanced on age at initial physical functioning measurement (mean 74.9 years) and initial physical functioning score (mean 71.3).

Each participant provided written informed consent and each institution obtained human subjects committee approval.

Assessment of lower arm and wrist fracture

Fractures were self-reported annually by participants. Participants were asked "Since the date on the front of this form, has a doctor told you for the first time that you have a new broken, fractured, or crushed bone?" Participants were asked to report the location of the fracture using the following response choices: hip, upper leg (not hip), pelvis, knee (patella), lower leg or ankle, foot (not toe), tailbone (not coccyx), spine or back (vertebra), lower arm or wrist, hand (not finger), elbow, upper arm of shoulder, jaw, nose, face, and/or skull, finger or toe, ribs and/or chest or breast bone, and cervical spine/neck. The fracture outcome of this study was lower arm or wrist fracture, to match the categories.

Assessment of other covariates

For each covariate, we used the most recent data available, i.e., at the time of, or the most recent measurement before, each participant's initial physical functioning measurement. At baseline, self-assessment questionnaires assessed participant age, race, ethnicity, highest educational attainment, and income. Subsequent questionnaires prospectively collected information regarding cigarette smoking, physical activity level, previous stroke, chronic obstructive pulmonary disease, diabetes mellitus, cancer, dementia or Alzheimer disease, and cardiovascular disease. For this study, we used the most recent information available for each participant, i.e., at the time of, or most recent prior to, initial physical functioning assessment.

Weight and height were measured at baseline and during follow-up (i.e., year three for observational study participants and annually for clinical trial participants during the clinical trial period). BMI was calculated as body weight in kilograms (kg) divided by the square of height in meters. The most recent BMI data (prior to, or at time of initial physical functioning assessment) was used for each participant.

Statistical analysis

We used SAS Proc Traj (SAS for Windows version 9.4, SAS Institute Inc., NC, USA), which is a trajectory procedure that uses a combination of hierarchical and latent growth curve modeling [26] to identify subgroups of participants with different physical functioning trajectories. We specified cubic modeling, which resulted in three physical functioning trajectory groups: decline in physical functioning, no change in physical functioning, and improving physical functioning. We fit logistic regression models with hierarchical adjustment levels, to examine associations of lower arm or wrist fracture with physical functioning trajectory group. The outcome of the logistic regression models was declining physical functioning trajectory, where the reference group was stable or improving physical functioning trajectory. Only 4.5% of cases and 5.4% of controls experienced improving physical functioning trajectory, and these participants were included in the combined reference group of improving or stable physical functioning trajectory.

In the regression models, we first adjusted for race, ethnicity, and WHI study component (Clinical Trial, Observational Study). Subsequent models further adjusted for cardiovascular disease, cancer, and treated diabetes at baseline. Fully adjusted models additionally included the following covariates: BMI, smoking, alcohol intake, and physical activity level. Covariates were *selected* a priori based on prior literature regarding factors associated with disability in older adults, e.g., cardiac disease, diabetes mellitus, cancer, and obesity [27]. Finally, we stratified results according to subgroups of interest designated a priori: age group at baseline (<70 years, 70–79 years, ≥ 80 years), baseline physical functioning score (0–60, 65–80. 85–100), BMI category (<25, 25 to <30, ≥ 30), baseline physical activity level (<5, 5 to <15, ≥ 15 metabolic equivalent-hours/week), and Alzheimer disease [28]. Due to imbalance of matching factors (i.e., age and initial physical functioning score) across certain subgroups, analyses stratified by body mass index, physical activity, cardiovascular disease, and Alzheimer disease status were additionally adjusted for age and physical functioning score.

In a sensitivity analysis, we repeated the regression models after excluding any participants ($n=1567$) who reported a fracture other than lower arm or wrist fracture at any point between their initial and final physical functioning measurement, additionally adjusting for initial physical functioning score and age at initial physical functioning assessment.

A two-sided $P < 0.05$ was considered statistically significant.

Results

The mean number of physical functioning measurements (including the measure prior to lower arm or wrist fracture event and measures after fracture event) was 5.2 (SD 1.5) for participants in the case group and 5.0 (SD 1.4) in the control group. Mean (SD) follow-up duration was 4.6 (1.4) years for cases and 4.5 (1.4) years for controls.

Table 1 displays characteristics of the 2097 cases and 20,970 control group participants. At the time of initial physical functioning measurement, mean (SD) age was 74.9 (6.8) years in both case and control group participants. Due to matching on age, the age distribution was identical among case and control group participants. One-thousand four hundred and thirty participants (6.2%) were under age 65 years at the time of their initial physical functioning measurement. One-quarter of women with lower arm or wrist fracture were aged between 59 and 69 years; 47% were aged between 70 and 79, and 28% were aged 80 and older. Compared with controls (without lower arm or wrist fracture), cases with lower arm or wrist fracture were more likely to be White and to report having Alzheimer disease. Participant characteristics are provided overall and according to physical functioning trajectory (declining vs. stable or improving) in Supplemental Table 2; overall, declining physical functioning trajectory was most common among women aged 70–79 years.

Figure 2 displays the three physical functioning trajectory groups in the overall sample. The three distinct physical functioning trajectory groups (stable, improving, declining) are apparent, and the model fit appears appropriate (mean *observed* physical functioning values in solid line, mean *predicted* physical functioning values in dotted line).

Average physical functioning level and physical activity level at baseline were very similar between cases and controls within each age subgroup (Supplemental Table 3).

Declining physical functioning was observed among 20.4% of cases and 16.0% of controls (p-value < 0.001) (Table 2). Compared to women without lower arm or wrist fracture, women with lower arm or wrist fracture were 35% more likely to experience declining physical functioning (unadjusted odds ratio [OR] 1.35, 95% confidence interval [CI] 1.21–1.51, reference group stable or improving physical functioning). The magnitude of the association was similar after adjustment for race, ethnicity, and WHI study component (adjusted OR 1.34, 95% CI 1.20–1.50), and not meaningfully altered by further adjustment for cardiovascular disease, cancer, treated diabetes, BMI, cigarette smoking, alcohol intake, and physical activity level (OR 1.33, 95% CI 1.19–1.49). The results of the sensitivity analysis, in which we excluded data from participants who experienced any non-lower arm or wrist fracture between initial and final physical functioning measurement, were similar to those of the main analysis, with p-values < 0.001 for all models (Supplemental Table 4).

There was evidence that the association of lower arm or wrist fracture with higher odds of declining physical functioning varied by age, with a more pronounced association among older women (interaction p-value 0.06) (Fig. 3). The OR was 1.56 (95% CI 1.29–1.88) among women aged ≥ 80 years, and 1.29 (95% CI 1.09–1.52) among women aged 70–79 years. In contrast, among women aged < 70 years, the OR was 1.15 (95% CI 0.86–1.53), which was not statistically significant. Associations did not vary by category of baseline physical functioning, BMI, physical activity level, and presence vs. absence of Alzheimer disease or cardiovascular disease (myocardial infarction, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, or stroke).

Discussion

In this large study with prospective measurements of physical functioning with approximately 5 years of follow-up duration, we found that women who experience lower arm or wrist fracture compared with those without lower arm or wrist fracture were slightly more likely to experience declines in physical functioning than women without lower arm or wrist fracture over the subsequent 5-year period, even after adjustment for covariates (age, race/ethnicity, and initial physical function level). This association was most evident among postmenopausal women aged ≥ 80 years. In contrast, the associations of lower arm or wrist fracture with likelihood of declining physical functioning trajectory did not differ by other baseline characteristics, including physical function level, BMI, physical activity level, and presence/absence of Alzheimer disease. Therefore, this study's results were consistent with our hypothesis that lower arm or wrist fracture would be associated with declining trajectory of physical functioning several years after fracture and that the declines in physical functioning following lower arm or wrist fracture would be more pronounced among older compared with younger subgroups of postmenopausal women.

Few North American studies of > 6 months duration compared Medical Outcomes Study Short-Form Physical Function scores (e.g., SF-36 [22], SF-12 [29]) among women with lower arm or wrist fracture vs. a control group of women without lower arm or wrist fracture [11–13], and only one previously published study compared associations of these fractures with physical functioning across age groups of postmenopausal women [12]. In contrast to findings of our

Table 1 Demographic and physiologic characteristics of study participants*

Variable	All participants ($n=23,067$)		Lower arm or wrist fracture				p-value
			No ($n=20,970$)		Yes ($n=2097$)		
	n	%	n	%	n	%	
Demographics							
Age (years), mean (SD)	74.9	(6.8)	74.9	(6.8)	74.9	(6.8)	1.00
< 70	5786	25.1	5260	25.1	526	25.1	
70–79	10,879	47.2	9890	47.2	989	47.2	
≥ 80	6402	27.8	5820	27.8	582	27.8	
Ethnicity							0.71
Hispanic/Latina	737	3.2	671	3.2	66	3.1	
Not Hispanic/Latina	22,282	96.6	20,257	96.6	2025	96.6	
Unknown/not reported	48	0.2	42	0.2	6	0.3	
Race							< 0.001
American Indian/Alaska Native	52	0.2	45	0.2	7	0.3	
Asian	450	2.0	417	2.0	33	1.6	
Native Hawaiian/other Pacific Islander	13	0.1	13	0.1	0	0.0	
Black	1380	6.0	1306	6.2	74	3.5	
White	20,669	89.6	18,729	89.3	1940	92.5	
More than one race	260	1.1	242	1.2	18	0.9	
Unknown/not reported	243	1.1	218	1.0	25	1.2	
Education							0.25
≤ High school/General Educational Development (GED)	4094	17.7	3693	17.6	401	19.1	
School after high school	8443	36.6	7683	36.6	760	36.2	
≥ College degree	10,380	45.0	9461	45.1	919	43.8	
Income (family)							< 0.001
< $20,000	2289	9.9	2028	9.7	261	12.4	
$20,000–$49,999	9191	39.8	8289	39.5	902	43.0	
≥ $50,000	10,446	45.3	9618	45.9	828	39.5	
Body mass index (kg/m^2), mean (SD)	28.1	(6.0)	28.1	(6.0)	27.6	(5.7)	< 0.001
< 25	7977	34.6	7201	34.3	776	37.0	
25– < 30	7993	34.7	7252	34.6	741	35.3	
≥ 30	7097	30.8	6517	31.1	580	27.7	
Physical function score (range 0–100), mean (SD)†	71.3	(26.3)	71.3	(26.3)	71.3	(26.3)	1.00
Medical history							
Cardiovascular disease	2137	9.3	1911	9.1	226	10.8	0.01
Myocardial infarction	866	3.8	780	3.7	86	4.1	0.38
Coronary artery bypass graft or percutaneous transluminal coronary angioplasty	1240	5.4	1103	5.3	137	6.5	0.01
Stroke	661	2.9	596	2.8	65	3.1	0.50
Cancer	4582	19.9	4159	19.8	423	20.2	0.71
Alzheimer disease	320	1.4	269	1.3	51	2.4	< 0.001
Treated diabetes mellitus	2697	11.7	2438	11.6	259	12.4	0.33
Treated hypertension	13,357	57.9	12,180	58.1	1177	56.1	0.14
Personal habits							
Smoking							0.33
Never	11,758	51.0	10,713	51.1	1045	49.8	
Past	10,532	45.7	9560	45.6	972	46.4	
Current	777	3.4	697	3.3	80	3.8	
Alcohol use (drinks/week)							0.49
< 1	13,929	60.4	12,643	60.3	1286	61.3	

Table 1 (continued)

Variable	All participants (*n* = 23,067)		Lower arm or wrist fracture				*p*-value
			No (*n* = 20,970)		Yes (*n* = 2097)		
	n	%	*n*	%	*n*	%	
1–<7	5827	25.3	5320	25.4	507	24.2	
≥7	3311	14.4	3007	14.3	304	14.5	
Physical activity (metabolic equivalent-hr/wk), mean (SD)	13.7	(14.3)	13.7	(14.3)	13.5	(14.2)	0.54
Women's Health Initiative (WHI) Study variables							
WHI study component							0.96
Clinical trial	10,285	44.6	9349	44.6	936	44.6	
Observational study	12,782	55.4	11,621	55.4	1161	55.4	
Enrolled in 2nd Women's Health Initiative Extension Study	21,609	93.7	19,794	94.4	1815	86.6	<0.001

*For each covariate, we used the most recent data available, i.e., at the time of, or before, each participant's initial physical function measurement. Missing data: education, *n* = 173; income, *n* = 1186

†RAND 36-item Short-Form Health Survey. Scores of 10 items averaged to obtain overall physical function score for each participant

study, the National Osteoporosis Risk Assessment study of 86,128 postmenopausal women (with 2-year follow-up duration) reported that recent wrist fractures were associated with significantly lower SF-12 physical function score in women younger than 65 years of age ($p < 0.001$), but not women 65 to 99 years old ($p > 0.10$) [12]. However, that study measured physical functioning only cross-sectionally at the 2 years follow-up visit, whereas the current study examined physical functioning trajectories over time. The other two studies did not compare results according to age. In the Global Longitudinal study of Osteoporosis in Women (GLOW) conducted in ten countries (*n* = 50,461 postmenopausal women mean age 69 years), physical function level was reported only cross-sectionally in relation to wrist fracture; SF-36 physical function score (cross-sectionally measured at 1-year follow-up) was not significantly different among the women who had incident wrist fracture vs. women who did not have wrist fracture [11]. The SF-36 physical function score at year 1 follow-up was 3.3 (95% confidence interval [CI] − 0.9, 7.5) among women who experienced wrist fracture and 4.1 (95% CI 3.3, 5.0) in participants who did not experience wrist fracture. Neither of those two published studies [11, 12] specifically defined which bones were considered to be "wrist fracture," so it is unclear whether wrist fractures were defined as carpal bone fracture (fracture of the bones of the wrist that connect the radius and ulna to the hand bones), distal radius fracture, distal radius and/or ulnar fracture, or any carpal, radius, or ulna fracture (which would align with our current study). Differences in skeletal sites defined as wrist fracture may partly explain differences in results across studies, as

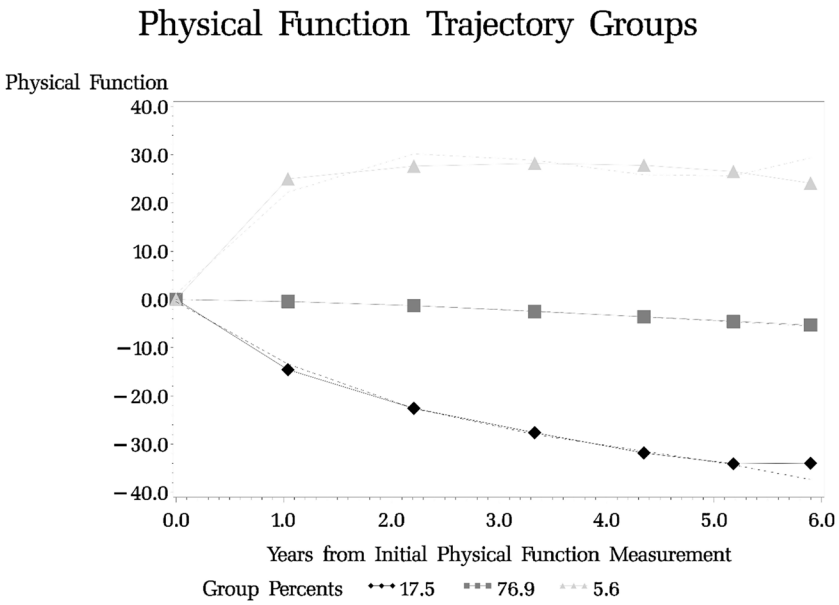


Fig. 2 Physical functioning trajectories. Three physical functioning groups based on cubic model fit

Table 2 Declining physical function trajectory as a function of lower arm or wrist fracture

	Lower arm or wrist fracture		
	No ($n=20,970$)	Yes ($n=2097$)	
Event totals	*n (%)*	*n (%)*	
Declining trajectory	3350 (16.0)	428 (20.4)	
Models	*OR (95% CI)*[*]	*OR (95% CI)*	*p-value*
Unadjusted	1.00 (ref)	1.35 (1.21, 1.51)	< 0.001
Model 1	1.00 (ref)	1.34 (1.20, 1.50)	< 0.001
Model 2	1.00 (ref)	1.33 (1.19, 1.49)	< 0.001
Model 3	1.00 (ref)	1.33 (1.19, 1.49)	< 0.001

Odds ratios, corresponding 95% confidence intervals, and *p*-values from a logistic regression model with decreasing physical function trajectory group classification (declining vs. stable/improving) as a function of lower/arm wrist event status. Model 1: adjusted for race, ethnicity, and Women's Health Initiative study component (clinical trial vs. observational study). Model 2: model 1 + cardiovascular disease, cancer, treated diabetes mellitus. Model 3: model 2 + body mass index, smoking, alcohol intake, physical activity level.

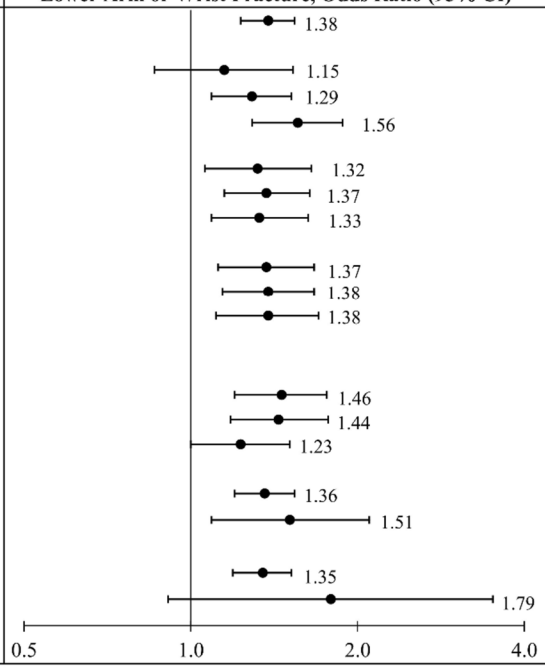
could differences in study duration across studies. Finally, the study of osteoporosis fractures, in which all participants were aged ≥ 65 years, distal radius or ulna fracture increased the odds of having a clinically important functional decline (defined as functional deterioration equivalent to one standard deviation decrease in functional ability) by 48% (odds ratio 1.48, 95% confidence interval 1.04 to 2.12) over a 7.6-year follow-up duration, even after adjustment for covariates including health status and baseline functional status, and comorbidities [13]. Although that study did not present results stratified by age subgroup, they are consistent with the findings of our study.

Our results are clinically relevant. We had previously reported the increased risk of subsequent fractures following an initial lower arm or wrist fracture among postmenopausal women, with more than one in ten women with a lower arm or wrist fracture experiencing a subsequent fracture [30]. While there is increasing awareness regarding the risk of subsequent fractures after initial lower arm or wrist fracture, attention has been focused on the adverse consequences of hip and vertebral, but not lower arm, fractures on well-being. The current findings will raise awareness of the potential impact of these common fractures beyond the immediate post-fracture period, particularly among older women. Multimorbidity, functional impairments, and frailty all increase with advancing age and may contribute to greater functional decline after lower arm or wrist fracture in older women. Future research should further evaluate whether specific interventions may help to avert such declines. Our findings suggest a need for additional studies that better characterize subpopulations of patients with wrist and lower arm fractures who are at high risk for physical functioning decline so that they can be targeted for interventions (such as physical therapy and occupational therapy) to prevent or reduce rates of decline.

Limitations of this study include that we cannot comment on whether it was the fracture itself, or other intervening health events, that were responsible for the differences we observed. For example, the higher incidence of subsequent additional fractures after an initial lower arm fracture could partly explain the decline in physical functioning. However, our sensitivity analysis found that exclusion of women with fractures locations other lower arm or wrist during the physical functioning follow-up period resulted in very similar findings. To be certain that the fracture preceded the physical function trajectory assessment, we only assessed incident, not prevalent, lower arm or wrist fracture, resulting in exclusion of data from 4498 participants who had such fractures before baseline physical functioning assessment. Physical functioning assessment began during the Extension phases of the WHI Study. Lower arm and wrist fractures were self-reported. However, in a previous validation study, agreement between self-report and medical record-confirmed lower arm/wrist fracture was high (81%) [31]. Consistent with prior epidemiologic studies [1], we found that lower arm or wrist fracture was less common among Asian and Black participants, so we could not reliably stratify our results regarding lower arm fracture and subsequent physical function trajectory by race. We could not specifically examine trajectory of upper extremity function and trajectory of lower extremity function. Finally, residual confounding is possible.

We did not have access to baseline objective measures of physical performance. However, the SF-36 physical function score has been shown to be correlated with objectively measured physical performance. Latham and colleagues reported that SF-36 physical function score was associated with objective performance-based measures of physical functioning, including the Short Physical Performance Battery (SPPB) and the 6-min walk test, in hip fracture patients [23]. Also, Syddall and colleagues reported that lower SF-36 physical function scores were associated with poorer performance on several objective measures of physical functioning, including grip strength, walking speed, and chair rise test times [24]. The SF-36 physical function score has also been linked with important health outcomes. For example, the RAND-36 physical function scale score predicts falls and mortality and is sensitive to important health events, including after surgery or cancer chemotherapy [22, 32–40]. Syddall and colleagues found that poor SF-36 physical function scores (lowest fifth of the gender-specific distribution) were related to lower grip strength as well as longer timed-up-and-go, 3-m walk, and chair rises test times in men and women [24]. A recent validation study based on data from the Women's Health Initiative found that each one standard deviation higher baseline RAND SF-36 physical function score was associated with

Subgroup	Total Participants, n	Declining Trajectory, n (%)	Lower Arm or Wrist Fracture, Odds Ratio (95% CI)[a]	Interaction p-value
All Participants	*23067*	*3778 (16.4%)*	1.38	
Age (years)				0.06[b]
< 70	5786	558 (9.6)	1.15	
70 – 79	10879	1760 (16.2)	1.29	
≥ 80	6402	1460 (22.8)	1.56	
Physical Function Score				0.90[b]
0 – 60	7117	907 (12.7)	1.32	
65 – 80	7293	1762 (24.2)	1.37	
85 – 100	8657	1109 (12.8)	1.33	
Body Mass Index (kg/m^2)				0.93[b]
<25	7977	1147 (14.4)	1.37	
25 - <30	7993	1359 (17.0)	1.38	
≥30	7097	1272 (17.9)	1.38	
Physical Activity (metabolic equivalent-hours/wk)				0.25[b]
< 5	7738	1369 (17.7)	1.46	
5 – <15	7040	1180 (16.8)	1.44	
≥ 15	8289	1229 (14.8)	1.23	
Cardiovascular Disease				0.55
No	20930	3331 (15.9)	1.36	
Yes	2137	447 (20.9)	1.51	
Alzheimers				0.41
No	21492	3500 (16.3)	1.35	
Yes	320	82 (25.6)	1.79	



[a]Odds ratios and corresponding 95% confidence intervals from a logistic regression model with decreasing physical function trajectory group classification (declining vs. stable/improving) as a function of lower arm or wrist fracture status, the subgroup of interest, and their interaction. Models are adjusted for age, race, ethnicity, initial physical function level, Women's Health Initiative Study component, cardiovascular disease, cancer, treated diabetes, treated hypertension, body mass index, smoking, alcohol, and physical activity. Due to imbalance of matching factors (i.e., age and initial physical function score) across certain subgroups, analysis stratified by body mass index, physical activity, cardiovascular disease, and Alzheimer disease status are additionally adjusted for age and physical function score. [b]Interaction p-value from a separate logistic model with decreasing physical function trajectory group classification (yes/no) as a function of lower arm or wrist fracture, linear trend over the subgroup, and their interaction, with the same adjustments.

Fig. 3 Forest plot of decreasing physical function trajectory as a function of lower arm or wrist fracture by subgroups. [a]Odds ratios and corresponding 95% confidence intervals from a logistic regression model with decreasing physical function trajectory group classification (yes/no) as a function of lower arm/wrist event status, the subgroup of interest, and their interaction. Models are adjusted for age, race, ethnicity, initial physical function level, WHI component, cardiovascular disease, cancer, treated diabetes, treated hypertension, body mass index, smoking, alcohol intake, and physical activity level. [b]Interaction *p*-value from a separate logistic model with decreasing physical function trajectory group classification (yes/no) as a function of lower arm/wrist fracture, linear trend over the subgroup, and their interaction, with the same adjustments

significantly lower all-cause mortality and that the discriminatory capacity was comparable to that of objective measure of physical performance (gait speed, chair stand), both in women aged < 70 and in women aged ≥ 70 years [25]. The SF-36 physical function score is a valid measure of mobility disability in epidemiologic studies.

This study also has several strengths. First, to our knowledge, this is the first published study to compare declines in physical functioning among women with, versus without, wrist or lower arm fracture prospectively over a duration of more than 1 year of follow-up, and to compare this association by age subgroups. Second, the prospective design helps to minimize the concern of reverse causality, i.e., physical functioning impairment preceding, instead of following, the increased risk of fracture. Third, we matched for time of initial measurement of physical functioning and age. Fourth, the RAND SF-36 physical function score is well-validated, including among WHI participants [25]. Finally, the study cohort had a large number of well-characterized participants, allowing for adjustment for numerous potential confounders. We were able to assess for interactions by age group (which showed a more pronounced association in women aged ≥ 80 years than women aged < 70 and women aged between 70 and 79 years), initial physical functioning level, body mass index, initial physical activity level, Alzheimer disease, and cardiovascular disease.

In conclusion, women with lower arm or wrist fracture were more likely to experience declines in physical functioning than women without such fractures, and this especially evident among women aged ≥ 80 years than among younger subgroups of postmenopausal women. Because these fractures are common in postmenopausal women, clinicians should have heightened awareness of the potential for declines in physical functioning even beyond the initial

post-fracture period, particularly among older women. Physical therapy may be especially important among these older women.

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https://www.whi.org/doc/WHI-Investigator-Long-List.pdf

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Data sharing.

The Women's Health Initiative Study data are available via the BioLINCC website of the National Heart, Lung, and Blood Institute at https://biolincc.nhlbi.nih.gov/home/.

Declarations

Competing Interests CJC, JL, AHS, JCW, KEE, NS, MSL, JWW, JAC, JS declare that they have no conflicts of interest. Dr. LeBoff is supported by grant R01 AR060574 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases and by grant R01AG071611 from the National Institute on Aging.

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