

Research Article

Sex Differences in Recovery Across Multiple Domains Among Older Adults With Hip Fracture

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Abstract

Background: Hip fractures are a public health problem among older adults, but most research on recovery after hip fracture has been limited to females. With growing numbers of hip fractures among males, it is important to determine how recovery outcomes may differ between the sexes.

Methods: 168 males and 171 females were enrolled within 15 days of hospitalization with follow-up visits at 2, 6, and 12 months postadmission to assess changes in disability, physical performance, cognition, depressive symptoms, body composition, and strength, and all-cause mortality. Generalized estimating equations examined whether males and females followed identical outcome recovery assessed by the change in each outcome.

Results: The mean age at fracture was similar for males (80.4) and females (81.4), and males had more comorbidities (2.5 vs 1.6) than females. Males were significantly more likely to die over 12 months (hazard ratio 2.89, 95% confidence interval: 1.56–5.34). Changes in outcomes were significantly different between males and females for disability, gait speed, and depressive symptoms ($p < .05$). Both sexes improved from baseline to 6 months for these measures, but only males continued to improve between 6 and 12 months. There were baseline differences for most body composition measures and strength; however, there were no significant differences in change by sex.

Conclusions: Findings confirm that males have higher mortality but suggest that male survivors have continued functional recovery over the 12 months compared to females. Research is needed to determine the underlying causes of these sex differences for developing future prognostic information and rehabilitative interventions.

Keywords: Body composition, Function, Gait speed, Mortality

Background

Every year more than 250 000 older adults are hospitalized for hip fracture in the United States (1). The age-adjusted annual incidence

of hip fracture is over 2 times higher in females, compared to males (2). Consequently, most studies examining sex differences in hip fracture recovery only include a relatively small number of males (3–5). However, by 2030, it is estimated that there will be a 51.8% increase

in the incidence of hip fractures in males, compared to a 3.5% decline in females (1). Sex may play an important role in health outcomes, including the extent of hip fracture recovery (3), and most posthip fracture care is not purposefully sex-specific. Additional data are needed to understand the impact of hip fracture on males and the extent to which recommendations for the management of care for females with a hip fracture can be generalized to males (3).

Prior studies have shown that males have higher postfracture mortality (4,6), which could be due to a greater disease burden at the time of fracture and susceptibility to infection after fracture among males (7). Studies of sex differences in physical function and disability less than 6 months postfracture are mixed with some showing better recovery in males (8), females (9–11), or no difference (10,12,13); however, studies with longer follow-up (≥ 6 months) find no sex differences (4,13–15). Few studies have examined recovery in other functional domains (ie, affect, cognition, quality of life) (3,8,10,13,14) or other postfracture changes (ie, body composition, bone mineral density [BMD], bone geometry, and muscle mass) (16,17).

This study was designed to determine whether male and female survivors experience the same recovery as measured by changes in multiple outcome domains from time of admission for fracture to 12 months postfracture. The study used data from the seventh cohort of the Baltimore Hip Studies (BHS-7), a sample that included equal numbers of male and female patients (18).

Method

Study Design and Study Sample

A prospective cohort study of male and female hip fracture patients was conducted at 8 hospitals selected from the BHS network. Patients admitted for a surgical repair of a nonpathological, low-energy hip fracture (ICD-9 codes 820.00–820.9) were screened by study research nurses for enrollment. For study inclusion, patients must have been 65 years of age or older, English-speaking, community-dwelling at the time of fracture, and ambulatory for the 6 months prior to the fracture. Patients were excluded if they resided ≥ 70 miles from the hospital, weighed ≥ 300 pounds (due to equipment restrictions), or had hardware in the contralateral hip. The patients received standard postfracture physical therapy care (lasting approximately 3 weeks posthospital discharge) intended to meet the minimum standards of domestic ambulation without falling (19). The average hospital length of stay in the United States is 6 days (20) and 90% of hip fracture patients are transferred to a skilled nursing facility for rehabilitative care (21).

Patients were consented either directly or via proxy consent with patient assent if the patient was not able to self-consent. Enrollment was required to occur within 15 days of hospital admission. To ensure equivalent numbers of males, females were frequency-matched to males by hospital and time of admission.

Enrolled participants completed a battery of assessments within 22 days of admission and again at 2, 6, and 12 months postadmission. All 4 study visits included questionnaires, cognitive testing, self-reported functional disability, and dual-energy x-ray absorptiometry (DXA) scans (18). Performance-based functional measures were assessed at the 3 follow-up time points. Interviews were completed by the participant or his/her proxy if the participant was not able (modified Mini-Mental State Examination (3MS) score < 36) (22). DXA scans were conducted at one of the 7 study DXA facilities using standard quality assurance procedures (16). Participants were

also contacted monthly by telephone. Protocols for this study were reviewed and approved by the University of Maryland Institutional Review Board (IRB) and the review boards of participating hospitals.

Figure 1 displays the flow diagram of study enrollment and sample sizes at each study visit. A total of 1 709 patients were approached for eligibility screening. Of the 405 eligible males, 168 (41.5%) were enrolled; 171 (33.4%) of the 512 eligible females were enrolled. Twenty-three patients were withdrawn, 5 for not providing data at baseline and 2-month visits and 18 due to an IRB-requested postprocedure audit (6 participants did not meet inclusion criteria and 12 were ineligible due to discrepancies in the informed consent process).

Measures

Demographics (age, race, marital status, living arrangement, years of education) and baseline clinical factors were obtained from patient (or surrogate) interviews, medical chart abstraction, and anthropometric measurements. We used a modified version of the Charlson Comorbidity Index (23) indicating liver disease as moderate or severe because we were not able to distinguish between mild and moderate severity from a medical chart (maximum score = 33).

Key outcome measures included physical and instrumental disability in activities of daily living, cognition, depressive symptoms, body composition, and strength assessed at all time points and performance measures at follow-up visits. Mortality was obtained

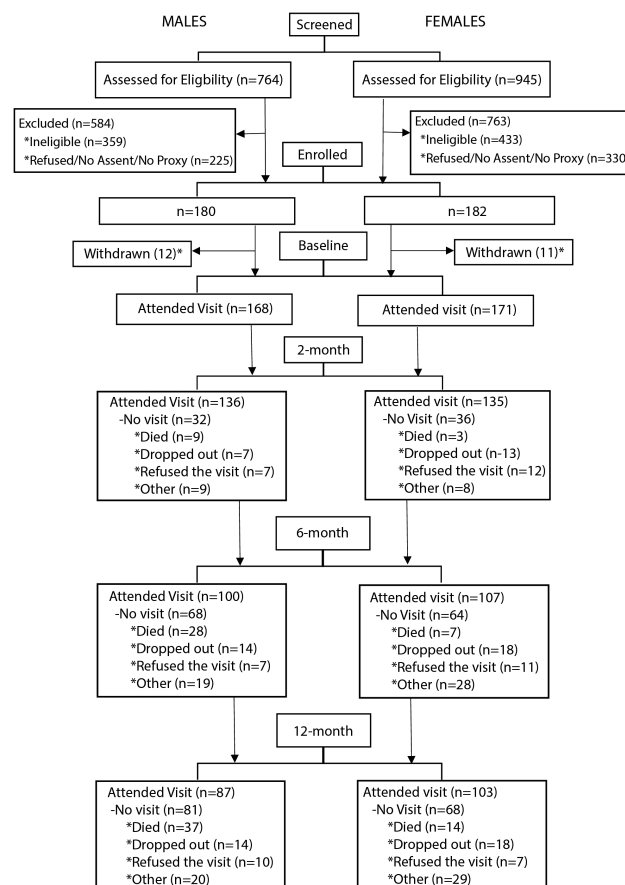


Figure 1. Flow diagram of study screening, enrollment, and follow-up, stratified by sex. *Participants were withdrawn either due to predetermined criteria for no data provided at baseline and 2-month follow-up visits or as a result of an Institutional Review Board-requested postprocedure audit.

through monthly telephone calls or reported any time from the time of consent during the 1-year follow-up period; therefore, those dying prior to being enrolled are not included.

Disability was evaluated using the Lower Extremity Physical Activities of Daily Living (LPADL) scale, which was modified for hip fracture patients from the Functional Status Index (24), and Instrumental Activities of Daily Living (IADL) scale, which stems from the Older Americans Resources and Services Instrument (25). Baseline disability reflects participants' report of disability status 1 week (LPADL) or 2 weeks (IADL) prior to the fracture. For both disability scales, the measurement value indicates the number of activities in which the participant reported needing equipment or human assistance, or the inability to carry out the activity due to a health-related reason. Higher scores indicate a worse disability.

Physical performance, or function, was assessed by grip strength, the Short Physical Performance Battery (SPPB) (26), the Lower Extremity Gait Scale (LEGS) (27), and gait speed. Grip strength was assessed using the JAMAR Hydraulic Hand Dynamometer (28). The SPPB includes items on walking, rising from a chair 5 times, and balance; scores range from 0 to 12 with higher scores indicating better function. The LEGS evaluates 9 lower extremity tasks thought to be relevant for the patient recovering from hip fracture: reach for an item on the ground from sitting position, put a sock on fractured side foot, put a shoe on fractured side foot, rise from armless chair, walk 10 feet, step up 4 steps, step down 4 steps, get on toilet, and get off toilet. Scores range from 0 to 36 with higher scores indicating better function. Gait speed was calculated from a timed 3-m walk test (29). A more complete description of study methods and measures is provided elsewhere (18).

Cognition and depressive symptoms were assessed using the 3MS (22,30), which includes items on orientation, registration, and recall with scores ranging from 0 to 100, and the Center for Epidemiologic Studies—Depression scale (CES-D) (31), which asks about frequency of a person's experience of 20 symptoms (range 0–60).

Body composition was assessed via DXA with a scan of the whole body. Total body lean mass, appendicular lean mass, and total body fat mass were calculated from whole-body DXA scans. Calculations were adjusted for the affected leg to reduce the possible influence of surgical site swelling by removing the value for the affected leg and doubling the value of the nonaffected leg. Femoral neck BMD was measured at the contralateral hip. Two different types of DXA machines were used—Hologic (Waltham, MA) and Lunar Prodigy (Madison, WI). Each participant had baseline and follow-up body composition measurements completed with the same machine type over time. However, to account for any systematic differences by machine type, all body composition measurements were adjusted for machine type and expressed as percentage change from baseline.

Statistical Methods

Distributions of baseline demographic and clinical factors and outcomes were examined, stratified by sex. Chi-square tests and *t*-tests were used to compare males and females at baseline.

Sex-stratified Kaplan–Meier curves with log-rank tests were used to examine survival over 12 months postadmission. For participants who reported being able to complete an LPADL without equipment or human assistance (no disability) prior to their fracture, new-onset disability was examined. Descriptive data on new-onset disability at 12 months postfracture are also reported. New-onset disability was operationalized as a composite outcome; such that for each activity, the proportion of participants with no disability in that LPADL at baseline who became disabled in that activity (needed assistance or

not able to perform for a health reason) or died at 12 months were estimated by sex. Raw proportions with new-onset disability or death were compared by sex with chi-square tests.

Longitudinal analysis using generalized estimating equations (GEEs) with robust standard errors was conducted to determine time-specific sex differences in each outcome measure. Given that the data had mortality as well as missingness due to nonresponse, weighted GEEs allow for the potential for data to be missing at random without an “immortal cohort” and separation of the missingness model from the outcome model. All participant data available at each time point were used. Thus, not all participants contributed data at all time points. Means of outcome measure were evaluated at each time point stratified by sex.

$$\begin{aligned} \text{Outcome} = & \text{Intercept} + b_1 (\text{male}) + b_2 (2 \text{ months}) \\ & + b_3 (6 \text{ months}) + b_4 (12 \text{ months}) \\ & + b_5 (\text{male} \times 2 \text{ months}) \\ & + b_6 (\text{male} \times 6 \text{ months}) \\ & + b_7 (\text{male} \times 12 \text{ months}) \end{aligned}$$

All GEEs were unadjusted for covariates in order to examine the natural course of recovery among males and females. However, total lean body mass, appendicular lean mass, and total body fat mass were adjusted for machine type in GEE models. Hypothesis tests assessed differences in changes in outcomes from baseline ($H_0: b_5 = b_6 = b_7 = 0$). A sensitivity analysis using observation-weighted estimating equations (WEEs) was conducted to ensure that results were not biased by either missing outcome data or differential survival between males and females.

Results

Baseline Differences

There were no statistically significant differences between males and females at the time of fracture with respect to age, race, education, fracture location, hospital length of stay, or body mass index. Males were significantly more likely to be married, reside with another individual, and have more comorbidities (2.5 [1.6] vs 1.6 [1.6], $p < .01$) than females (Table 1). Nearly 100% of participants were in a nursing home or rehabilitation care facility at the baseline assessment with men being more likely to be in a facility over time, but the percentage decreased over time with 10% or less of men and women living in a facility at 6 and 12 months (data not shown). For comorbidities with a prevalence greater than 5%, males had significantly more peripheral vascular disease, myocardial infarctions, and moderate renal disease. Males also had significantly worse 3MS scores (82.3 [16.4] vs 86.2 [16.4], $p = .03$) and prefracture IADL disability (2.2 [1.5] vs 1.8 [1.5], $p < .01$). Males and females were significantly different at baseline for all DXA and strength measures with males having greater grip strength, lean body mass, and BMD values than females, but lower fat mass.

Mortality

Males had a higher risk of death (hazard ratio 2.89, 95% confidence interval: 1.56–5.34) over the 12 months postadmission for hip fracture, compared to females (log-rank test $p < .01$) with 37 males dying by 12 months compared to 14 females (Figure 2).

New-Onset Disability or Death

Figure 3 displays the proportion of males and females with no disability in each LPADL item in the 1 week prior to fracture who

Table 1. Baseline Demographic and Clinical Characteristics of Hip Fracture Patients, Stratified by Sex

Variable	Males (<i>n</i> = 168)	Females (<i>n</i> = 171)	<i>p</i> *
Age, mean (<i>SD</i>)	80.4 (7.8)	81.4 (7.9)	.20
Race (%)			.62
White	147 (87.5)	152 (88.9)	
Non-White	16 (9.5)	12 (7.0)	
Unknown	5 (3.0)	7 (4.1)	
Married (%)	87 (51.8)	47 (27.5)	<.01
Live alone (%)	39 (23.2)	81 (47.4)	<.01
Education (years), mean (<i>SD</i>)	13.2 (3.8)	13.0 (3.0)	.74
Length of stay (days), mean (<i>SD</i>)	5.4 (2.4)	5.2 (2.7)	.10
Fracture location (%)			.20
Femoral neck	74 (44.0)	93 (54.4)	
Intertrochanteric	73 (43.5)	62 (36.3)	
Other	19 (11.3)	16 (9.4)	
Body mass index, mean (<i>SD</i>)	25.6 (4.5)	25.0 (5.6)	.29
Charlson comorbidity index, mean (<i>SD</i>)	2.5 (1.9)	1.6 (1.6)	<.01
Congestive heart failure (%)	32 (19.2)	25 (14.6)	.26
Peripheral vascular disease (%)	35 (21.0)	19 (11.1)	.01
Myocardial infarction (%)	37 (22.2)	17 (9.9)	<.01
Stroke (%)	31 (18.6)	25 (14.6)	.33
Transient ischemic accident (%)	15 (9.0)	13 (7.6)	.65
Dementia/Alzheimer's (%)	28 (16.8)	18 (10.5)	.09
Respiratory disease (%)	45 (27.0)	32 (18.7)	.07
Diabetes (without end-stage organ damage) (%)	36 (21.6)	32 (18.7)	.51
Moderate renal disease [†] (%)	12 (7.2)	4 (2.3)	.03
Any tumor (%)	43 (25.8)	30 (17.5)	.07
Physical and instrumental disability			
LPADL, mean (<i>SD</i>)	2.4 (2.6)	2.7 (2.6)	.27
IADL, mean (<i>SD</i>)	2.2 (1.5)	1.8 (1.5)	<.01
Physical performance [‡]			
Gait speed (m/s), mean (<i>SD</i>)	0.32 (0.26)	0.37 (0.24)	.13
SPPB, mean (<i>SD</i>)	2.9 (2.7)	3.6 (2.7)	.07
LEGS, mean (<i>SD</i>)	14.4 (10.8)	16.7 (9.8)	.14
Cognition			
3MS, mean (<i>SD</i>)	82.3 (16.4)	86.2 (16.4)	.03
Depressive symptoms			
CES-D, mean (<i>SD</i>)	17.4 (10.4)	17.7 (11.4)	.82
DXA measurements			
Adjusted total body lean mass (kg), mean (<i>SD</i>)	51.3 (7.74)	37.0 (6.1)	<.01
Adjusted appendicular lean mass (kg), mean (<i>SD</i>)	21.5 (4.1)	14.9 (3.2)	<.01
Adjusted total body fat (kg), mean (<i>SD</i>)	21.0 (8.6)	23.4 (9.9)	.0465
Femoral neck BMD, mean (<i>SD</i>)	0.7392 (0.1370)	0.6802 (0.1333)	<.01
Grip strength (kg), mean (<i>SD</i>)	29.3 (9.7)	18.6 (6.7)	<.01

Note: LPADL = Lower Extremity Physical Activities of Daily Living; IADL = Instrumental Activities of Daily Living; SPPB = Short Physical Performance Battery; LEGS = Lower Extremity Gain Scale; 3MS = Modified Mini-Mental State Examination; CES-D = Center for Epidemiologic Studies—Depression scale; BMD = bone mineral density; DXA = dual-energy x-ray absorptiometry.

**p* value from *t*-test for continuous variables and chi-squared test for categorical variables.

[†]Moderate renal disease was defined as not on dialysis, but creatinine >3 mg%.

[‡]All baseline physical performance assessments were completed at 2 months.

developed a new-onset disability or died over 12 months. New-onset disability or death was greatest for both sexes for climbing 5 stairs. Among those without disability in a given LPADL, males had significantly greater new-onset disability or death, compared to females, in walking 10 feet ($p = .048$; 62% males vs 47% females), getting into a car ($p = .01$; 46% males vs 28% females), getting in/out of bed ($p < .01$; 44% males vs 20% females), putting on socks and shoes ($p = .02$; 58% males vs 42% females), washing all parts of the body ($p = .02$; 54% males vs 36% females), and reaching for an item on the ground ($p = .02$; 44% males vs 30% females).

Outcomes Over 12 Months

Figure 4 displays the mean of outcome measures at each time point stratified by sex. Only outcomes with significant or borderline significant differences in slopes are displayed in Figure 4. All other outcomes are displayed in Supplementary Appendix A.

Physical and instrumental disability

There was a significant difference in mean changes between males and females for LPADLs ($p = .015$), but not IADLs ($p = .439$; note: the reporting period for baseline LPADLs and IADLs was prior to the fracture). For LPADLs, Figure 4A demonstrates that both sexes

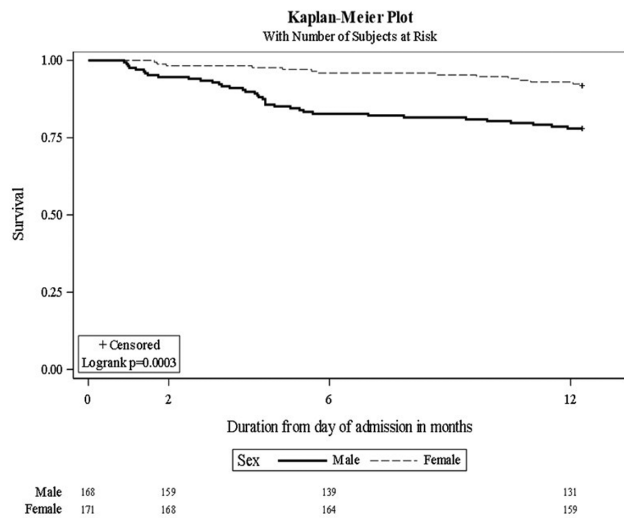


Figure 2. Kaplan–Meier survival curve comparing survival over 12 months postadmission, stratified by sex.

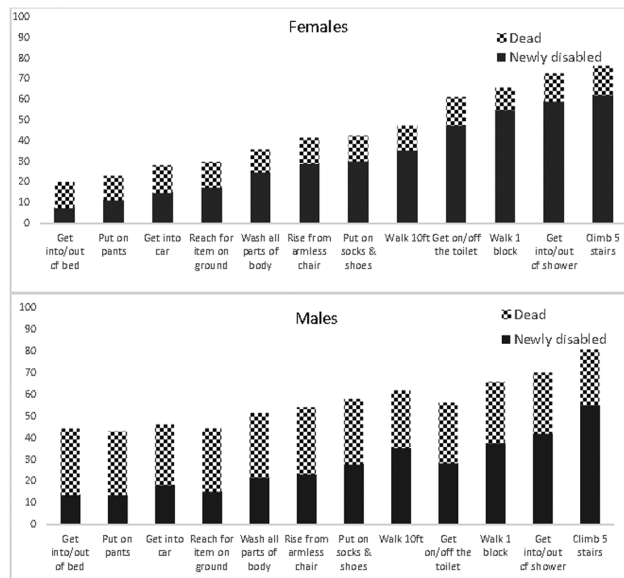


Figure 3. Proportion of participants not disabled in lower extremity activities of daily living activity prior to admission who became newly disabled or died by 12 months, stratified by sex.

report similar levels of disability prior to fracture. At 2 months, there was a large increase in lower extremity disability for both sexes with males reporting more disability (7.87 vs 7.08) which remained higher over the follow-up period. Females experience a reduction in disability from 2 to 6 months, which remained stable between 6 and 12 months. Males experienced improvements between 2 and 6 months as well as between 6 and 12 months. Both sexes reported, on average, disability in more than 5 activities over the year compared to only 2.5 prior to the fracture.

Physical performance

Significant differences in mean changes between males and females are present for gait speed ($p = .019$). Differences in mean changes were borderline significantly different for SPPB ($p = .067$) but not

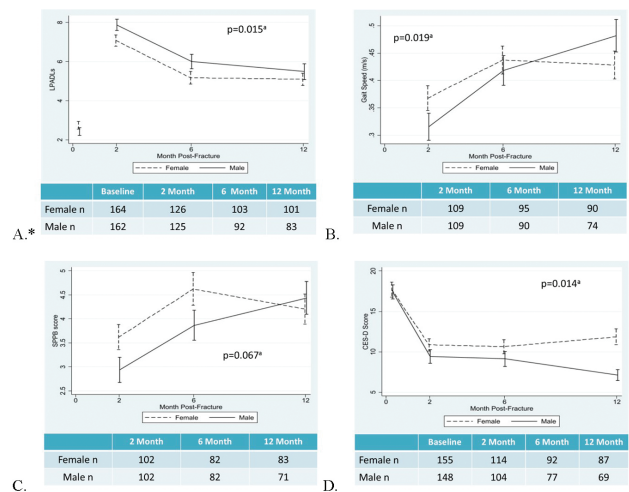


Figure 4. Mean changes in outcome measures with significant or borderline significant differences in slopes by sex. LPADL = Lower Extremity Physical Activities of Daily Living; SPPB = Short Physical Performance Battery; CES-D = Center for Epidemiologic Studies–Depression scale. *The reporting period for the baseline assessment of LPADLs was during the 1 week prior to the fracture. * p value for a hypothesis test of difference in slopes. Full color version is available within the online issue.

for LEGS ($p = .206$). Females had faster gait speeds than males at 2 months (Figure 4B) and continued to have improvements at 6 months but plateaued between 6 and 12 months with a 12-month gait speed of 0.43 m/s. Males appeared to catch up to females at 6 months and, unlike the females, continued to improve in gait speed out to 12 months, walking faster than females (0.48 m/s). A similar pattern was seen for SPPB (Figure 4C), where females had better SPPB at 2 months (3.62 vs 2.94) and improved between 2 and 6 months but had a slight decline by 12 months (4.20). While males started out with worse scores, they continued to improve over this time period with an SPPB score of 4.44 at 12 months.

Cognition and depressive symptoms

There were no sex differences in the mean change in outcome from baseline for the 3MS ($p = .180$), but there were significant sex differences in the mean change from baseline for the CES-D ($p = .014$; Figure 4D). Females and males experienced declines in depressive symptoms from baseline to 2 months (females, 17.59–10.86; and males, 17.28–9.34). Males continued to improve throughout the study (12-month CES-D 8.13); however, females plateaued and had a slight worsening of symptoms from 6 to 12 months (12-month CES-D 12.03).

Body composition

There were no significant sex differences ($p > .05$) in the mean change from baseline for any body composition measure (adjusted total body lean mass, adjusted appendicular lean mass, and femoral neck BMD).

Strength

Males and females did not demonstrate significant differences in mean change in grip strength from baseline ($p = .161$).

Sensitivity Analysis and Missing Value Bias

For the purpose of sensitivity analysis and to assess the potential for missing value bias in the trajectory results, the models were

re-run restricted to those with complete data available at baseline and at 2, 6, and 12 months postadmission and compared to original analyses. This comparison revealed potential missing value bias for 3 outcomes based on moderate differences in effect sizes: gait speed, LEGS, and CES-D (32). For these outcomes, WEEs (33,34) were used to test whether the time-specific effect sizes were seriously biased, and the results were in the same direction and do not change the overall conclusions. The largest difference found between the reported time-specific results and those from the WEEs was less than 0.1 *SD*, which is considered very small, suggesting that missing value bias is unlikely to explain the observed results among survivors.

Discussion

Overall, males were in poorer health at the time of fracture and were more likely to die over the 12 months after hip fracture. Despite poorer survival and worse initial health, among survivors, males had continued recovery in LPADLs, gait speed, and depressive symptoms. Both sexes had improvements in these 3 outcomes over the first 6 months, but males continued to improve over the next 6 months while females remained stable or declined.

While there was an improvement in 12 months, the average gait speed for males (0.48 m/s) and females (0.43 m/s) at 1-year postfracture is very slow. Cummings et al. (35) suggested that a gait speed of ≤ 0.6 m/s may be used to define a diagnosis of dysmobility in clinical care settings, and research has shown that gait speeds below 0.6 m/s predict 1-year hospitalization, worse quality of life, poor survival, and greater limitations in IADL (36–38). In this sample, 75% of females and 64% of males were walking less than 0.6 m/s at 12 months postfracture. A gait speed of 0.46 m/s is consistent with a state-like condition of disability reported by Miller et al. (39) that reflects a dramatic reduction in gait speed. Among community-dwelling older adults, men have faster gait speeds on average compared to women (40) and slower gait speeds predicted greater disability and poor survival in both men and women (41). This sex-based difference in gait speed may be due to differences in body composition, whereas women are more likely to have higher total body fat and intermuscular fat which has been associated with slower gait speed and poorer physical performance (42).

The LPADL measure is unique because an actual comparison can be made between disability status before the fracture and over the follow-up period. Among survivors, the prefracture disability level was still much better than the 12-month level. While surviving hip fracture patients may have had reductions in disability over the postfracture period, they did not get back to their prefracture level of function reporting twice the amount of disability at 12 months. Among those without disability in a given LPADL prior to the fracture, male survivors had a significantly greater new-onset disability in 6 activities compared to female survivors, suggesting that the hip fracture had a greater impact on the men who were healthier at the time of fracture. No significant difference in change was found when the analysis was conducted on individual LPADL items (eg, walk 10 feet, walk 1 block, and climb 5 stairs), suggesting that the significant difference found by sex is an overall assessment of ability and not specific to any single activity.

Although nonsignificant, the same general pattern was also observed for the SPPB. One year after hip fracture, the SPPB scores of males and females are quite low (females, 4.2; males, 4.4). Specifically, SPPB scores below 10 have been shown to be predictive of adverse outcomes such as mobility disability, lower forced expiratory volume, nursing home admission, and mortality in older adults (26,43–48). Prior research has shown that women on average score lower on the SPPB compared to men in the community (49,50), and

there are sex differences in SPPB score over time with women having a faster decline in SPPB score with increasing age (48). Additionally, poorer SPPB performance can be attributed to higher rate of depression in women compared to men (50). It is notable that 12-month values for SPPB (and gait speed) in this study differ from those in other studies of hip fracture patients, which may be due to differences in eligibility criteria as well as case-mix of patients at the study hospitals, care provided in the hospital and whether there is specialized orthogeriatric care, length of hospital stay, and the rehabilitation course postdischarge including the location, intensity, and duration.

These findings are contrary to prior studies that reported better outcomes among females (9–11) or no difference in outcomes by sex both in short-term (10,12,13) and long-term follow-up studies (4,13–15). To the best of our knowledge, only one prior study (8) demonstrated better short-term recovery among male hip fracture patients in functional independence (assessed with the Functional Independence Measure as opposed to self-reported ADLs in our study) and depressive mood (measured by the Short Zung Interviewer-assisted Depression Rating Scale while our study used the CES-D). However, this study of 64 female and 35 male hip fracture patients conducted assessments only at patient admission and discharge from geriatric rehabilitation (mean follow-up time = 49.5 days) (8).

The better performance among male survivors in our study may be driven by multiple factors. First, males were significantly more likely to live with another individual and be married than females at the time of fracture; social connectedness is associated with improved hip fracture recovery (51,52). Second, depressive symptoms are associated with reduced rehabilitation participation (53) and worse recovery after fracture (53,54). Consequently, the lower disability and better physical performance in male survivors, particularly after 6 months, could be a reflection of lower depressive symptoms. Third, although there were no sex differences in changes in body composition over time, males had significantly greater lean body mass, BMD, and strength at baseline, compared to females. These differences in body composition at baseline may have a long-term rehabilitative benefit for males with respect to LPADL, SPPB, and gait speed improvements after fracture. Fourth, because males generally demonstrated worse impairment at the time of hip fracture, they had a greater opportunity to demonstrate improvement and/or this recovery could be more protracted in time.

The poorer health at the time of fracture among male patients may have yielded a selective survival of the healthiest males that could be an additional factor explaining some of the sex differences in recovery. The divergence in survival between males and females is most strongly noted from baseline to 6 months postadmission, when mortality risk is the greatest (55). The sensitivity analysis conducted sheds some light on any bias due to selective survival. In the sensitivity analysis, 2 of the outcomes, where significant sex differences were seen in mean changes from baseline, gait speed, and the CES-D, yielded different results than in the full analysis. However, for both of these outcomes, the overall direction remained the same and there were only small changes in the estimates. As a result, selective survival may explain some, but not all, of the differences in recovery between males and females between 6 and 12 months postadmission. These results may support the emerging literature on personalized rehabilitation strategies based on specific comorbidities while also considering sex. Shibasaki et al. (56) found that interventions targeted to manage behavioral and psychological symptoms of dementia can have a positive effect on overall posthip fracture rehabilitation. There is also evidence that depressive symptoms (57) or a specific

comorbidity can affect posthip fracture recovery in a particular outcome. For example, diabetes was important for global measures of physical and mental health recovery, whereas, osteoporosis mostly affected functional recovery (58).

The study sample may not be representative of the larger population of hip fracture patients and is limited to predominantly White patients entering 8 hospitals in Baltimore, MD. Additional research is needed in more diverse groups of hip fracture patients to identify whether there are comparable sex differences by race and/or ethnicity. The study's findings are only generalizable to those who survive the initial acute period, recognizing that research on sex differences in mortality during the first 2 weeks of hospitalization is needed. Functional measures such as LPADLs and IADLs were based on subjective report versus observations and thus, may have been biased; however, having a measure of prefracture disability is unique for assessing recovery. Additionally, we were unable to compare individuals to their prefracture status for other measures. Still, we were able to describe the changes in these measures from the time of fracture to 12 months among those who survived. Lastly, we were not able to capture real-world mobility represented by a number of steps covered in a typical day or time spent in activity, nor did we collect important information about patient's perspectives on changes in their mobility (eg, Patient Reported Outcomes), measures that will need to be incorporated into future studies. However, real-world mobility depends on behavior, performance, and environment. While real-world behavior is an important outcome worthy of research, especially for interventions, it would be difficult to discern if differences between men and women reflect sex differences in either performance, behavior, or environment. These limitations are offset by the fact that this is the largest longitudinal study of hip fracture patients to date that specifically addresses sex differences in multiple outcomes over 1-year posthip fracture.

Overall, this study confirms the finding that males die at a higher rate than females after hip fracture and suggests that males who survive have better functional recovery and a more pronounced return to independence after hip fracture than females. Additional analysis is needed to determine the mechanisms (eg, perioperative events, surgical approach, pain, biomarkers, resilience) contributing to the higher mortality in males and better long-term outcomes in males among those who survive, and on how this information can be leveraged to inform prognosis and rehabilitative interventions.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

D.L.O., D.S.A., M.C.H., A.R.C., J.G., A.G.-B., G.E.H., B.R., M.S., and R.S.S. have no conflicts of interest to disclose. J.M. reports personal fees from Pluristem Pharma. J.M.G. reports personal fees from Pluristem Pharma, Boehringer-Ingelheim, and Viking Therapeutics. R.R.M. is a full-time employee of the Novartis Institutes for BioMedical Research.

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Author Contributions

D.L.O., J.M., D.S.A., and A.G.-B. had access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: D.L.O., J.M., M.C.H., A.R.C., A.G.-B., G.E.H., R.R.M., B.R., and R.S.S. Acquisition of data: D.L.O., J.M., M.C.H., and A.G.-B. Analysis and interpretation of data: All authors. Drafting of the manuscript: D.L.O., J.M., D.S.A., and R.B. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: D.S.A., A.G.-B., J.G., and M.S. Obtained funding: D.L.O., J.M., M.C.H., A.G.-B., A.R.C., G.E.H., R.R.M., B.R., and R.S.S.

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