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Persistence of Depressive Symptoms and Gait Speed Recovery in Older Adults after Hip Fracture

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Abstract

Objective—Depression after hip fracture in older adults is associated with worse physical performance; however, depressive symptoms are dynamic, fluctuating during the recovery period. The study aim was to determine how the persistence of depressive symptoms over time cumulatively affects the recovery of physical performance.

Methods—Marginal structural models estimated the cumulative effect of persistence of depressive symptoms on gait speed during hip fracture recovery among older adults (n=284)

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Ethics statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Conflict of interest

Dr. Jay Magaziner has consulting agreements with Ammonett, Novartis, Viking, and Pluristem. Dr. Denise Orwig has consulting agreements with Kinexum and Viking. Drs. Alan M. Rathbun, Michelle D. Shardell, Elizabeth A. Stuart, Ann L. Gruber Baldini, Glenn V. Ostir, Gregory E. Hicks, and Marc C. Hochberg have no conflicts of interest to declare.

Author contributions

AMR participated in study design and data acquisition, conducted statistical analyses, interpreted results, and drafted and wrote the manuscript. MDS and EAS participated in study design and statistical analyses, interpreted results, and critically revised the manuscript for important intellectual content. ALG, DO, GEH, MCH, and JM participated in study design and data acquisition, interpreted results, and critically revised the manuscript for important intellectual content. GVO interpreted results and critically revised the manuscript for important intellectual content. AMR had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final version of the manuscript for publication.

enrolled in the Baltimore Hip Studies 7th cohort. Depressive symptoms at baseline and at 2 and 6 months post-admission for hip fracture were evaluated using the Center for Epidemiological Studies Depression (CES-D) Scale and persistence of symptoms was assessed as a time-averaged severity lagged to standardized 3-meter gait speed at 2, 6, and 12 months.

Results—A one-unit increase in time-averaged CES-D score was associated with a mean difference in gait speed of -0.0076 standard deviations (95% confidence interval [CI]: -0.0184 , 0.0032 ; $p = 0.166$). The association was largest in magnitude from baseline to 6 months: -0.0144 standard deviations (95% CI: -0.0303 , 0.0015 ; $p = 0.076$). Associations for the other time intervals were smaller: -0.0028 standard deviations (95% CI: -0.0138 , 0.0083 ; $p = 0.621$) at 2 months and -0.0121 standard deviations (95% CI: -0.0324 , 0.0082 ; $p = 0.238$) at 12 months.

Conclusion—Although not statistically significant, the magnitude of the numerical estimates suggests that expressing more depressive symptoms during the first 6 months after hip fracture has a meaningful impact on functional recovery.

Keywords

Aging; Hip fracture; Depressive symptoms; Physical performance

Introduction

Depressive symptoms develop in approximately 50% of the many older adults who annually experience a hip fracture, an acute medical event that is associated with excess morbidity and mortality.^{1–3} Research has consistently demonstrated that post-fracture depressive symptoms are associated with greater functional disability.^{4–8} Therefore, depressive symptoms are an important sequela and their deleterious impact on functional recovery may account (in part) for why 50–75% of hip fracture patients never regain their pre-fracture physical function.^{1, 7, 9} Depressive symptoms after hip fracture are dynamic, but existing research has largely evaluated the transient effects of depressive symptoms measured at one point in time.^{8, 10}

The relationship (Figure 1) between depressive symptoms and physical performance after hip fracture is likely bidirectional. More specifically, increases in depressive symptoms are associated with worse gait speed, and poor gait speed predicts greater depression severity.¹¹ In addition to physical performance, depressive symptoms may affect the likelihood of future depressed mood and severity or status of time-varying confounders (e.g., cognitive functioning) involved in hip fracture recovery and vice versa. These dynamic interactions may explain why depressive symptoms that persist after hip fracture are associated with significant deficits to physical performance.^{4, 5} However, the effects of persistently high levels of depressive symptoms during the recovery period may accumulate over time even after the resolution of depressed mood, a paradigm that has been observed in other musculoskeletal conditions among older adults.¹²

The study objective was to evaluate how the persistence of depressive symptoms cumulatively affects the recovery of gait speed after hip fracture. It was hypothesized that

persistent post-fracture depressive symptoms would be associated with worse gait speed after hip fracture and that the magnitude of the association would increase over time.

Methods

Study Data & Sample

Baltimore Hip Studies 7th cohort (BHS-7) participants were recruited from 2006 to 2011 from eight participating BHS network hospitals in the Baltimore metropolitan area, and detailed study methodology is available elsewhere.^{13, 14} Briefly, protocols were reviewed and approved by the University of Maryland Baltimore Institutional Review Board and the review boards of participating hospitals. Participants were aged 65 years or older at the time of hospitalization for hip fracture and consented to enroll or had a proxy provide informed consent within 15 days of admission. Exclusion criteria included pathologic fracture, not community dwelling at the time of fracture, non-English speaker, being bedbound for 6 months before fracture, residence of greater than 70 miles from the hospital, weight of more than 300 pounds, not undergoing surgery, and hardware in the non-fractured hip. Participants were evaluated within 22 days of hospital admission (baseline) and at 2, 6, and 12 months post-admission. Data were collected by trained research staff and included medical record abstractions, questionnaires, and measures of body composition and functional performance.

A total of 362 hip fracture patients were enrolled (180 males and 182 females). Five participants did not provide data at the baseline or 2-month follow-up visit and another 18 participants were removed from the analysis sample as a result of an IRB-requested post procedure audit (6 participants were subsequently found to be ineligible because they did not meet study inclusion criteria and 12 participants were determined to be ineligible secondary to failures of the informed consent process), leaving a sample of 339 participants. In the overall BHS-7 cohort (n=339), there were 55 and 21 participants with missing data on time-invariant and time-varying covariates at baseline (Figure 2), respectively. Among those with complete baseline data: 182 participants had complete data at baseline and 2 months; 122 participants had complete data at baseline and 2 and 6 months; and 82 participants had complete data at baseline and at 2, 6, and 12 months.

Gait Speed

Physical performance was measured using 3-meter gait speed assessed at 2, 6, and 12 months post-admission. Participants were instructed to stand with both feet together at the starting line, to walk to the other end of the course “at your usual speed just as if you were walking down the street to go to the store,” to keep walking through the end of the course, and to only stop after crossing the finish line. Participants were permitted to use walking aids when recommended to do so by their treating physician; however, they were otherwise encouraged to walk without using any assistive devices. Physical performance outcome values were standardized using the pooled mean (0.4082055) and standard deviation (0.2535071) from 2, 6, and 12 months among surviving participants across multiply imputed datasets so that associations could be interpreted per standard deviation of gait speed. A clinically meaningful effect-sized based difference is approximately 0.2 standard deviations

and translates to a change in gait speed of 0.03 m/s.¹⁵ Gait speed was both an outcome variable and time-varying confounder.

Depressive Symptoms

Depressive symptoms were measured at baseline and at 2, 6, and 12 months follow-up using the 20-item Center for Epidemiological Studies Depression (CES-D) Scale.¹⁶ To ensure temporality between exposure and outcome, only CES-D scores at baseline and at 2 and 6 months post-admission were used, lagged to physical performance assessments at 2, 6, and 12 months follow-up. Depressive symptoms occur on a continuum such that greater severity is attributed to having a larger number of symptoms. Moreover, the reference timeframe for CES-D items corresponds to how participants felt during the previous week, and diagnostic criteria for major depressive disorder requires the core symptoms of depression to be present for at least two weeks.^{16, 17} The noted assessment characteristics for measuring depressive symptoms highlight their stability over time, and studies indicate the median time to recovery from major depression ranges from 6 to 12 months, and chronic depressive episodes can last for more than 2 years.^{18, 19} Therefore, persistence of depressive symptoms for each participant at each time point was operationalized as a time-averaged severity, reflecting aggregative effects, calculated as the product of exposure intensity and duration.²⁰ Given the between-visit follow-up variability, depressive symptom exposure was computed as a time-averaged score, and depressive symptom severity was assumed to be constant for each time interval: baseline to 2 months, 2 months to 6 months, and 6 months to 12 months. For example, CES-D scores of 30 at baseline, 20 at 2 months, and 10 at 6 months were used to calculate time-averaged depressive symptom scores as $(30 \times (2/2))$ at 2 months, $(30 \times (2/6)) + (20 \times (4/6))$ at 6 months, and $(30 \times (2/12)) + (20 \times (4/12)) + (10 \times (6/12))$ at 12 months.

Covariate Measures

Baseline variables abstracted from patients' medical records included age (years), sex, body mass index (BMI, kilograms per meters squared), pre-fracture depressive illness, and number of comorbid conditions measured using a modified Charlson Comorbidity Index that omitted mild liver disease.²¹ Patient-reported surveys assessed the following baseline covariates: race (white or nonwhite), education (years), marital status (never, married, widowed, divorced, or separated), and pre-fracture functional disability using Instrumental Activities of Daily Living (IADL) data obtained from a modified version of the Older Americans Resources and Services Instrument.²²

Time-varying covariates measured at baseline and at 2 and 6 months post-admission were potential confounders for gait speed at 2, 6, and 12 months, respectively. Patient-reported surveys evaluated the following time-varying confounders: 1) social interaction (number of social activities) using a social activity measure adapted from House and colleagues;²³ 2) Modified Mini-Mental State (3MS) Examination used to assess cognitive status;²⁴ 3) hip pain (yes or no) based on the presence of "pain in or around either hip joint, including the buttocks, groin, or either side of the upper thigh"; and 4) antidepressant use (never, past, or current) from a single-item question asking about the current use of antidepressants (fluoxetine, sertraline, paroxetine, or bupropion).

Statistical Analysis

Missing values for time-varying variables were imputed using multiple imputation in participants (n=284) with complete baseline data on time-invariant covariates.²⁵ Missing values for time-varying covariates at baseline and 2 and 6 months, including depressive symptoms (n=187), social interaction (n=136), cognitive status (n=136), hip pain (n=191), and antidepressant use (n=142), were imputed in surviving participants at baseline and at 2 and 6 months. Missing gait speed values (n=274) were imputed among non-censored participants: n=80 at 2 months, n=94 at 6 months, and n=100 at 12 months. The potential analysis sample consists of 1019 observations (339×3), while the effective complete case analysis sample included 182 participants with 386 data points. Based on a conservative missing data rate of approximately 60%, sixty datasets were imputed and analyzed.

Participants' baseline characteristics were compared between the depressed (CES-D 16) and non-depressed. Proportions and means with 95% confidence intervals were estimated for categorical and continuous variables, respectively. Descriptive statistics were averaged values from all 60-imputed data-sets. Regression models (linear, logistic, or multinomial) for multiply-imputed data were used to evaluate the association between baseline depressive symptoms and each covariate and to obtain a P-value from the model F statistic. Baseline characteristics were compared among participants (n=263) with complete data at study enrollment between complete cases (n=82) and individuals (n=181) with missing information during follow-up to evaluate differences between those with and without missing data.

Marginal structural models (MSMs) are an epidemiologic method explicitly developed to evaluate the cumulative effects of dynamic exposures.²⁶ MSMs use inverse probability of exposure weights and censoring weights to control for time-dependent confounding and mitigate selective attrition. MSMs yield unbiased estimates conditional on five (some untestable) assumptions: exchangeability, positivity, consistency, correct model specification, and no measurement error.²⁶ Exchangeability implies no unmeasured confounding; positivity assumes there are both unexposed and exposed persons at all levels of the confounders; and consistency assumes a subject's observed outcome is their potential outcome under the exposure history they actually had.²⁷

The analysis was implemented in two stages: 1) models predicting the probability of exposure and censoring at each time point and 2) structural models of outcomes fit using weights generated in the first stage.²⁶ At the first stage, subjects' CES-D scores at baseline and at 2 months and 6 months were categorized using quantile binning with ten bins, which has been shown to perform well in practice.²⁸ Pooled ordinal logistic models were used to estimate the probability of membership to each category conditional on baseline and time-varying confounders. Time-specific exposure probabilities were cumulatively multiplied across time points to weight an individual's observation at a given visit by the inverse probability of having the exposure history he or she had up until that time point. The inverse of the conditional probability of membership to a given quantile grouping at each time point was stabilized with the estimated exposure probability given time-invariant confounders to improve structural outcome model estimation efficiency.²⁶ Censoring weights were calculated in a similar manner to the exposure weights and accounted for selective survival.

²⁶ The final weights were the cross product of the exposure weights and censoring weights at each time point.

In the second stage, weighted linear models were used to determine how time-averaged CES-D scores were associated with standardized gait speed after hip fracture. CES-D values at baseline and at 2 months and 6 months were modeled as a continuous, time-averaged score, representing the mean persistence of depressive symptoms from baseline through a given visit on future gait speed assessed at 2, 6, and 12 months follow-up. Structural outcome models included time-averaged CES-D scores, visit indicators, and interactions between time-averaged CES-D scores and visit. MSMs were fit for all 60 imputed datasets and then pooled to obtain summary estimates. Structural outcome models estimated slopes for the association between time-averaged CES-D scores and standardized gait speed. Also, parameter estimates were used to compute associations for 16-unit differences in time-averaged CES-D scores and standardized gait speed. Statistical tests were two-sided, significance was set at an alpha level of 0.05, and analyses were conducted using Stata (Version 13.1, Stata Corp, College Station, Texas, USA). Sensitivity analyses testing the robustness of the results are described in the Appendix.

Results

The distributions of covariate values were similar between depressed and non-depressed participants at study enrollment across multiply-imputed datasets (Table 1). The mean time-averaged depressive symptom scores were 17.6 ± 10.8 from baseline to 2 months, 12.9 ± 8.1 from baseline to 6 months, 11.4 ± 7.1 from baseline to 12 months, and 14.1 ± 9.3 across all these intervals. Average gait speeds were $0.34 \text{ m/s} \pm 0.24$ at 2 months, $0.43 \text{ m/s} \pm 0.26$ at 6 months, and $0.44 \text{ m/s} \pm 0.25$ at 12 months. Loss to follow-up from death resulted in 9 participants censored at 2 months, 16 subjects censored at 6 months, and 12 subjects censored at 12 months, yielding an effective sample size of 284 subjects with 781 analytic observations for each imputed dataset. Participants with missing data during follow-up had greater baseline comorbidity and pre-fracture functional disability and were more likely to experience hip pain, while complete cases had more social interactions and better cognitive function (Supplementary Table 1).

The point estimate (Table 2) representing the marginal association between post-fracture depressive symptoms and gait speed averaged across all time intervals was not statistically significant ($p = 0.166$) and implied that for each 1-unit increase in time-averaged CES-D score there was a corresponding mean decrease in gait speed of 0.0076 standard deviations (95% confidence interval [CI]: $-0.0184, 0.0032$). Thus, the marginal difference (Table 3) in gait speed during the year after hip fracture between participants with (i.e., CES-D=16) and without (CES-D=0) depressive symptoms defined by a time-averaged CES-D score meeting threshold screening criterion was -0.1219 standard deviations (95% confidence interval [CI]: $-0.2949, 0.0511$).

The time-specific associations (Table 2) indicated the relationship between time-averaged CES-D scores and standardized gait speed was strongest from baseline to 6 months: $\beta = -0.0144$ standard deviations (95% CI: $-0.0303, 0.0015$; $p = 0.076$). The estimated beta

coefficients for the other time periods (2 and 12 months) were lower in magnitude: -0.0028 standard deviations (95% CI: $-0.0138, 0.0083$; $p = 0.621$) at 2 months and -0.0121 m/s (95% CI: $-0.0324, 0.0082$; $p = 0.238$) at 12 months. These effect estimates translated to mean differences in gait speed of -0.0443 (95% CI: $-0.2209, 0.1324$; $p = 0.621$), -0.1886 (95% CI: $-0.4204, 0.0431$; $p = 0.110$), and -0.1527 (95% CI: $-0.4793, 0.1438$; $p = 0.356$) standard deviations between participants with and without depressive symptoms defined by a time-averaged CES-D score from baseline to 2 months, baseline to 6 months, and baseline to 12 months, respectively (Table 3). Despite the heterogeneity, neither the time-specific associations nor interaction ($p = 0.300$) between time-averaged depressive symptom scores and visit were statistically significant.

Sensitivity analyses using generalized estimating equations (GEEs) across multiply-imputed datasets generally yielded similar estimates (Supplementary Table 2) and time trends compared to the main results. Notably, the main effect across all time intervals was statistically significant, and differences between the time-specific associations were smaller in magnitude. Findings from GEEs applied in the context of a complete case analysis, consisting of 182 participants with 386 observations with complete data, produced estimates (Supplementary Table 3) comparable to the primary results for the main effect and time-specific associations at 2 and 6 months but not 12 months.

Discussion

This study evaluated how the persistence of post-fracture depressive symptoms during the year after hip fracture was associated with gait speed, and findings illustrated different patterns of effect accumulation that did not reach statistical significance. Depressive symptoms that persisted from baseline to 2 months had the smallest impact on gait speed, less than 0.05 standard deviations for a CES-D score meeting threshold screening criterion. By contrast, the influence of persistent depressive symptoms after hip fracture was largest from baseline to 6 months, with an estimated mean decrease of approximately 0.2 standard deviations in gait speed at 6 months for a 16-unit difference in time-averaged CES-D score. However, the magnitude of the association decreased for depressive symptoms persisting throughout the entire year after hip fracture. Although the observed associations were not statistically significant ($p > 0.05$), the magnitude of the association between persistent depressive symptoms and gait speed during the first 6 months after hip fracture may be clinically meaningful.¹⁵

The results are consistent with prior studies demonstrating that longer periods of depressive symptoms after hip fracture are associated with greater decreases in physical function.^{4–8} Yet, the results diverge from prior research and show temporal trends illustrating non-linear effects of persistent depressive symptom on gait speed over time. Specifically, the association between time-averaged CES-D scores and gait speed was weakest at 2 months after hip fracture, strongest at 6 months post-fracture, and intermediate at 12 months. Thus, the most clinically meaningful impact was in participants with more persistent depressive symptoms at baseline and 2 months post-fracture with respect to 6 month gait speed, when hip fracture patients experience the largest improvements in physical function.^{2, 15} These data support previous BHS research findings that demonstrated the presence of depressive

symptoms 2 months after hip fracture was associated with clinically significant, smaller improvements in physical performance, when compared to non-depressed individuals at 12 months follow-up.⁸ Experiencing a catastrophic medical event, like hip fracture, may create vulnerability and a loss of self-control among older adults, and optimal psychosocial functioning is integral to achieving ideal rehabilitation outcomes.²⁹ Thus, routine screening to diagnose persistent depressive symptoms after hip fracture may be useful in identifying individuals in this vulnerable population who are at risk of poor functional recovery.³⁰ Through the appropriate recognition of depressive symptoms that remain unresolved, it is possible to initiate treatment early during the post-fracture recovery period, when patients are most susceptible to being adversely affected by mood disorders.

Depression affects biological, psychological, and behavioral processes, and several mechanisms could account for the negative effects of persistent depressive symptoms on functional recovery after hip fracture. For example, increases in inflammation after hip fracture that are of consequence of depression could cause greater hip pain and indirectly lead to decreases in post-fracture gait speed.^{6, 10, 31} Alternatively, depression is associated with painful emotional states (e.g., negative affect) and may decrease patients' self-efficacy and affect their adherence and compliance to medical care during the rehabilitation process.^{32–34} There also is a strong physical activity component to depression, and behavioral patterns that develop during extended periods of depressed mood could result in greater sedentary activity after hip fracture and have adverse effects on body composition and gait speed.^{11, 35} However, neither the marginal or time-specific associations were statistically significant in the current study, and it is possible that the magnitude of effect of persistent depressive symptoms on gait speed over time is not large enough to detect using the BHS-7 study sample. In addition, the use of multiple imputation and inverse probability weighting are known to increase variation, and therefore, decrease statistical power.^{25, 27} Whether a consequence of the sample size or increased measurement variability, a lack of power could have inhibited the identification of statistically significant associations. Given the potential for a clinically significant effect of depressive symptoms on functional recovery after hip fracture, validation research evaluating the observed relationships using larger hip fracture samples is warranted.

There are several study limitations and strengths. Depressive symptoms were evaluated using a patient-reported questionnaire, which is not equitable to clinically diagnosed depression. Fluctuations in depressive symptoms may have occurred between visits; however, in contrast to the operationalization used herein, most previous work has not operationalized depressive symptoms in a way that leverages multiple measures (e.g., pooled cross-sectional) or accounts for any changes (e.g., baseline measure only). BHS-7 was originally powered to detect signals for time-invariant variables, and there may have been insufficient power to detect associations for a dynamic exposure. There were substantial missing data, which creates the potential for selection bias, but this limitation was mitigated using validated approaches to handle missingness. Lastly, the cohort was primarily white older adults from the Baltimore metropolitan area, and the results may lack generalizability to more diverse samples of hip fracture patients. The BHS-7 sample is small, but it is one of the largest cohorts comprising both men and women with hip fracture. Moreover, the operational definition for depressive symptoms leveraged information about measured

longitudinal depressive symptom history. An objective measure, gait speed, was used to assess physical function, rather than a subjective metric. Additionally, BHS-7 collected extensive clinical and patient-reported measures at multiple time points in the year after hip fracture that were used to control for a wide variety of potential confounders. Lastly, robust statistical methods also were used to address missing data, time-dependent confounding, and selective survival. This study is the first to evaluate how the persistence of depressive symptoms cumulatively affects functional recovery over time after hip fracture.

Conclusion

In summary, depressive symptoms that arise after hip fracture and continue to persist throughout the first six months of recovery may have a clinically meaningful impact on the restoration of gait speed. Our findings underscore the need to consider psychosocial functioning when designing integrated medical management strategies for rehabilitation after hip fracture in order to optimize functional recovery. Future research should strive to determine whether depression modifies the effect of rehabilitation activities on physical performance after hip fracture and to identify depressed patient subgroups in which interventions for persistently high levels of post-fracture depressive symptoms may be most effective.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Key Points

- Depressive symptoms may influence gait speed in the first 6 months after hip fracture
- Early depression screening and treatment after hip fracture may improve functional recovery

Figure 1.

Figure 2.

Table 1

Baseline sample (n=284) characteristics pooled across imputed datasets (m=60).

Variable	Depressed (% or mean, 95% CI)	Non-Depressed (% or mean, 95% CI)	P Value
Female	48.0%	39.9, 56.1	55.2% 46.7, 63.7 0.226
Age (years)	80.8	79.6, 82.0	80.5 79.1, 81.8 0.708
White	93.3%	89.3, 97.3	89.6% 84.4, 94.8 0.265
Education (years)	13.0	12.4, 13.5	13.4 12.8, 14.0 0.285
Marital Status			0.413
<i>Never</i>	6.5%	2.5, 10.5	4.7% 1.2, 8.3
<i>Married</i>	37.5%	29.7, 45.3	44.6% 36.1, 53.1
<i>Widowed</i>	46.0%	37.9, 54.1	41.1% 32.7, 49.5
<i>Divorced</i>	6.7%	2.7, 10.7	8.9% 4.1, 13.8
<i>Separated</i>	3.3%	0.4, 6.3	0.7% -0.7, 2.2
BMI (kg/m ²)	25.5	24.7, 26.3	25.2 24.3, 26.1 0.657
Depression History	24.6%	17.6, 31.5	20.3% 13.4, 27.1 0.390
Charlson Comorbidity	2.1	1.8, 2.4	2.0 1.7, 2.3 0.417
IADL	2.0	1.7, 2.2	2.0 1.7, 2.2 0.962
Social Interaction	9.4	8.0, 10.8	11.4 9.9, 12.9 0.065
3MS	84.8	82.6, 87.0	87.2 85.0, 89.3 0.130
Hip Pain	17.2%	10.8, 23.6	14.9% 8.6, 21.2 0.599
Antidepressant Use			
<i>Never</i>	64.0%	56.3, 71.8	67.1% 59.1, 75.1 0.757
<i>Past</i>	8.0%	3.6, 12.4	5.9% 1.9, 10.0
<i>Current</i>	27.9%	20.7, 35.2	27.0% 19.4, 34.5

95% CI: 95% confidence interval; BMI (kg/m²): Body mass index (kilograms per meters squared); IADL: Instrumental Activities of Daily Living; 3MS: Modified Mini-Mental State Examination.

Table 2

Associations between time-averaged CES-D scores and standardized 3-meter gait speed after hip fracture.

Persistence of Depressive Symptoms	Gait Speed Assessment	β	95% CI	P Value
Baseline to 12 months	2, 6, and 12 months	-0.0076 ^{a,b,c}	-0.0184, 0.0032	0.166
Baseline to 2 months	2 months	-0.0028 ^{b,c}	-0.0138, 0.0083	0.621
Baseline to 6 months	6 months	-0.0144 ^{b,c}	-0.0303, 0.0015	0.076
Baseline to 12 months	12 months	-0.0121 ^{b,c}	-0.0324, 0.0082	0.238

β : beta in standardized gait speed ((gait speed-0.4082055)/0.2535071) per unit of time-averaged CES-D score estimated from marginal structural models pooled from across (m=60) multiply-imputed datasets; 95% CI: 95% confidence interval.

^a Adjusted for time but no time-by-depressive symptom interaction terms.

^b Adjusted for confounders from study baseline: sex, age, race, education, marital status, BMI, depression history, Charlson comorbidity, and IADL.

^c Adjusted for time-varying confounders concurrent to depressive symptoms: social interaction, 3MS, hip pain, antidepressant use, and gait speed.

Table 3

Associations between a 16-unit difference in time-averaged CES-D scores and standardized 3-meter gait speed after hip fracture.

Persistence of Depressive Symptoms	Gait Speed Assessment	β	95% CI	P Value
Baseline to 12 months	2, 6, and 12 months	-0.1219 ^{a,b,c}	-0.2949, 0.0511	0.166
Baseline to 2 months	2 months	-0.0443 ^{b,c}	-0.2209, 0.1324	0.621
Baseline to 6 months	6 months	-0.1886 ^{b,c}	-0.4204, 0.0431	0.110
Baseline to 12 months	12 months	-0.1527 ^{b,c}	-0.4793, 0.1438	0.356

β : beta in standardized gait speed ((gait speed-0.4082055)/0.2535071) per 16-unit difference in time-averaged CES-D score estimated from marginal structural models pooled from across (m=60) multiply-imputed datasets; 95% CI: 95% confidence interval.

^a Adjusted for time but no time-by-depressive symptom interaction terms.

^b Adjusted for confounders from study baseline: sex, age, race, education, marital status, BMI, depression history, Charlson comorbidity, and IADL.

^c Adjusted for time-varying confounders concurrent to depressive symptoms: social interaction, 3MS, hip pain, antidepressant use, and gait speed.