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Research Article

Inflammation, Depression, and Slow Gait: A High Mortality Phenotype in Later Life

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Abstract

Background. Inflammation, slow gait, and depression individually are associated with mortality, yet little is known about the trajectories of these measures, their interrelationships, or their collective impact on mortality.

Methods. Longitudinal latent class analysis was used to evaluate trajectories of depression (Center for Epidemiologic Studies Depression ≥ 10), slow gait (<1.0 m/s), and elevated inflammation (interleukin 6 > 3.2 pg/mL) using data from the Health Aging and Body Composition Study. Logistic regression was used to identify their associations with mortality.

Results. For each outcome, low-probability ($n_{\text{inflammation}}$ = 1,656, $n_{\text{slow gait}}$ = 1,471, $n_{\text{depression}}$ = 1,458), increasing-probability ($n_{\text{inflammation}}$ = 847, $n_{\text{slow gait}}$ = 880, $n_{\text{depression}}$ = 1,062), and consistently high-probability ($n_{\text{inflammation}}$ = 572, $n_{\text{slow gait}}$ = 724, $n_{\text{depression}}$ = 555) trajectories were identified, with 22% of all participants classified as having increasing or consistently high-probability trajectories on inflammation, slow gait, and depression (meaning probability of impairment on each outcome increased from low to moderate/high or remained high over 10 years). Trajectories of slow gait were associated with inflammation (r = .40, p < .001) and depression (r = .49, p < .001). Although worsening trajectories of inflammation were independently associated with mortality (p < .001), the association between worsening trajectories of slow gait and mortality was only present in participants with worsening depression trajectories (p < .01). Participants with increasing/consistently high trajectories of depression and consistently high trajectories of inflammation and slow gait (n = 247) have an adjusted-morality rate of 85.2%, greater than all other classification permutations.

Conclusions. Comprehensive assessment of older adults is warranted for the development of treatment strategies targeting a high-mortality risk phenotype consisting of inflammation, depression, and slow gait speed.

Key Words: Frailty—Depression—Inflammation—Slow Gait—Mortality

Human aging is associated with chronic, low-grade inflammation (inflammaging) (1). Levels of pro-inflammatory cytokines such as interleukin 6 (IL-6) on average increase with age and peak in late life. Inflammaging has adverse affective, cognitive, motor, and neurostructural consequences for older adults (2). In addition to these pathological changes in later life, inflammation is associated with

morbidity and mortality by contributing to syndromes such as depressive illness (3) and frailty (4).

Inflammatory processes may play a causal role in the development of depression. Adults treated with the inflammatory cytokine interferon alpha were at risk for developing a major depression (5,6) characterized by symptoms of fatigue, psychomotor retardation, and decreased appetite (6). The inflammation-depression association has consequences for treatment, as elevated inflammatory markers in depressed individuals are associated with resistance to some antidepressant medications (3). The depression associated with an elevated inflammatory response is phenomenologically similar (7) to the syndrome of frailty (8), which itself is linked to inflammation and characterized by slowness, fatigue, weakness, shrinkage, and low physical activity (4). Of these characteristics, decreased gait speed (9,10), considered a "vital sign" to monitoring older adults (11–13), may have an important influence on the inflammation-depression relationship. Dopaminergic dysfunction in the basal ganglia that may be caused or made worse by inflammatory processes is associated with increased slowing (1,14,15). Similarly, slow gait in the context of depression is associated with higher mortality (16) and increased cardiovascular risk (17).

Despite the prognostic risk independently associated with inflammation, depression, and slow gait and the bivariate relationships shared between them (7,18), the nature of the relationship within the triad remains unknown. We believe this triad represents a clinical phenotype at grave risk for poor outcomes. Its deconstruction allows for the identification of targets for interventions (19) to alter the clinical trajectory of this high-risk cohort. The aims of this study were to (i) identify longitudinal trajectories of inflammation, depression, and slow gait and determine their association, (ii) determine the order in which the conditions manifest, and (iii) investigate the individual and joint associations between mortality and trajectories for these conditions. Using data from the Health Aging and Body Composition study, we tested the hypotheses that inflammation (i) would initiate a cascade of events leading to the development of slow gait and depression and (ii) would moderate the associations between slow gait and mortality and depression and mortality in late life, thus resulting in greater mortality.

Methods

Study Participants

The Health Aging and Body Composition Study is a National Institute on Aging project launched in 1997 to characterize the extent of change in body composition in older adults and examine the impact of these changes. Data were obtained in November 2013 and consist of 3,075 persons aged 70–79 years at baseline. Participants were selected if they were (i) free of difficulty in activities of daily living with (ii) no baseline functional limitation (difficulty walking ¼ mile or upto 10-steps without resting). Prior work has detailed criterion for inclusion and exclusion (20,21). Variables of interest were measured serially over 10 years, with mortality status available 15.9 years after baseline.

Age, gender, body mass index, Modified Mini-Mental Status Exam (22), medical comorbidity, and anti-inflammatory pharmacotherapy use were used as covariates (level of education and race were unrelated to mortality and not included as covariates). Dichotomous comorbidity variables were created from baseline questionnaires and grouped into six disease categories (0 = no diseases in that class, 1 = one or more diseases): physical (arthritis, osteoporosis), respiratory (asthma, chronic bronchitis, emphysema, chronic obstructive pulmonary disease), vascular (hypertension, diabetes mellitus, and current smoker, a vascular risk factor), cardiovascular (myocardial infarction, angina pectoris, congestive heart failure, coronary bypass/coronary artery bypass grafting), cerebrovascular (transient ischemic attack, stroke/cerebrovascular accident), and cancer (any type). A dichotomous variable for baseline anti-inflammatory pharmacotherapy (Cox II inhibitor, nonsteroidal anti-inflammatory medication, oral steroid medications, or oral salicylates) was classified.

Depression

Depressive symptoms were assessed using the original 20-item Center for Epidemiologic Studies Depression Scale at years 1, 4, 6, 8, and 10 (23). Scores range from 0 to 60 with a cutoff of ≥10 used to create a dichotomous variable (0 = nondepressed, 1 = depressed). This level, denoting significant subthreshold depressive symptoms, is associated with greater frailty and poorer prognosis (16,24).

Inflammatory Markers

Elevated levels of IL-6 were used to represent inflammation (1,25). IL-6 was assessed in years 1, 2, 4, 6, 8, and 10. A detailed explanation of the measurement procedures was previously described (18). The value that denotes the highest baseline quartile was used to represent inflammation (3.2 pg/mL). Although no normative data exist for IL-6 (26), a recent report showed comparable levels of IL-6 that represented an inflammatory response (27).

Slow Gait

Participants' usual walking speed was assessed at years 1, 2, 4, 6, 8, and 10 (6-meters in years 1, 4, 6, and 10, 20-meters in years 2 and 8). Gait was classified as slow if participants' usual walking speed was slower than 1.0 m/s. This cutoff marked the slowest baseline quartile and has been used to identify elders at risk for poor outcomes (20,28).

Statistical Analyses

Multivariate longitudinal latent class analysis was used to simultaneously model the trajectories of depression, inflammation, and slow gait. The longitudinal latent class analysis estimates class-specific probabilities of the dichotomous measures being positive at each time point, determining class-specific trajectories for each over time. Each individual's probability of class membership is estimated. The highest probability class assignments for each variable were extracted from the best fitting longitudinal latent class analysis and used as independent variables in subsequent analyses. Longitudinal latent class analysis models were fit using MPlus (Version 7.2) with full information maximum likelihood, accommodating missing data via a missing at random assumption. Fit was compared between 1-, 2-, 3-, and 4-class models using the Bayesian Information Criterion (BIC) (29). Baseline characteristics were compared across inflammation trajectory classes using one-way analysis of variance (continuous) and chi-square tests (categorical). Polychoric correlations were used to test the association between membership in trajectory classes.

The order in which each of the three conditions manifest was examined using lagged longitudinal logistic regression models. A separate model was fit for each outcome such that the outcome at each time *t* was predicted by all three of the measures at the previous time point (*t* – 1) with baseline age, sex, body mass index, Modified Mini-Mental Status Exam, comorbidities, and anti-inflammatory pharmacotherapy use entered as covariates and a random intercepts by person included to control for repeated measures. This lagged model estimates and tests the odds ratio of each outcome occurring at the next time point conditional on the presence of each at the current time point. SAS (version 9.4) Proc Glimmix was used to fit the lagged models.

Finally, logistic regression models were used to examine the association between mortality and the trajectory classes. Separate models initially examined associations between trajectories of each variable with mortality to test if each class assignment differed in its association with mortality. If not, these assignments were combined for the main analysis. The main logistic regression model including trajectory assignments for all three variables allowing for two- and three-way interactions was fit, with baseline age, sex, body mass index, Modified Mini-Mental Status Exam, comorbidities, and anti-inflammatory pharmacotherapy use entered as covariates. An identical covariate adjusted logistic model was conducted using baseline values of inflammation, slow gait, and depression to compare the use of longitudinal trajectories with baseline values. SAS (version 9.4) Proc Genmod was used to fit the logistic models and calculate the covariate-adjusted mortality rates (ILINK) across each permutation of class assignment for all three variables.

Results

Trajectories of Inflammation, Slow Gait, and Depression

A series of multivariate longitudinal latent class analysis models were fit to simultaneously derive trajectories for inflammation, slow gait, and depression. The model with each dichotomous variable having three trajectory classes fit the data best (BIC = 43386, 37239, 37084, 37246 for 1-, 2-, 3-, and 4-class models, respectively). Figure 1A, B, and C depict the three trajectories for each variable. The classes represent consistently low-, gradually increasing-, and consistently high-probability trajectories. The low-probability trajectory for each variable identifies older adults with a low likelihood of developing inflammation, slow gait, or depression over 10-years. Among the full sample, 53.9% were classified as consistently having a low-probability for inflammation, 47.8% for slow gait, and 47.4% for depression. Over the 10-year follow-up, 21.3% had a low-probability of impairment on all three conditions.

The increasing-probability trajectory identifies older adults whose likelihood of impairment gradually increases from low to moderate/high over 10-years. Twenty-eight percent of the sample had an increasing probability of inflammation, 28.6% of slow gait, and 34.5% of depression, with 3.1% of the sample having an increasing-trajectory on all three variables.

The consistently high-probability classification identifies older adults with a high-likelihood of inflammation, slow gait, or depression from beginning to end of follow-up. Nineteen percent of the sample had a consistently high classification for inflammation,

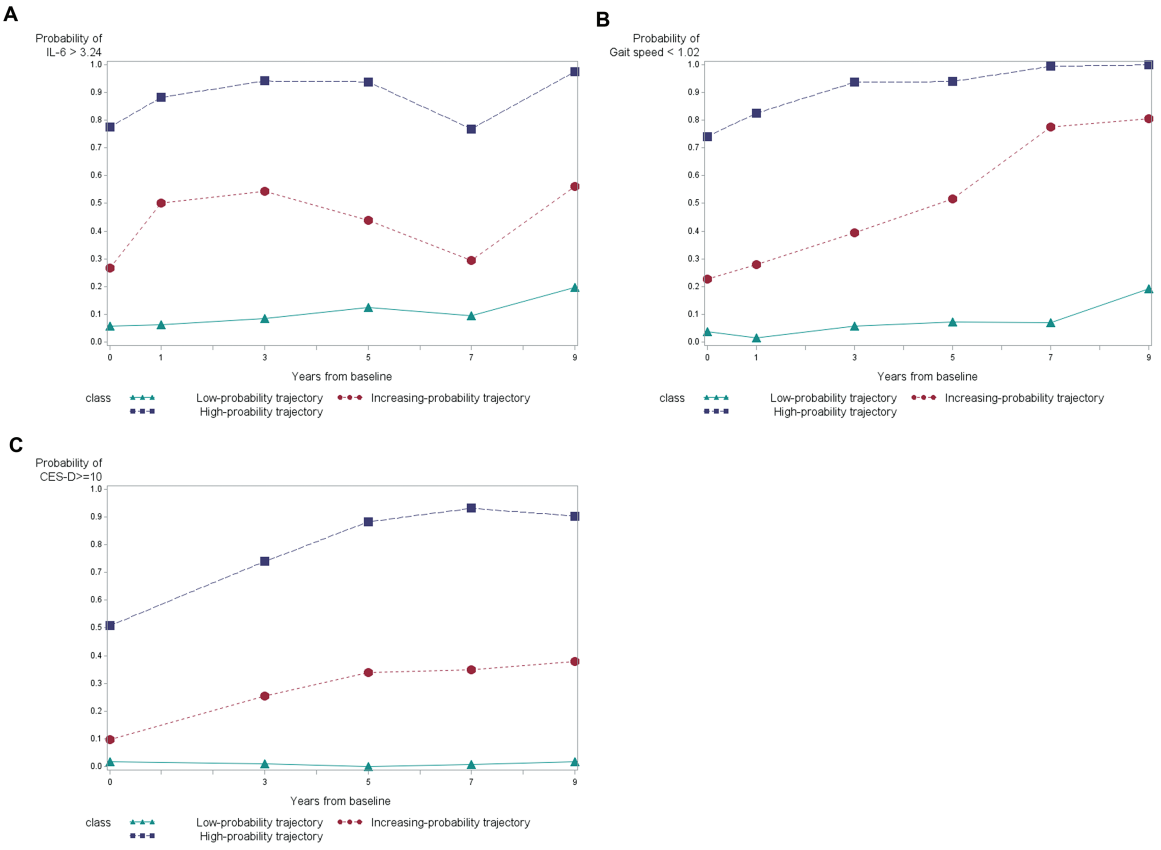

Figure 1. Mean trajectories of inflammation, slow gait, and depression over 10 years among functionally intact older adults. CES-D = Center for Epidemiologic Studies Depression Scale; IL-6 = interleukin-6. Increasing probability, Increasing risk class assignment; Low probability, Low risk class assignment; Consistently high probability, Consistently high risk class assignment. Depression defined as CES-D ≥ 10; Slow gait defined as usual walking speed < 1.0 m/s; Inflammation defined as IL-6 ≥ 3.2 pg/mL.

23.5% for slow gait, and 18.1% for depression. Over 10-years, 2.0% had high probability of impairment on all three.

Table 1 depicts baseline characteristics across inflammation trajectories. Individuals with an increasing or consistently high probability of inflammation were older and more often black, with lower levels of education, higher body mass index, and poorer cognition than those in the low probability class for inflammation ($p < .01$). This group had higher baseline prevalence of vascular, respiratory, and cardiovascular diseases, slower gait speed, lower energy and physical activity levels, and reported more weight loss ($p < .01$) as well. Trajectories of inflammation were moderately associated with trajectories of slow gait ($r = .40$, $p < .001$) and weakly associated with trajectories of depression ($r = .11$, $p < .001$). Trajectories of slow gait were moderately correlated with trajectories of depression ($r = .49$ $p < .001$).

Manifestation of the Phenotype

The odds of each condition occurring given the presence of it or the other conditions at the previous time point are shown in Table 2. Inflammation was associated with previous inflammation ($p < .001$), but not previous slow gait ($p = .087$) or depression ($p = .959$). Slow gait was associated with previous slow gait ($p < .001$), inflammation ($p = .008$), and depression ($p < .001$). Depression was associated with previous depression ($p < .001$) and slow gait ($p = .005$) but not inflammation ($p = .729$).

Mortality Risk

In separate unadjusted logistic regression models, worsening trajectories of slow gait and inflammation were associated with increased mortality. Consistently high and increasing-trajectories of depression, however, did not differ from each other in their association with mortality ($p = .748$). Thus, these classifications were collapsed to create a dichotomy for depression trajectories in the main analysis (low vs increasing/consistently high). In the covariate-adjusted simultaneous logistic regression model, there was a significant main effect of increasing and consistently high-probability classifications of inflammation on mortality ($p < .001$). A significant two-way interaction was observed between trajectories of depression and slow gait ($p < .001$), such that worsening trajectories of slow gait were associated with greater mortality risk only in elders with increasing- or

Table 1. Baseline Characteristics for the Sample and Across Classes for Elevated Interleukin-6 From the Health Aging and Body Composition Study*

Characteristic	Total Sample ($n = 3,075$)	Low Probability of Elevated IL-6 ($n = 1,656$)	Increasing Probability of Elevated IL-6 ($n = 847$)	Consistently High Probability of Elevated IL-6 ($n = 572$)
	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)
Demographic				
Age, y	73.6 (2.87)	73.5(2.81)	73.8 (2.94)†	73.8 (2.93)‡
Educational level	2.17 (0.80)	2.24 (0.79)	2.11 (0.80)†	2.0 (0.81)‡
Sex, No. M/F (% F)	51.5%	54.1%	48.5%†	48.4%
Body mass index	27.4 (4.82)	26.6 (4.29)	27.8 (4.81)†	29.1 (5.72)‡,§
White/black (% black)	41.7%	36.9%	45.2%†	50.2%‡
3MS total score	90.1 (8.42)	91.0 (7.90)	89.5 (8.34)†	88.3 (9.55)‡
Medical comorbidities				
Vascular disease % Yes	60.3%	54.2%	65.0%†	71.0%‡
Physical diseases % Yes	57.6%	57.3%	56.1%	60.5%
Respiratory disease % Yes	18.8%	15.7%	21.6%†	23.8%‡
Cardiovascular disease % Yes	22.3%	18.8%	22.2%	32.6%‡,§
Cerebrovascular disease % Yes	7.5%	6.9%	7.1%	9.7%
Cancer malignant % Yes	5.1%	4.7%	6.1%	4.5%
Anti-inflammatory use % Yes	52.9%	53.0%	50.2%	56.8%
Frailty				
Gait speed (m/s)	1.18 (0.24)	1.21 (0.23)	1.15 (0.24)†	1.10 (0.23)‡,§
Slow gait	25.9%	19.7%	28.9%	39.4%
Grip strength (kg/f)	31.6 (10.57)	31.6 (10.57)	32.2 (10.59)	30.7 (10.50)
Activity levels (kcal)	7.7 (17.68)	8.7 (19.65)	7.1 (16.45)	5.5 (12.41)‡
Energy levels low No/Yes (% Yes)	15.8%	12.2%	17.5%†	23.7%‡,§
Weight loss No/Yes (% Yes)	15.9%	12.9%	18.4%†	20.8%‡
Depression scores				
CES-D	4.7 (5.36)	4.42 (5.00)	5.3 (5.85)†	4.7 (5.55)
(% ≥ 10)	14.3%	12.7%	17.6%	13.9%
Inflammatory marker				
Interleukin 6	2.8 (2.61)	1.8 (1.14)	2.8 (1.93)†	6.1 (3.75)‡,§
% elevated IL-6	25.0%	4.3%	24.4%	88.7%

Notes: CES-D = Center for Epidemiologic Studies Depression Scale; IL-6 = interleukin-6; 3MS = Modified Mini-Mental Status Exam. Elevated CES-D defined as CES-D ≥ 10; Slow gait defined as usual walking speed < 1.0 m/s; Elevated IL-6 defined as IL-6 ≥ 3.2 pg/mL; Education defined as 1 = less than high school, 2 = high school graduation, 3 = secondary education. Grip strength assessed in kilograms of force; Energy levels low if participant reports getting tired walking ¼ of a mile or climbing a flight of stairs at baseline; Weight loss defined as a self-reported loss of 10 lbs or 5% of body weight in year prior to baseline.

*Data presented as mean (*SD*) unless otherwise indicated.

†Significant difference in post hoc comparisons between low probability and increasing probability classes for elevated IL-6 ($p < .01$).

‡Significant difference in post hoc comparisons between low probability and consistently high probability classes for elevated IL-6 ($p < .01$).

§Significant difference in post hoc comparisons between increasing probability and consistently high probability classes for elevated IL-6 ($p < .01$).

Table 2. Covariate-Adjusted Odds Ratios (95% confidence intervals) Examining the Lagged Association Between Inflammation, Slow Gait, and Depression*

Predictor (t – 1)	Elevated CES-D	
	Odds Ratio	95% Confidence Interval
Elevated CES-D	8.711	7.446, 10.190 ‡
Elevated IL-6	1.030	0.871, 1.218
Slow gait	1.270	1.075, 1.502 †
	Slow Gait	
	Odds Ratio	95% Confidence Interval
Elevated CES-D	1.371	1.172, 1.603 ‡
Elevated IL-6	1.220	1.053, 1.414 †
Slow gait	5.333	4.632, 6.141 ‡
	Elevated IL-6	
	Odds Ratio	95% Confidence Interval
Elevated CES-D	0.996	0.850, 1.167
Elevated IL-6	5.108	4.468, 5.840‡
Slow gait	1.140	0.981, 1.324

Notes: CES-D = Center for Epidemiologic Studies Depression Scale; IL-6 = interleukin-6. Increasing, Elevated CES-D defined as CES-D ≥ 10; Slow gait defined as usual walking speed <1.0 m/s; Elevated IL-6 defined as IL-6 ≥ 3.2 pg/mL.

*Covariates adjusted for include baseline age, sex, BMI, 3MS, medical comorbidity and anti-inflammatory medication use.

†$p < .01$.

‡$p < .001$.

consistently high-probability trajectories of depression. This finding differs from an identical covariate adjusted logistic regression model that utilized baseline values for inflammation, slow gait, and depression. Main effects of baseline inflammation ($p < .001$) and slow gait ($p < .001$) were evident. No main effect of baseline depression ($p = .361$) and no interactions between the variables were observed.

In older adults with a low probability of depression trajectory (Figure 2A), trajectories of slow gait have no association with mortality (Gait trajectory p values > .35). In this low probability of depression group, mortality risk increases only as trajectories of inflammation worsen (adjusted mortality rates: low-probability$_{inflammation}$: 48.2%; increasing-probability$_{inflammation}$: 64.0%; consistently high-probability$_{inflammation}$: 72.5%, p values comparing each < .01). In older adults with increasing/high probability of depression trajectories (Figure 2B), mortality rates increase as trajectories of slow gait ($p < .01$) and inflammation worsen ($p < .01$). Elders with increasing or consistently high-probability for depression and a high-probability for both inflammation and slow gait ($n = 247$) have an adjusted morality rate of 85.2%, significantly greater than every permutation of class across the three conditions. These elders are 36.9% more likely to die during the 15-year follow-up than elders with low-probability trajectories for inflammation, depression, and slow gait ($n = 656$; adjusted morality rate: 48.3%).

Discussion

This investigation showed that inflammation, depression, and slow gait are defining features for a high-risk mortality phenotype in late life. Specifically, inflammation had a strong independent association with mortality. There was no evidence of an interactive effect on mortality between inflammation and both slow gait and depression as hypothesized. Rather, an interactive effect on mortality was identified between trajectories of slow gait and depression, such that as the probability of slow gait worsened, the risk of death increased only in those individuals at increased or high-risk for depression. Although this differs from prior research (30,31), these studies investigated only individual effects rather than synergistic relationships that may and apparently do exist. The cumulative impact of inflammation, depression, and slow gait results in an adjusted mortality rate of 85.2% in the highest-risk cohort.

The investigation into the manner in which the phenotype manifests showed that previous inflammation results in the development of subsequent slow gait but not depression. This finding supports previous research identifying an association between inflammation and incident cognitive and motor slowing (6,32). Additionally, previous slow gait resulted in subsequent depression and vice versa. This apparent bidirectional relationship between slow gait and depression combined with the association between their longitudinal trajectories highlights a distinct and clinically relevant association between mobility deficits and depression in later life.

The identification of this phenotype and the multiple pathways in which the phenotype may manifest suggest that evaluations of elders should include markers of inflammation, mobility, and depressive symptoms. Determining the presence of one or more of these factors may facilitate primary and secondary preventative strategies. For example, exercise (33) improves strength and decreases fall risk, but exercise may do little for comorbid depressive illness, itself associated with increased fall risk (34,35). Similarly, although antidepressant medications are effective for treating late life depression (36), there is no evidence to suggest a beneficial effect of antidepressant medications on mobility in late life. Thus, treating one component of the phenotype but not the others may continue to leave these elders at risk. Inflammation may provide an optimal target for treatment to alter the trajectory of this phenotype. Anti-inflammatory pharmacotherapies are effective treatments for chronic inflammatory conditions in late life (37). More recently, an antidepressant effect of a cytokine inhibitor compared to placebo was observed for the treatment of adults with treatment-resistant depression and elevated C-reactive protein (38). Future research on the effectiveness of anti-inflammatory medications in this high-risk phenotype is needed to determine the risks and benefits of their use in these populations (39).

The identification of three clinical trajectories is consistent with prior research on gait speed (31) and similar to that conducted in depression (30). In an investigation of depression trajectories over 20-years, four latent classes were identified, two of which (increasing and consistently high) are similar to those observed in this study. The previous model identified depression trajectories for adults at minimal and persistently low risk over 20-years, counter to the one consistently low-risk class identified in this study. To the best of our knowledge, this is the first article that investigated the latent trajectories of inflammation (40). It should be noted that, although the number and depiction of the trajectories were similar across the three conditions, the shape, particularly for the increasing-probability trajectory, differed. There is a nonlinear increase over 10-years for the increasing-probability trajectory for inflammation, with probability peaking at moderate levels (.50). This differs from the linear increase in risk identified for slow gait, with probability peaking at high levels (.80). The increasing-probability trajectory for depression depicts a linear increase in risk as well, but this risk peaks at only moderate levels (.35) at the end of the study. This latter finding may be due to the nature of the sample. The Health Aging and Body Composition study

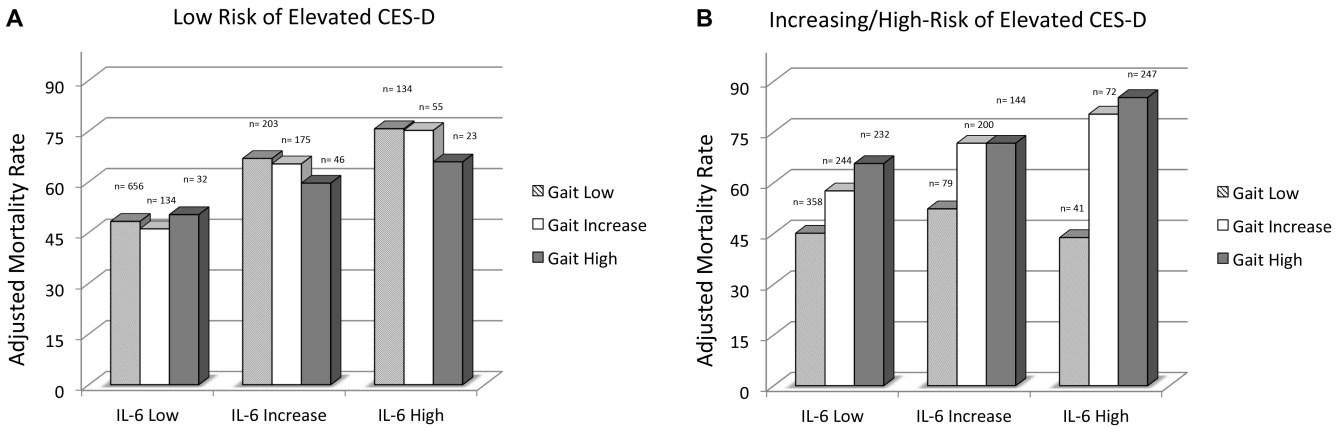

Figure 2. Covariate-adjusted* mortality rates across clinical trajectories of elevated depression, gait impairment, and elevated inflammation. CES-D = Center for Epidemiologic Studies Depression Scale; IL-6 = interleukin-6. Elevated CES-D defined as CES-D ≥ 10; Slow gait defined as usual walking speed < 1.0 m/s; Elevated IL-6 defined as IL-6 ≥ 3.2 pg/mL. Sample sizes for each subgroup included. *Covariates adjusted for include baseline age, sex, BMI, 3MS, medical comorbidity, and anti-inflammatory medication use.

recruited functionally intake older adults. Given the strong bidirectional relationship between functional impairment and depression (41), recruiting functionally intact elders may have limited the inclusion of those with a history of or current struggles with depression. Thus, those at greater risk for developing depression may have been initially excluded from the study.

Other limitations to consider include the measures and cut-points used to evaluate depression, inflammation, and gait. The Center for Epidemiologic Studies Depression scale is a screening instrument rather than a diagnostic tool for depressive illness, and the cutoff used denotes elevated depressive symptoms, not depressive illness (42). Additionally, two items from the Center for Epidemiologic Studies Depression scale that assess energy are used to assess the frailty characteristic of fatigue (8). Thus, some of the symptomatology captured by the Center for Epidemiologic Studies Depression scale total score may be attributable to underlying fatigue. Regarding frailty characteristics, although gait was used as a marker for frailty, other frailty characteristics were considered. Given the subjectivity of the assessment of weight loss, fatigue, and physical activity levels (weight loss prior to baseline was self-reported) and their similarity to specific depressive symptoms (7,8,16), the use of these characteristics was not optimal. Additionally, grip strength was not used because a prior investigation showed no relationship between low grip strength and mortality in depressed older adults (16,43). Cutoffs used to indicate slow gait and elevated IL-6 were identified via the most impaired baseline quartile. Although not ideal, these levels are nearly identical to those associated with poor outcome in prior research (20,27,28). The inclusion of a cognition trajectory would be desirable. Modeling trajectories of cognitive function were not possible from this data set, however, as measures were not assessed as often during follow-up.

Offsetting these limitations are considerable strengths. Previous studies that analyzed the bivariate relationships between inflammation, gait, and depression often relied on single point prevalence as predictors of outcome. Relying on single assessment points (baseline values) may ignore potential change in conditions that worsen (inflammation (1,26,32), gait speed (31)) or whose impact increases (depression) with age. The use of longitudinal data in this study identified a slow gait by depression interaction not observed using baseline values. Thus, a more nuanced understanding of the depression–mobility relationship was observed using the longitudinal data.

In conclusion, a high-mortality risk phenotype was identified that included older adults with inflammation, depression, and slow gait speed. The identification of this late life phenotype supports the comprehensive assessment of older adults and compels research to develop intervention and prevention strategies.

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