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Allostatic Load and Frailty in Older Adults

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Abstract

OBJECTIVE—To examine the association between allostatic load (AL), an index of multisystem physiological dysregulation, and frailty development over a 3-year follow-up in a sample of older adults.

DESIGN—Longitudinal cohort study.

SETTING—Community.

PARTICIPANTS—High-functioning men and women aged 70–79 at study entry.

MEASUREMENTS—Multisystem physiological dysregulation, or AL, was assessed according to 13 biomarkers of cardiovascular, endocrine, immune, and metabolic function. An AL score was computed as the total number of biomarkers for which participant values fell into high-risk biomarker quartiles. Frailty status (not frail, intermediate frail, frail) was determined according to the total number of five indicators of frailty: weight loss, exhaustion, weak grip, slow gait, and low physical activity. The association between level of AL at baseline and frailty status 3 years later was examined using ordinal logistic regression in 803 participants not frail at baseline.

RESULTS—In a multivariable model adjusting for sociodemographic, health, and behavioral characteristics, each 1-unit increase in AL at baseline was associated with a 10% greater likelihood of frailty at the 3-year follow-up (cumulative adjusted odds ratio = 1.10, 95% confidence interval = 1.03–1.19).

CONCLUSION—These findings support the hypothesis that dysregulation across multiple physiological systems is associated with greater risk of frailty. Greater levels of multisystem physiological dysregulation may serve as a warning sign of frailty development in later life.

Keywords

frailty; allostatic load; physiological dysregulation; older adults

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CONFLICT OF INTEREST

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INTRODUCTION

Clinicians have long used the term frail to describe older adults with low functional reserve who are vulnerable to stressor experiences and at risk for adverse health outcomes.^{1–3} A number of clinical operational definitions of frailty have been proposed,^{1,4,5} including different combinations of age-associated deficits, such as weakness, fatigue, slowness, poor balance, slowed motor performance, low physical activity, weight loss, sarcopenia, and cognitive impairment. Multi-indicator measures of frailty have been found to be associated with, but different from, measures of comorbidity and disability and to independently predict fractures, falls, physical disability, hospitalization, and death.^{1,6}

The clinical expression of frailty is thought to result from alterations in multiple molecular, cellular, and physiological systems. A number of physiological systems are hypothesized to be involved in frailty development, including the cardiovascular, neuroendocrine, metabolic, immune, and nervous systems.^{3,7} Positive cross-sectional associations between frailty and measures of inflammation have been observed,^{8,9} and elevations in inflammatory markers are associated with many frailty indicators, including fatigue, weight loss and anorexia, and loss of muscle mass and strength.^{10–14} Levels of anabolic hormones (e.g., insulin-like growth factor-1, dehydroepiandrosterone sulfate) have been found to be lower in frail older adults,¹⁵ and a number of the characteristics of frailty and aging (e.g., sarcopenia) are thought to be associated with declines in anabolic hormones and increases in catabolic hormones (e.g., hormones of the hypothalamic pituitary adrenal axis (e.g., cortisol) and the sympathetic nervous system (e.g., norepinephrine, epinephrine)).^{16–19} Levels of metabolic markers also vary according to frailty status, with higher levels of fasting glucose, insulin, triglycerides, and cholesterol in frail older adults.⁹ Although these cross-sectional associations are compelling, data on links between multi-system physiological dysregulation and the development of frailty over time is limited.

It has been postulated that dysregulation across a critical mass of the systems noted above may be necessary to induce frailty.³ The number of dysregulated systems that constitutes a “critical mass” has not been hypothesized, but it is plausible that dysregulation across a greater number of systems may render an individual more vulnerable to frailty development. The current study examined the association between allostatic load (AL), an index of multisystem physiological dysregulation, and frailty development in a sample of older adults from the MacArthur Study of Successful Aging (MSSA). AL includes biomarkers from a range of physiological systems hypothesized to be involved in frailty development, including the cardiovascular, metabolic, inflammatory, and neuroendocrine systems.

AL is conceptualized as a cumulative index of wear and tear across multiple physiological systems involved in the body's effort to adapt to internal and external stressors over time²⁰ and has been examined as a preclinical physiological marker of risk for adverse health outcomes. In the MSSA cohort, greater levels of AL have been shown to predict greater risk of cognitive and physical disability and all-cause mortality over time.^{21,22} Frailty is also linked to disability and mortality in the MSSA cohort; a recent analysis indicated that older adults who developed frailty at 3-year follow-up had greater odds of incident physical disability or mortality at 7-year follow-up.²³ The current analysis examines whether AL at baseline might serve as a marker of risk of frailty development at 3-year follow-up in MSSA participants free of frailty at baseline.

METHODS

The MSSA is a prospective cohort study of high-functioning older adults recruited on the basis of age (aged 70–79 at study entry) and cognitive and physical functioning levels from

three community-based cohorts of the Established Populations for the Epidemiologic Studies of the Elderly.²⁴ Detailed information on selection criteria are provided elsewhere,²⁴ but the aim of selection criteria was to screen out individuals with manifest cognitive and physical disability and to obtain a cohort of older adults who represented the top third of their age group in terms of functional ability at study enrollment.

Of 4,030 age-eligible men and women screened, 1,313 met all screening criteria, and 1,189 (90.6%) agreed to participate and provided informed consent. The sample was predominantly Caucasian (80.7% Caucasian, 18.8% African American, 0.5% other) and had slightly higher numbers of women (55.4%). Information obtained from participants at the baseline (1988–1989) and 3-year follow-up (1991–1992) examinations were used for analyses in the present investigation; data were collected during an in-home interview at baseline and in-home and telephone interviews at follow-up. Detailed information on the selection, reliability, and validity of study measures is available elsewhere.²⁴ Of the 1,189 participants enrolled at baseline, 1,103 completed interviews at the 3-year follow-up. (Seventy-one participants died over the follow-up, and 13 refused participation or could not be contacted.) Although MSSA baseline data were collected 20 years ago, the rich battery of sociodemographic and biomedical measures and longitudinal design provide a unique opportunity to examine the association between AL and frailty development.

Measures

Measurement of AL—Consistent with previous research,^{21,22} an AL summary score was computed as the total number of 13 biomarkers for which a participant's value fell into the highest-risk quartile of the biomarker's distribution. (See Table 1 for specific biomarkers and risk cutpoints; detailed information on biomarker measurement is available elsewhere.²²) The original AL index²¹ included biomarkers of cardiovascular, metabolic, and endocrine stress regulatory systems. Biomarkers of inflammation were added at a later time,²² in recognition of the important role of inflammation in response to stress and many diseases and disorders of aging.²⁵ A dichotomous high-risk score was constructed for each biomarker by assigning a value of 1 to participants whose scores fell into the quartile of highest clinical risk for the biomarker and a value of 0 otherwise. An AL score was computed by taking the mean of the 13 dichotomous (0/1) biomarker risk scores and multiplying by 13, yielding a possible score range of 0 to 13; scores were calculated only for participants with information on at least eight of the 13 biomarkers.

Assessment of Frailty Status—Frailty status was measured with the operational definition developed by Fried and colleagues¹ using five criteria: weight loss, weak grip strength, exhaustion, slow gait, and low physical activity level. Weight loss was calculated as the percentage of body weight lost (or gained) over the 3-year follow-up. Grip strength was assessed using a handheld dynamometer (average of 3 measures using dominant hand). Exhaustion was assessed according to an item on the Hopkins Symptom Checklist, “During the past week, how much have you been distressed by feeling low in energy or slowed down?” (not at all, a little, quite a bit, extremely). Gait speed was measured as the time taken (in seconds) to complete a 10-foot walk (usual pace). Physical activity was quantified using energy expenditure-weighted frequency assessments of engagement in recreational and exercise, housework, and yardwork activities from the Yale Physical Activity Survey and other physical activity surveys.²⁶ Average monthly frequencies (in days) of engagement in activities in each domain (recreational and exercise, housework, yardwork) were multiplied by weights for intensity level of each activity set (light-2; moderate-5; heavy-7) to produce a summary score for each of the three domains. Total physical activity scores were calculated at each examination by summing scores across the three activity domains.

A dichotomous variable was created for each of the five frailty indicators using cutpoint criteria that were the same or similar to that used in the operational definition developed by Fried and colleagues in analysis of Cardiovascular Health Study (CHS) data. (See Table 2 for details.) The same absolute cutpoints were used for weight loss and weak grip strength. Similar to the method used for the CHS cohort, MSSA participants who endorsed a high frequency of experience of exhaustion symptoms were classified as exhausted, although an item from the Hopkins Symptom Checklist, rather than items from the Center for Epidemiologic Studies Depression Scale, was used to assess exhaustion in the MSSA cohort. The MSSA used a 10-foot walk to measure gait speed, whereas the CHS used a 15-foot walk. Consistent with the scoring method used in the CHS cohort, sex- and height-specific cutoffs were based on lowest quintile scores. The cutpoints in the MSSA cohort were slightly lower than those used in the CHS cohort (MSSA cutpoints ranged from 0.84 to 0.95 feet per second; CHS cut-points ranged from 2.1 to 2.5 feet per second), indicating that MSSA participants classified as having slow gait were slower in completing their timed walk than CHS participants classified as exhibiting slow gait. Low physical activity was defined as the sex-specific lowest quintile on the summary physical activity score assessed in the MSSA (men 51.3, women 47.1; possible score range 0–252). Physical activity cutpoints in the CHS and MSSA cohorts cannot be directly compared, because the average time expended during each activity session was not assessed in the MSSA, precluding the ability to assess total kilocalories expended in physical activity, as was assessed in the CHS. However, inspection of those classified as having low levels of physical activity in the MSSA cohort indicated that few engaged in any recreational or exercise activity, approximately half engaged in some yardwork (median frequency 5.1 days per month for light yardwork and 0 days per month for strenuous yardwork), and most engaged in some housework (median frequency = 6 days per month for light housework and 1.25 days per month for strenuous housework). If a duration of 1 hour is assumed for each occurrence of these activities, then levels of energy expenditure are similar in the low physical activity groups across the MSSA and CHS cohorts.

For the five frailty criteria, those with no criteria were considered nonfrail, those with one or two criteria were considered intermediate frail, and those with three or more criteria were considered frail. Frailty status was determined at the baseline and 3-year follow-up examinations using the same criteria, although weight loss information was not available for the baseline examination. Thus, frailty classification at baseline was based on four indicators.

Sociodemographic and Health Status Covariates—Sociodemographic covariates included age at the baseline examination, sex, self-reported race (white or black), and educational attainment (<high school degree, high school degree). Health status covariates included the presence or absence of one physical ability limitation from an eight-item index of mobility and strength disability screener,^{27,28} the total number of six self-reported chronic or major health conditions (cancer, diabetes mellitus, hypertension, myocardial infarction, stroke, and broken hip) experienced up to the baseline examination, and smoking status (smoker, ex-smoker, nonsmoker).

Analyses

The objective was to examine the association between baseline AL level and odds of frailty at the 3-year follow-up in participants who were not frail at baseline. A total of 1,016 participants had sufficient information (24 of the 5 frailty criteria) to compute a frailty score in 1991. Of these, 213 participants were excluded from analyses: 181 participants did not have sufficient biomarker information (data on at least 8 of the 13 indicators) at the baseline examination, three participants were missing data on frailty status at baseline, and 29

participants were frail at baseline. The exclusions yielded a final analytical sample of 803 individuals free of frailty at baseline. Of these 803, five were missing data on race, and five were missing data on number of chronic health conditions; missing data were replaced with the mode in each case (mode 5 white for race and 1 for chronic conditions).

Variations in the pattern of scores on sociodemographic and health status variables for individuals with different levels of frailty at the 3-year follow-up were examined using chi-square and linear trend analyses. The association between baseline AL level and frailty at follow-up was assessed using multivariable ordinal logistic regression. Cumulative odds of frailty (frail vs intermediate frail or nonfrail, and frail or intermediate frail vs nonfrail) were examined as a function of AL measured continuously and in quintile groupings (lowest quintile served as referent group). Three models were examined: one adjusted for intermediate frailty status (yes/no) at baseline, one with sociodemographic covariates added, and one that additionally included baseline health status and behavior covariates. The proportional odds assumption was met for each analysis. All analyses were conducted with commercially available software (SPSS version 5.0, SPSS, Inc., Chicago, IL; SAS version 9.1, SAS Institute, Inc., Cary, NC).

RESULTS

At baseline, 54.8% (n = 440) of the 803 participants in the analytical sample were classified as nonfrail, and 45.2% (n = 363) were classified as having intermediate frailty. At the 3-year follow-up examination, 44.1% (n = 354) of participants were classified as nonfrail, 49.9% (n = 401) as intermediate frail, and 6.0% (n = 48) as frail.

The pattern of scores on sociodemographic and health status variables according to frailty status at the 3-year examination are displayed in Table 3. Participants with greater levels of frailty were older, had a greater average number of health conditions, were more likely to report having one physical ability limitation, and were more likely to have had intermediate frailty at baseline. Sex, race, education, and smoking status distributions did not significantly vary according to frailty status.

The AL score ranged from 0 to 9.1 (mean $\pm$ SD = 3.2 ± 2.0 , median = 3). Quintile ranges were as follows: lowest, 0.0 to 1.3, second, 1.4 to 2.9; third, 3.0 to 3.9; fourth, 4.0 to 5.0; and highest, 5.1 and above. The prevalence of each category of frailty at the 3-year follow-up according to quintile of baseline AL is depicted in Figure 1. In general, a lower prevalence of nonfrailty and a higher prevalence of intermediate frailty and frailty were observed with higher levels of AL.

The results of ordinal logistic regression analyses examining baseline AL as a predictor of the cumulative odds of frailty at the 3-year follow-up are displayed in Table 4. Adjusted odds ratio (AOR) estimates from the first model adjusting for baseline intermediate frailty status suggest that higher levels of AL are associated with higher cumulative odds of frailty at the follow-up (Model 1: AOR 5 1.12, 95% confidence interval (CI) 5 1.05–1.21). The cumulative AOR remained unchanged with the addition of sociodemographic covariates into the model (Model 2: AOR 5 1.12, 95% CI 5 1.04–1.20), whereas the addition of health status and health behavior covariates led to a slight reduction in the magnitude of the AOR estimate, but the association between higher AL and greater odds of frailty remained statistically significant (Model 3: AOR 5 1.10, 95% CI 5 1.03–1.19). Results from analyses substituting quintiles of allostatic load at baseline as predictors of 3-year frailty level are detailed in the bottom of Table 4 and confirm the linear increase in frailty risk with increasing AL. There was a statistically significant trend of increasing cumulative odds of

frailty with higher AL, although only participants in the highest two AL quintiles had significantly greater odds of frailty than those in the lowest AL quintile.

Supplemental Analyses

Because information on weight loss was not available at the baseline examination, frailty classification at baseline was based on four of the five frailty indicators. Thus, estimates of frailty prevalence at the baseline and 3-year follow-up examinations may not be comparable, and frailty prevalence may have been underestimated at the baseline examination. Supplemental analyses explored the association between baseline AL and frailty at the 3-year follow-up using a frailty classification variable that omitted information on weight loss over the follow-up. The results were similar to those obtained using a frailty variable based on all five indicators; higher levels of AL at baseline were associated with greater cumulative odds of frailty at the follow-up examination (Model 1: AOR 5 1.13, 95% CI 5 1.05–1.21; Model 2: AOR 5 1.12, 95% CI 5 1.04–1.21; Model 3: AOR 5 1.11, 95% CI 5 1.03–1.20). Similar and significant linear trends were found for analyses using AL quintiles as predictors of frailty (data not shown).

An additional set of supplemental analyses further explored the question of whether dysregulation across multiple physiological systems was associated with greater risk of frailty development. For these analyses, a physiological systems dysregulation score was computed as the sum of the four systems (cardiovascular or blood pressure, metabolic, hormone, and inflammation) for which a participant had evidence of dysregulation in the system (defined as at least 1 of 2 high-risk blood pressure markers, at least 1 of 3 high-risk inflammation markers, at least 2 of 4 high-risk hormone markers, at least 2 of 4 high risk metabolic markers). The results of the fully adjusted model indicate greater cumulative odds of frailty development for participants with a greater number of dysregulated systems (AOR 1 dysregulated system = 1.39, 95% CI = 0.95–2.03; AOR 2 dysregulated systems = 1.59, 95% CI = 1.08–2.33; AOR 3 or 4 dysregulated systems = 1.78, 95% CI = 1.05–3.03; those with 0 dysregulated systems served as referent).

DISCUSSION

In the present study, higher levels of allostatic load were associated with a greater level of frailty 3 years later in a sample of high-functioning nonfrail older adults. This association remained statistically significant after accounting for presence of intermediate frailty, disability, comorbidity, smoking behavior, and sociodemographic variables; in the fully adjusted model, each unit increase in AL was associated with a 10% greater odds of developing frailty 3 years later. Parallel analyses examining quintiles of AL as predictors of frailty level also suggest a trend for greater likelihood of frailty with increasing levels of AL, although only participants in the highest two AL quintiles had significantly greater odds of frailty than those with the lowest AL levels. These findings extend those of a recently published analysis that found that greater AL was cross-sectionally associated with greater level of frailty in the Women's Health and Aging Studies I and II cohorts,²⁹ which represent a sample of women with more-varied functional status than is the case for MSSA participants. The prospective ability of AL to predict frailty in men and women of a wide range of functional status should be an important objective of future research.

Greater AL is thought to result from greater cumulative experience of internal and external stressors across the life course,^{20,21} and empirical research supports an association between greater AL and greater age and psychosocial stress experience.^{21,30–32} Frailty is a state characterized by vulnerability to the negative effects of stressor experience. Whether the finding of an association between greater AL and greater frailty level represents direct effects of physiological dysregulation on observable indicators of frailty or a state of

biological vulnerability that manifests as frailty under conditions of further stress remains to be determined, although the findings of the current investigation point to levels of AL as a potentially useful preclinical indicator of the risk of frailty development. The findings also suggest potential biological pathways to explore in understanding links between psychosocial factors and frailty risk that have been observed in other studies.^{5,33}

The AL index used in the present investigation incorporated presence of potential dysregulation in multiple physiological systems, including the immune, neuroendocrine, metabolic, and cardiovascular systems, each of which is hypothesized to contribute to the development of frailty in older adulthood.³ Scores on this index do not indicate the specific mix of systems for which individual values fall into high-risk ranges. Substantial heterogeneity has been found in the specific patterns of biomarkers that predict mortality in this cohort,³⁴ indicating that diverse patterns of physiological dysregulation predict adverse health outcomes in this group. Unfortunately, the small event rates for full-blown frailty in the current analyses limit the ability to examine the specific combinations of biological systems associated with frailty development. Such explorations in other samples may yield fruitful information regarding the underlying physiology of frailty in later life. Although these analyses do not answer the question of what defines a “critical mass” of dysregulated systems, supplementary analyses indicated that dysregulation across a greater number of the four physiological systems represented in the AL index was associated with greater level of frailty 3 years later, supporting the hypothesis that dysregulation across a critical mass of systems may render individuals more vulnerable to frailty development. An important aim of future research is the examination of a broader range of physiological risk factors, as well as the specific mix and number of dysregulated systems, involved in the development of the clinical manifestations of frailty.

Limitations

An important limitation of this study is that the relatively high functional status of study participants at baseline limits the potential generalizability of study findings, although the criteria used to classify frailty status in this study were the same or similar to those used in other cohorts of older adults. The upshot of this classification scheme is that, despite the overall lower rates of frailty in the sample, frail participants in the MSSA should be similar to frail participants identified in other study cohorts. Furthermore, although MSSA participants were recruited based on higher levels of functioning than in same-age peers, at baseline, one-quarter of MSSA participants exhibited one mobility or range of motion limitation and two-thirds had one or more chronic health conditions; thus MSSA participants do not possess perfect health, and the presence of frailty indicators in this group is not unlikely. The presence of a substantial burden of frailty was also found in another sample of non-disabled, community-dwelling older adults using the index developed by Fried and colleagues³⁵ and the assessment of frailty as an index of cumulative deficits across a large array of indicators.³⁶

Another potential limitation is that the baseline prevalence of frailty may have been underestimated because of the lack of information on weight loss as an indicator of frailty at study entry, but supplemental analyses indicated no substantial effect on the association between AL and frailty when also omitting weight loss as an indicator of frailty at the 3-year follow-up. The follow-up time between assessment of AL at baseline and frailty development 3 years later is another potential limitation; substantial changes in physiological status that affected frailty level, as well as transitions in frailty status occurring during the intervening period, may have been missed.³⁵ Finally, it was decided to measure frailty according to a commonly used operational definition,¹ but geriatric researchers are using many other important definitions of frailty; it is unclear whether the current findings regarding the association between level of AL and frailty would generalize to other

operational definitions that include additional or alternative indicators. Another commonly used classification scheme measures frailty as the sum of deficits across a large number of measures of poor cognitive and physical functioning, self-assessed and clinically diagnosed poor health, and low physical activity and poor affective well-being.^{4,37,38} It is likely that greater AL would be associated with greater frailty as measured using this deficit accumulation approach. Given demonstrated links between AL and many of the deficits typically included in this frailty index,²¹ future studies should examine this empirically.

CONCLUSION

High levels of AL, indexed with a summary measure of potential dysregulation in neuroendocrine, immune, cardiovascular, and metabolic systems, was associated with a greater likelihood of frailty development over a 3-year follow-up in a sample of initially high-functioning older adults. This association held even when accounting for co-occurring physical disability and comorbidity that may be associated with alterations in biomarker levels. These findings support the hypothesis that observable indicators of frailty may result from dysregulation in multiple physiological systems and suggest that it might be useful to monitor the function of several biological systems for warning signs of potential frailty risk in later life.

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Figure 1.
Prevalence of Frailty Status at 3-Year Follow-Up Exam as a Function of Quintile of Allostatic Load at Baseline Exam

Table 1**Biomarkers in Allostatic Load Score**

Biomarker	N	High-Risk Quartile Cutpoint
Systolic blood pressure (mmHg)	800	148.00
Diastolic blood pressure (mmHg)	800	83.33
HDL cholesterol (mg/dL)	801	36.00
Total/HDL cholesterol	801	5.92
Glycosylated hemoglobin (%)	793	7.10
Waist-hip ratio	802	0.94
DHEAS (mg/dL)	794	5.00
Urinary cortisol (ug/g creatinine)	647	25.69
Urinary norepinephrine (ug/g creatinine)	643	48.12
Urinary epinephrine (ug/g creatinine)	652	5.00
Fibrinogen (mg/dL)	745	336.00
C-reactive protein (mg/L)	750	3.19
Interleukin-6 (pg/mL)	745	4.65

Abbreviations. HDL: high-density lipoprotein; DHEAS: dehydroepiandrosterone sulfate.

Table 2

Indicators of Frailty

Frailty Characteristic	Indicator in MacArthur Study of Successful Aging	
Weight Loss	Loss of >5% of body weight over 3-year follow-up. Gender- and BMI-specific lowest quintile of grip strength:	
	<i>Men:</i>	<i>Cutoff (Kg of grip strength):</i>
	BMI < 24	29
	BMI 24.1 – 26	30
	BMI 26.1 – 28	30
	BMI > 28	32
Weakness (weak grip)	<i>Women:</i>	
	BMI < 23	17
	BMI 23.1 – 26	17.3
	BMI 26.1 – 29	18
	BMI > 29	21
Exhaustion	Response of “quite a bit” or “extremely” to question, “During the past week, how much have you been distressed by feeling low in energy or slowed down?”	
	Gender- and height-specific lowest quintile * on timed 10-foot walk at usual pace:	
Slowness (slow gait)	<i>Men:</i>	<i>Cutoff (seconds):</i>
	Height < 173 cm	10.7 seconds
	Height > 173	10.5 seconds
	<i>Women:</i>	
	Height < 159 cm	11.9 seconds
	Height > 159 cm	11.1 seconds
Low physical activity	Gender-specific lowest quintile of physical activity on energy-expenditure weighted activity scale.	
Frailty Status	Scoring Criteria:	
Not frail	0 positive indicators	
Intermediate frail	1 – 2 positive indicators	
Frail	3 or more positive indicators	

Note.

Abbreviations. BMI: body mass index.

* A 10-foot walk was used in the MacArthur Study of Successful Aging as compared to a 15-foot walk used in the Cardiovascular Health Study sample which Fried and colleagues utilized for the development of their operational definition of frailty. Cutpoints for slow gait above reflect gender- and height-specific lowest quintiles in the MacArthur sample.

Table 3

Characteristics of Study Participants by Frailty Status in 1991

	Non-frail (n = 354) mean ($\pm$ SD) or%	Intermediate frail (n = 401) mean ($\pm$ SD) or %	Frail (n = 48) mean ($\pm$ SD) or%	P
Age	73.9 (2.7)	74.4 (2.7)	75.4 (2.9)	0.000
Gender				0.755
Male	46	43	46	
Female	54	57	54	
Race				0.514
White	84	81	85	
Black	16	19	15	
Education				0.779
< high school degree	51	53	56	
high school degree	49	47	44	
Physical disability				0.036
None	79	74	63	
1 physical limitation	21	26	37	
# major/chronic health conditions	0.8 (0.8)	0.9 (0.9)	1.5 (0.9)	0.000
Smoking Status				0.764
Non-smoker	48	51	56	
Ex-smoker	37	36	33	
Current smoker	15	13	10	
Frailty status (baseline)				0.000
Non-frail	71	44	25	
Intermediate frail	29	56	75	

Table 4

Cumulative Odds of Frailty (ordered as Non-Frail, Intermediate Frail, Frail) at the 3-Year Follow-Up Exam by Continuous and Quintile Allostatic Load Scores at Baseline Exam

Allostatic Load Score	Model 1:	Model 2:	Model 3:
	+ baseline intermediate frailty (yes/no)	Model 1 + sociodemographics [*]	Model 2 + disability, comorbidity, smoking [†]
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Continuous score	1.12 (1.05 – 1.21)	1.12 (1.04 – 1.20)	1.10 (1.03 – 1.19)
Quintile score			
1 st (<=1.3)	Ref.	Ref.	Ref.
2 nd (1.4–2.9)	1.32 (0.85 – 2.03)	1.31 (0.85 – 2.04)	1.28 (0.83 – 1.99)
3 rd (3.0–3.9)	1.40 (0.91 – 2.14)	1.33 (0.86 – 2.05)	1.30 (0.84 – 2.00)
4 th (4.0–5.0)	1.60 (1.05 – 2.43)	1.63 (1.06 – 2.50)	1.60 (1.04 – 2.45)
5 th (>=5.1)	2.14 (1.35 – 3.38)	2.06 (1.29 – 3.28)	1.88 (1.17 – 3.01)
<i>P</i> value for linear trend across quintiles	.001	.002	.005

Note.

^{*} Model 2 sociodemographic covariates include gender, race (white/black), and age.

[†] Model 3 covariates include disability (presence/absence of 1 strength or mobility limitation), comorbidity, and smoking status at baseline.