Cross-Sectional Associations of Albuminuria and C-Reactive Protein With Functional Disability in Older Adults With Diabetes

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OBJECTIVE—To examine the relationship between albuminuria, inflammation, and disability in older adults with diabetes.

RESEARCH DESIGN AND METHODS—Data were from 1,729 adults (≥60 years) with diabetes in the National Health and Nutrition Examination Survey, 1999–2008. Disability in activities of daily living (ADL), instrumental activities of daily living (IADL), leisure and social activities (LSA), general physical activities (GPA), and lower-extremity mobility (LEM) was obtained from self-reports. Urinary albumin-to-creatinine ratio (UACR) (mg/g) was categorized into normal (UACR <30 mg/g), microalbuminuria (UACR 30–300 mg/g), and macroalbuminuria (UACR >300 mg/g). C-reactive protein (CRP) levels were quantified by latex-enhanced nephelometry.

RESULTS—In the full-adjusted model, microalbuminuria was associated with disability in ADL, LSA, and LEM with corresponding odds ratios (ORs) (95% CIs) of 1.51 (1.16–1.98), 1.62 (1.23–2.14), and 1.34 (1.03–1.74), respectively, compared with participants without albuminuria. Macroalbuminuria was associated with disability in ADL, IADL, and LEM with corresponding ORs (95% CIs) of 1.94 (1.24–3.03), 1.93 (1.23–3.02), and 2.20 (1.38–3.49), respectively, compared with participants without albuminuria. Elevated CRP (>0.3 mg/dL) was associated with increased odds of disability in ADL and LEM, with corresponding ORs (95% CIs) of 1.28 (1.00–1.62) and 1.68 (1.34–2.11), respectively. Subjects with both albuminuria and elevated CRP had higher odds of disability than individuals with no albuminuria and normal CRP.

CONCLUSIONS—Albuminuria and inflammation were independent correlates for disability among older adults with diabetes. There was an interaction of albuminuria and elevated CRP on disability, suggesting that the presence of subclinical inflammation may amplify the effect of albuminuria on disability in older adults living with diabetes.

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The adverse effects of diabetes in late life on functional ability have been well characterized. Data from the U.S. national survey (1,2) or population-based epidemiological studies (3) indicated that individuals with diabetes generally have two to three times greater odds of functional disability in terms of activities of daily living (ADL), instrumental activities of daily living (IADL), or mobility-related tasks compared with individuals without diabetes. Diabetes-related disability is especially common in the elderly population, with ~60% of elderly patients with diabetes participating in the 1989 National Health Interview Survey and reporting one or more limitations in their daily activities (4). More recent data from the National Health and Nutrition Examination Survey (NHANES) 1999–2006 showed that the estimated prevalence of self-reported difficulties in performing any functional tasks with daily activities among elderly people with diabetes had increased to ~77% (2). Preventing onset of disability in the increasing elderly population with diabetes is a public health issue.

An important step toward preventing diabetes-related disability is a better understanding of predisability indicators that can identify older adults with diabetes at the highest risk of becoming disabled. Previous studies suggest that late complications of diabetes, such as cardiovascular diseases, foot ulcers, amputation, retinopathy, or nephropathy, are important predictors of subsequent functional disability among people with diabetes (1–3). Because accelerated atherosclerosis is a common pathway for the majority of diabetes-related complications, past studies have provided evidence supporting key roles of albuminuria and subclinical low-grade inflammation as antecedents of diabetes complications and subsequent disability (5,6). Both albuminuria and high proinflammatory cytokines have been linked to endothelial dysfunction, as well as initiation and progression of atherosclerosis (5,6). Albuminuria is an early indicator for diabetic end-organ complications including nephropathy (7) and cardiovascular morbidity/mortality (8). On the other hand, subclinical chronic inflammation, as measured by interleukin-6 or C-reactive protein (CRP), has been shown to be an important correlate for frailty and late-life disability among the general population (9,10). In fact, albuminuria accompanied by subclinical inflammation, or "inflammatory microalbuminuria," may have an additive effect on such outcomes as atherosclerosis or metabolic disarray (11). Although diabetes complications and cardiovascular comorbidities have been extensively documented as crucial factors of disability among older adults with diabetes, data examining the associations of preclinical disease indicators such as urinary albumin

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excretion or inflammation with disability are relatively sparse.

Therefore, the objective of this study was to examine the association between urinary albumin excretion, chronic inflammation, and disability among older adults with diabetes. We hypothesized that higher urinary albumin excretion and chronic inflammation are associated with disability and that albuminuria and chronic inflammation have a combined effect on disability.

RESEARCH DESIGN AND METHODS

Data source and study sample

The data come from NHANES, a population-based cross-sectional survey designed to collect information on the health and nutrition of the U.S. civilian noninstitutionalized population. Beginning in 1999, NHANES became a continuous annual survey rather than the periodic survey that it had been in the past. The survey data are released every 2 years. Detailed survey operations manuals, consent documents, and brochures of the NHANES 1999–2008 are available on the NHANES website (http://www.cdc.gov/nchs/nhanes.htm).

A total of 2,399 older adults (≥60 years of age) with diabetes completed the physical function questionnaires for assessment of functional disability. Among them, 1,804 participants had complete data in the laboratory measurements and comorbidities questionnaires. Given that advanced kidney disease is a known predictor of functional limitation (12), we further excluded 75 participants with advanced kidney disease (estimated glomerular filtration rate [eGFR] <30 mL/min per 1.73 m^2) to minimize the confounding effect of chronic kidney disease on the association between urinary albumin-to-creatinine ratio (UACR) and functional disability. Compared with excluded subjects (n = 670), current analytic sample (n = 1,729) tended to be younger (70.6 vs. 72.2 years, $P < 0.001$), male (52.8 vs. 44.9%, P = 0.001), and less disabled in all disability domains ($P \leq 0.001$).

Assessment of disability

There were 19 questions in the physical functioning questionnaire designed to assess the functional status of participants. These questions were phrased to assess the individual's level of difficulty in performing the task without using any special equipment. The 19 questions of functional dependence were categorized into five major domains according to published definitions (10): *1*) ADL (eating, walking, dressing, and getting out of bed); *2*) IADL (managing money, housekeeping, and food preparation); *3*) leisure and social activities (LSA; attending social events, going out to movies, in-home leisure activities); *4*) lower-extremity mobility (LEM; walking for a quarter mile and walking up 10 steps); and *5*) general physical activities (GPA; stooping, bending, standing, sitting, lifting, reaching, and grasping). A subject's answer to a given question was coded as "no difficulty," "some difficulty," "much difficulty," or "unable to do." Functional disability was defined as any difficulty in performing one or more activities within a given domain.

UACR

A casual urine specimen was collected and stored under frozen condition (−20°C). A solid-phase fluorescent immunoassay, specifically useful for measurement of low levels of urinary albumin not detectable by dipstick methods, was used for the measurement of urinary albumin. Urine creatinine was analyzed with the Jaffe reaction, in which creatinine reacts with picrate in an alkaline solution to form a red creatinine-picrate complex. The UACR, in milligrams per gram, was calculated by dividing the urinary albumin value by the urinary creatinine concentration. Microalbuminuria and macroalbuminuria were defined if UACR was 30–300 and >300 mg/g, respectively (13).

Assessment of demographics, comorbidities, and laboratory examinations

Age, sex, and race were obtained by self-report. BMI, calculated as weight in kilograms divided by the square of height in meters, was categorized according to the National Institutes of Health obesity standards: <18.5 kg/m^2 = underweight, 18.5–24.9 kg/m^2 = normal weight, 25.0–29.9 kg/m^2 = overweight, and >30 kg/m^2 = obese (14). Using their serum cotinine concentrations (ng/mL), we classified smoking status of participants in four groups: nonsmoker (<14), light smoker (14–99), moderate smoker (100–199), and heavy smoker (>200) (15). Comorbidities, including heart disease (defined as a history of myocardial infarction, coronary heart disease, congestive heart failure, or angina), chronic lung disease (defined as emphysema or chronic bronchitis), arthritis and stroke, use of cholesterol-lowering medications, and use of antihypertensive medications were ascertained by self-report. Diabetes was defined by self-report of a physician's diagnosis, the presence of a fasting (fasting >6 h) plasma glucose level >126 mg/dL or a nonfasting (fasting <6 h) glucose level >200 mg/dL, A1C ≥6.5% (16), or the use of diabetic medications. Use of diabetic medications was classified in four groups: oral antidiabetic medication alone, insulin alone, both, or none. Hypertension was defined as mean systolic BP >140 mmHg, mean diastolic BP >90 mmHg, physician diagnosis, or use of antihypertensive medications. Mean BP was composed of up to four readings on two separate occasions. eGFR was calculated by using the modification of diet in renal disease (MDRD) study equation (17). CRP was quantified by utilizing latex-enhanced nephelometry with a Behring Nephelometer Analyzer System. A1C was measured using high-performance liquid chromatography assay standardized to the Diabetes Control and Complications Trial values by the National Glycohemoglobin Standardization Program (18). Levels of serum total cholesterol and triglycerides were measured enzymatically.

Analysis

Demographic and clinical characteristics of the study population were presented according to UACR categories, namely, normal UACR (n = 1,124), microalbuminuria (n = 475), and macroalbuminuria (n = 140). χ^2 test or ANOVA was used to determine differences between groups. Multiple logistic regression analysis was used to examine the relationship between microalbuminuria and macroalbuminuria, with functional disability as a function of UACR with the normal group (UACR <30 mg/g) as a reference category. We used an extended-model approach for covariate adjustment: model 1 = age, sex, and race; model 2 = model 1 + BMI category, smoking status, systolic blood pressure, chronic comorbidities (heart disease, chronic lung disease, stroke, and arthritis), eGFR, A1C, total cholesterol, use of antihypertensive medications, use of cholesterol-lowering medications, and use of diabetic medications; and model 3 = model 2 + log-transformed CRP level.

Given the fact that chronic inflammation has been shown as an important

correlate of disability in the general population (9,10), the association of CRP and functional disability among participants with diabetes was examined using a similar statistical approach. We further evaluate the joint effect of UACR and inflammation on functional disability by reclassifying study participants in one of the four groups based on UACR (UACR <30 and ≥30 mg/g) and CRP (CRP >0.3 and ≤0.3 mg/dL). The adjusted odd ratios (ORs) for disability were obtained using multiple logistic regression with participants with UACR <30 mg/g and CRP ≤0.3 mg/dL as the reference group.

Because NHANES weights apply to prevalence estimates of the entire population and our study aimed to evaluate associations in certain subsets of elderly participants with diabetes, no NHANES weights were adjusted in the analyses. Data analyses were performed using STATA 10.0 software (STATA Corporation, College Station, TX).

RESULTS—The mean age of the study population was 70.6 years and 52.8% was male. The mean A1C was 7.2. Characteristics of the study sample by UACR were summarized (Table 1). Participants with higher UACR were more likely to have hypertension, stroke, and heart disease. They tended to have lower eGFR, higher blood pressure, higher A1C, and higher CRP levels. There was no difference in terms of race, smoking status, BMI, chronic lung disease, and arthritis. Participants with normal UACR were more likely to be independent in all aspects of functional disability ($P < 0.01$). The percentages of participants according to numbers of limitation in the five disability domains by UACR were plotted in Fig. 1.

Urinary albumin excretion, chronic inflammation, and functional disability

The results of multiple logistic regression analysis for the association between UACR and functional disability are summarized in Table 2. After adjusting for age, sex, and race, both macroalbuminuria and microalbuminuria were associated with disability in ADL, LSA, and

Table 1—*Characteristics of study participants with diabetes according to UACR: NHANES 1999–2008*

	UACR			
	Normal (<30 mg/g)	Microalbuminuria (30–300 mg/g)	Macroalbuminuria (>300 mg/g)	*P*
n	1,121	470	138	
Age (years)	70.1 (7.0)	71.6 (7.6)	70.6 (7.6)	0.001
Female*	554 (49.4)	200 (42.6)	63 (45.7)	0.04
Race*				0.608
Mexican American	249 (22.1)	114 (24.2)	33 (23.9)	
Other Hispanics	53 (4.7)	21 (4.5)	11 (8.0)	
Non-Hispanic white	533 (47.6)	213 (45.3)	55 (40.0)	
Non-Hispanic black	255 (22.8)	107 (22.8)	36 (26.0)	
All others	32 (2.8)	15 (3.2)	3 (2.1)	
Nonsmoker*	942 (84.0)	396 (84.3)	107 (77.5)	0.317
BMI (kg/m^2)	30.6 (5.9)	30.4 (6.3)	30.4 (6.5)	0.774
Systolic blood pressure (mmHg)	132.9 (19.4)	142.4 (22.8)	154.8 (26.6)	<0.001
Diastolic blood pressure (mmHg)	64.8 (14.2)	66.6 (16.1)	69.6 (14.9)	0.001
A1C (%)	7.0 (1.4)	7.4 (1.7)	7.8 (2.1)	<0.001
eGFR (mL/min per 1.73 m^2)	81.2 (24.5)	77.9 (25.7)	67.4 (24.6)	<0.001
Total cholesterol (mg/dL)	193.0 (43.8)	194.0 (46.9)	200.1 (44.5)	0.208
CRP (mg/dL)†	0.29 (0.46)	0.32 (0.58)	0.42 (0.60)	<0.001†
Hypertension*	852 (76.0)	373 (79.4)	129 (93.5)	<0.001
Stroke*	93 (8.3)	60 (12.8)	26 (18.8)	<0.001
Heart diseases*	279 (24.9)	150 (31.9)	51 (37.0)	0.001
Chronic lung diseases*	121 (10.8)	57 (12.1)	17 (12.3)	0.687
Arthritis*	586 (52.3)	232 (49.4)	62 (44.9)	0.196
Use of antihypertensives*	695 (62.0)	292 (62.1)	100 (72.5)	0.052
Use of oral antidiabetic agents*				<0.001
None	345 (30.8)	139 (29.6)	35 (25.4)	
OAD alone	543 (48.4)	240 (51.1)	67 (48.6)	
Insulin alone	81 (7.2)	52 (11.0)	29 (21.0)	
Both OAD and insulin	152 (13.6)	39 (8.3)	7 (5.0)	
Functional disability*				
ADL	318 (28.4)	170 (36.2)	63 (45.7)	<0.001
IADL	365 (32.6)	168 (35.7)	63 (45.7)	0.007
LSA	275 (24.5)	153 (32.6)	47 (34.1)	0.001
GPA	783 (69.9)	353 (75.1)	110 (79.7)	0.012
LEM	523 (46.7)	258 (54.9)	94 (68.1)	<0.001

Data are means (SD) or *n (%) unless otherwise specified. *n* = 1,729. †Values are expressed as median (interquartile range) because of right skewness and *P* for log-transformed values. OAD, oral antidiabetic.

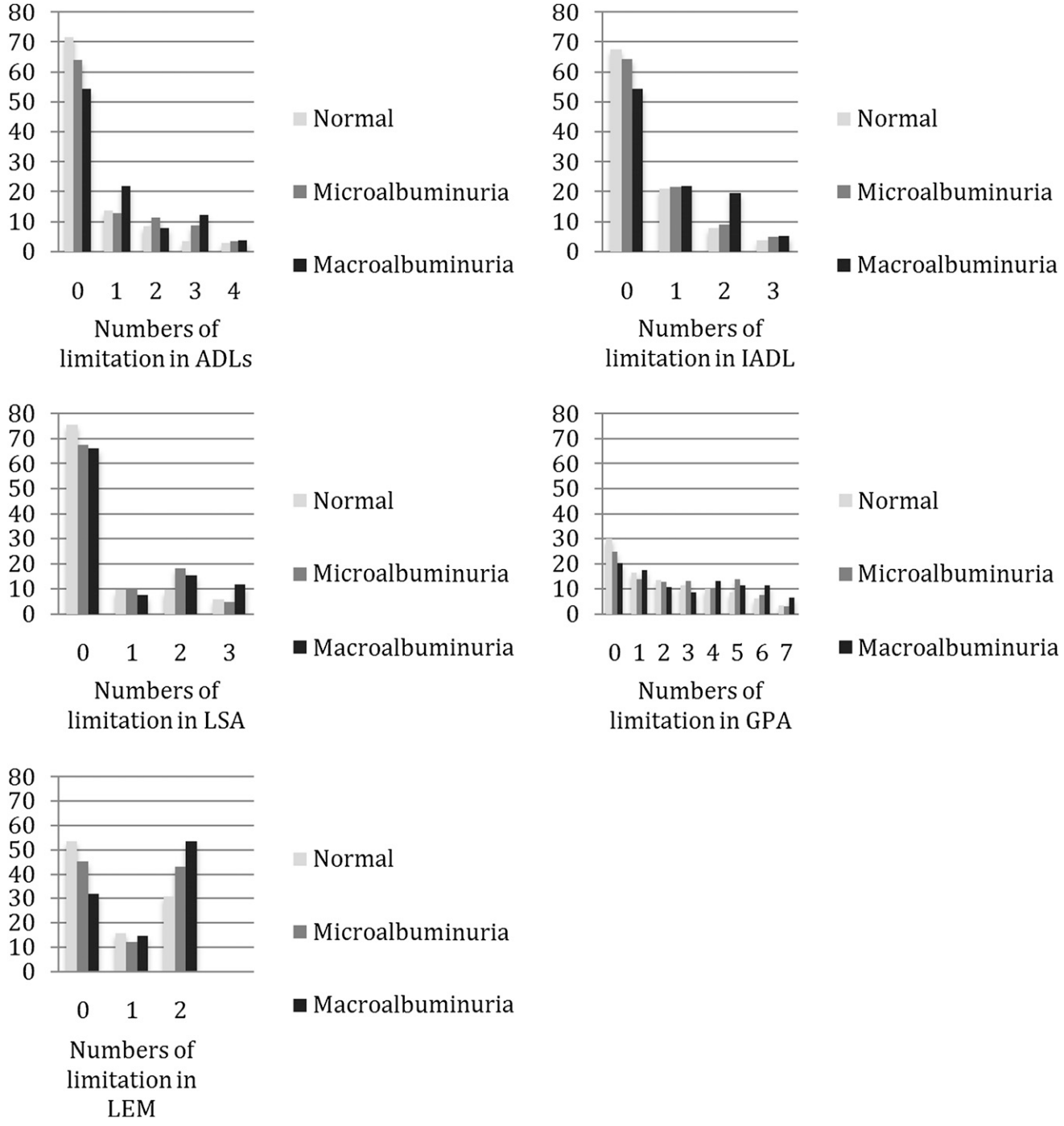

Figure 1—*Crude percentage of participants according to numbers of limitation in the five disability domains by status of albuminuria. The* y*-axis stands for the percentage of participants within each category of albuminuric status. The* x*-axis stands for the numbers of limitation in each disability domain.*

LEM, respectively. Further covariate adjustment, including chronic inflammation (model 2 to model 3), only mildly attenuated the association between UACR and disability in ADL, LSA, and LEM. We also found that macroalbuminuria was associated with IADL disability from model 1 to model 3. Of note, the trends of disability remained statistically significant across different models and all disability outcomes.

In another set of multiple logistic regression analysis (table not shown), we examined associations between chronic inflammation (elevated CRP) and disability among participants with diabetes. After adjusting for age, sex, and race, elevated CRP (>0.3 mg/dL) was associated with disability in ADL, IADL, LSA, GPA, and LEM. The ORs (95% CI) were 1.61 (1.30–1.98), 1.55 (1.26–1.90), 1.57 (1.26–1.95), 1.65 (1.33–2.06), and 2.15 (1.76–2.62), respectively. Further covariate adjustment (model 2 covariates + log-transformed UACR levels) diminished the association between elevated CRP and functional disability.

Table 2—*Association between UACR with functional disability*

Model	UACR groups	ADL disability		IADL disability		LSA disability		GPA disability		LEM disability	
		OR* (95% CI)	*P* for trend	OR* (95% CI)	*P* for trend	OR* (95% CI)	*P* for trend	OR* (95% CI)	*P* for trend	OR* (95% CI)	*P* for trend
1	UACR <30 mg/g	1.0 (ref)	<0.001	1.0 (ref)	0.001	1.0 (ref)	<0.001	1.0 (ref)	0.003	1.0 (ref)	<0.001
	UACR 30–300 mg/g	1.45 (1.15–1.83)		1.21 (0.96–1.52)		1.52 (1.20–1.94)		1.31 (1.02–1.68)		1.40 (1.12–1.75)	
	UACR >300 mg/g	2.12 (1.47–3.05)		1.83 (1.27–2.64)		1.63 (1.11–2.38)		1.71 (1.10–2.66)		2.55 (1.73–3.75)	
2	UACR <30 mg/g	1.0 (ref)	<0.001	1.0 (ref)	0.004	1.0 (ref)	0.001	1.0 (ref)	0.026	1.0 (ref)	<0.001
	UACR 30–300 mg/g	1.55 (1.18–2.02)		1.19 (0.91–1.56)		1.65 (1.25–2.17)		1.28 (0.96–1.70)		1.38 (1.06–1.78)	
	UACR >300 mg/g	2.02 (1.30–3.15)		1.99 (1.28–3.12)		1.64 (1.02–2.62)		1.62 (0.97–2.72)		2.34 (1.47–3.70)	
3	UACR <30 mg/g	1.0 (ref)	<0.001	1.0 (ref)	0.007	1.0 (ref)	0.002	1.0 (ref)	0.046	1.0 (ref)	<0.001
	UACR 30–300 mg/g	1.51 (1.16–1.98)		1.17 (0.90–1.53)		1.62 (1.23–2.14)		1.25 (0.93–1.67)		1.34 (1.03–1.74)	
	UACR >300 mg/g	1.94 (1.24–3.03)		1.93 (1.23–3.02)		1.59 (0.99–2.54)		1.55 (0.92–2.60)		2.20 (1.38–3.49)	

Adjusted covariates: Model 1 = age, sex, and race. Model 2 = model 1 + BMI category, smoking status, systolic blood pressure, comorbidities (heart diseases, chronic obstructive pulmonary disease, stroke, and arthritis), eGFR, levels of A1C and total cholesterol, use of antihypertensive agents, use of cholesterol-lowering agents, and use of antidiabetic medications. Model 3 = model 2 + log-transformed CRP. *ORs are for disability comparing participants with macroalbuminuria (UACR >300 mg/g) and microalbuminuria (UACR 30–300 mg/g) to participants with UACR <30 mg/g.

Elevated CRP was associated with disability in ADL and LEM in the full-adjusted models, with corresponding ORs (95% CIs) of 1.28 (1.00–1.62) and 1.68 (1.34–2.11), respectively.

Joint effect of albuminuria and elevated CRP on disability

We computed the ORs for disability in analyses where study participants were reclassified into four groups: UACR <30 mg/g and CRP ≤0.3 mg/dL (n = 577, reference group); UACR ≥30 mg/g and CRP ≤0.3 mg/dL (n = 278); UACR <30 mg/g and CRP >0.3 mg/dL (n = 544); and UACR ≥30 mg/g and CRP >0.3 mg/dL (n = 330). We found additive effects of albuminuria and elevated CRP on disability in older adults with diabetes (Fig. 2). Participants with both elevated UACR and CRP tended to have higher likelihoods of being disabled. The ORs (95% CIs) for disability in ADL, IADL, LSA, GPA, and LEM were 2.01 (1.42–2.84), 1.58 (1.12–2.23), 2.05 (1.43–2.93), 1.58 (1.09–2.29), and 2.49 (1.77–3.49), respectively, compared with participants with UACR ≥30 mg/g and CRP >0.3 mg/dL versus the reference group.

CONCLUSIONS—Among 1,729 noninstitutionalized elderly adults with diabetes, increased urinary albumin excretion is associated with functional disability in ADL, IADL, LSA, GPA, and LEM, independent of chronic comorbidities (heart disease, chronic lung disease, stroke, and arthritis), systolic blood pressure, glycemic control (A1C), renal function (eGFR), total cholesterol, and chronic inflammation (log-transformed CRP). We also found a previously unreported interactive effect of albuminuria and elevated CRP on functional disability. Subjects with albuminuria and increased CRP values were significantly more likely to have higher odds of disability than individuals with albuminuria and normal CRP values. The interaction between albuminuria and high CRP values on functional disability suggests that the presence of subclinical inflammation may amplify the effect of albuminuria on functional disability in older adults living with diabetes.

Our study supports and extends previous studies examining the association between albuminuria and disability among people with diabetes. Bruce et al. (19), using data from the Fremantle Diabetes Study, showed that microalbuminuria, or increased UACR, was

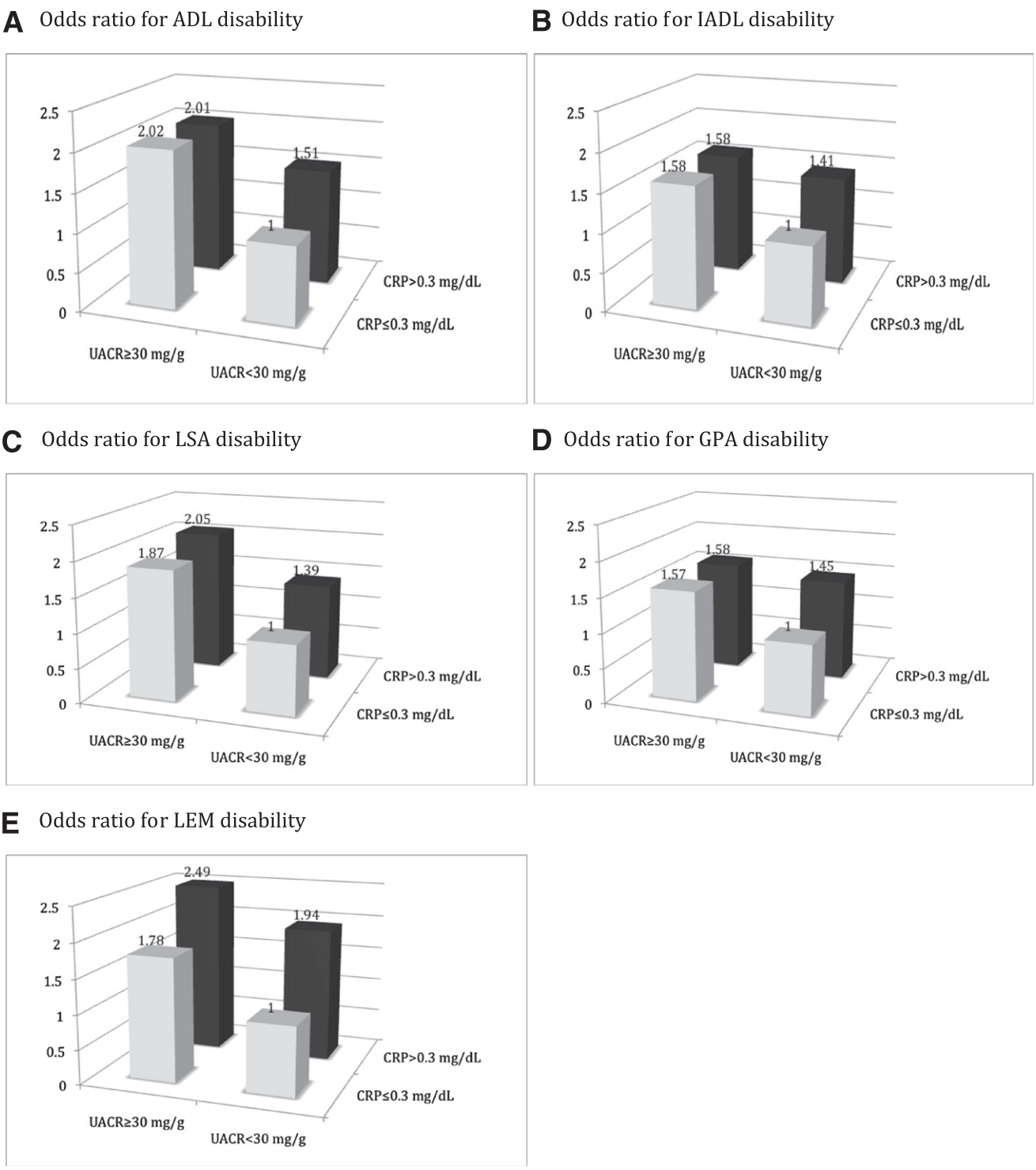

Figure 2—*Joint effect of UACR and CRP on functional disability. Study participants were reclassified into one of four groups based on UACR (>30 vs. <30 mg/g) and CRP (>0.3 vs. <0.3 mg/dL) levels. The ORs for disability in respective disability domains were obtained with participants with UACR <30 mg/g and CRP <0.3 mg/dL as the reference group. The analyses were adjusted for age, sex, race, BMI category, smoking status, systolic blood pressure, comorbidities (heart diseases, chronic obstructive pulmonary disease, stroke, and arthritis), eGFR, glycemic control (A1C), levels of total cholesterol, use of antihypertensive agents, use of cholesterol-lowering medications, and use of antidiabetic medications.*

independently associated with mobility impairment among patients without a baseline mobility problem who were followed for an average of 4.6 years. Ghanassia et al. (20) found that albuminuria/renal impairment was associated with ADL disability after 6.5 years of follow-up among patients with diabetes and foot ulcers. Diabetes studies with functional disability as outcomes have typically focused on ADL, IADL, and/or mobility limitation. In developing

potential interventions to slow diabetes-related disability in the elderly, it is clinically relevant to consider all domains of disability, including ADL, IADL, social activities, and leisure activities. To the best of our knowledge, this is the first report to describe the association between albuminuria and disability by using a geographically dispersed and ethnically diverse national sample of community-dwelling older adults with diabetes and disability outcomes covering not just ADL and IADL, but other clinically relevant disability domains such as leisure and social activities (e.g., attending social events), lower-extremity mobility (e.g., walking for a quarter mile), and general physical activities (e.g., stooping, bending, and lifting). Potential confounders were comprehensively considered, and the interaction effect of albuminuria and inflammation on disability was also investigated.

Several mechanisms might explain the association of albuminuria and inflammation with increased risk of disability. Both albuminuria and inflammation, important markers for endothelial dysfunction and atherosclerosis, are related to cerebral atherosclerosis and peripheral vascular disease. Peripheral vascular disease is associated with slow gait speed, decreased muscle strength, and physical disability (21). Cerebral atherosclerosis precedes both cerebral macroangiopathy (large observable stroke) and cerebral microangiopathy (leukoaraiosis). These cerebral lesions thus interrupt the integrity of frontal-subcortical circuits that are associated with a magnitude of aging phenotypes, including cognitive impairment, functional decline, and slow walking speed (22), all of which are documented risk factors for disability. Vascular lesions, either directly or indirectly, therefore provide convincing mechanisms for the associations between albuminuria, inflammation, and disability. Second, there is often an essential joint effect between various cardiovascular disease or risk factors on a variety of clinical outcomes (23). Thus, it is physiologically plausible for older people with both albuminuria and elevated CRP to have greater odds of functional disability.

Our study has several implications. First, in addition to being predictors of cardiovascular or survival outcomes, albuminuria and/or CRP appear to have functional implications among older adults with diabetes. These two markers, either alone or in combination, may be useful in early identification and targeting patients with diabetes who may require intervention to avoid or delay functional dependence. Second, our findings may serve as a theoretical basis for pharmaceutical approach. Both albuminuria and elevated CRP can be managed pharmaceutically, with ACE inhibitors and angiogensin-receptor blockers known to reduce the magnitude of albuminuria, whereas statins have a CRP-lowering effect (24). Moreover, a recent study has shown that treatment with either ACE inhibitors or angiogensin-receptor blockers was protective against cognitive decline in patients with diabetes (25). Future studies (e.g., randomized controlled trials) are needed to ascertain the roles of pharmaceutical agents and lifestyle approaches in preventing disability among people with diabetes.

Our study has potential limitations deserving comments. Because of the cross-sectional design, a causal relationship between albuminuria, inflammation, and disability cannot be established and should be explored longitudinally. Second, variables of diabetes complications in NHANES, such as foot ulcer, ophthalmological examination, or peripheral neuropathy, are not complete from 1999 to 2008. Therefore, we are not able to ascertain the role of diabetes complications in functional disability. Lastly, blood glucose at any time point has an important effect on physical ability. Specifically, extremes of blood glucose may have an acute effect on function; but we have no data to explore that important effect.

In conclusion, albuminuria and inflammation were associated with functional disability among older people with diabetes. Albuminuria and inflammation had an interaction effect on disability. We provided new information and a possible implication on the associations between UACR, CRP, and disability among community-dwelling older adults living with diabetes. The findings raise a number of important questions for future research. Can level of albuminuria identify older adults with diabetes at highest risk for subsequent disability? Can reduction of proinflammatory markers moderate the disability impact of albuminuria in people with diabetes? Examining these questions may provide evidence of potentially modifiable predisability indicators in the setting of diabetes. An important step toward reducing the disabling impact of diabetes is early identification of (and potential interventions for) older adults with diabetes at the highest risk of becoming disabled.

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H.-K.K. developed the study concept and design. H.-K.K., S.A.S., Y.-F.K., and M.A.R. performed the data analysis and data interpretation and prepared the manuscript.

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