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Research Article

Gender Differences in the Combined Effects of Cardiovascular Disease and Osteoarthritis on Progression to Functional Impairment in Older Mexican Americans

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Abstract

Background: Comorbidity (COM) is an important issue in aging. Cardiovascular disease (CVD) and osteoarthritis separately and together may modify the trajectories of functional decline. This analysis examines whether specific and unrelated COMs influence functional change differently and vary by gender.

Methods: A cohort study of 1,789 (aged 60 years and older) Mexican Americans was followed annually for up to 10 years. We created four groups of COM (CVD alone, lower body osteoarthritis alone [OA], neither, or both). We employed mixed effects Poisson models with Instrumental Activities of Daily Living (IADL) as the outcome. We tested whether the association between COM and decline in functional status differed by gender.

Results: IADL impairments in those with CVD, OA, or both were significantly higher at baseline and increased more rapidly over time compared to those with neither condition. Compared to women with no COM, the number of IADL impairments in women with CVD alone were 1.36 times greater, with OA were 1.35 times greater, and both conditions were 1.26 times greater. Compared to men with no COM, IADL impairments in men with CVD alone were 1.15 times greater, OA alone were 1.12 times greater, and both were 1.26 times greater.

Conclusions: Over time, the influence of COM on functional decline differs by specific combinations of COM and by gender. Aggregate COM scales obscure the biological and temporal heterogeneity in the effects of COM. Time-dependent-specific COMs better assess the development of impairment. Women experience a higher burden of functional impairment due to COM than men.

Key Words: Epidemiology—Cardiovascular—Functional performance—Arthritis—Minority aging

As populations and people age, chronic diseases and conditions accelerate in number and severity more rapidly over time. A number of reports of this process have suggested that women decline in function more rapidly than men (1,2). Gill and coworkers (3) reported that women progress more rapidly than men to severe impairment. Analyses from the Leiden 85-plus study also found important gender differences in progression to disability (4). Gender differences in functional impairment may vary by type of task, for example, women may decline more rapidly than men in activities requiring physical effort. As well, the influence of specific comorbid conditions on functional ability is likely to vary by gender (5). Grunau and coworkers (6) have suggested that disease-specific models perform better than a summary score when evaluating prognosis for a specific outcome.

The most common methodological approaches to measuring comorbidities (COMs) use scales that sum the number of COMs (7). These measures are often weighted by prognostic severity of the condition based on a prediction of death or other clearly defined

outcome such as institutionalization. This approach to quantifying COM yields a predictable result, namely, that COM increases risk of death, institutionalization, and impairment. Performance of several different measures of aggregated COM indices with respect to timing of COM have been examined by Tang and coworkers (8). That work found that a summative index, the Charlson scale, performed better when measured at baseline, whereas a similar scale performed better when assessed closer to outcomes of interest.

Additive approaches such as these may include biologically disparate conditions that influence functional decline by different pathways or in different directions. Two or more conditions may be associated because they have a common antecedent, but are not necessarily biologically related. An example of this is the influence of obesity on osteoarthritis and hypertension/cardiovascular disease (CVD). The relative joint timing of multiple COMs is also important. Very few studies have traced the trajectory of concurrent change in COMs or the influence of such changes on functional decline. Wang and coworkers (9) has demonstrated that the use of time-dependent COMs is a more effective model for looking at the relationship between COMs and mortality. The use of time-dependent accumulation of COMs more accurately reflects the changing nature of the exposure over time. Time-dependent covariates are allowed to change over time. Time-dependent changes in multiple COMs are likely to influence the trajectory of change in functional status. The focus of this article is on gender differences in change over time in Instrumental Activities of Daily Living (IADL) as predicted by two time-dependent major COMs—lower body osteoarthritis alone (OA) and CVD.

Study Design and Methods

The Sacramento Area Latino Study on Aging (SALSA) is a population-based longitudinal study of older Mexican Americans (n = 1,789) living in the Sacramento Valley area of California who were 60–101 years old at baseline in 1998–1999 (10). We designed SALSA to examine the effects of sociocultural, metabolic, and cardiovascular risk factors on dementia incidence and cognitive decline in this ethnic group. Participants were interviewed and underwent clinical examinations in their homes every 12–15 months to 2008 for up to seven examinations. The study also interviewed participants by telephone biannually to update medication use and health status. Study questionnaires were available in Spanish and English. Interviews were conducted in the language that participants preferred. A detailed description of study procedures has been published previously (10). The Institutional Review Boards of the University of California San Francisco and Davis and the University of Michigan approved the study.

Measurement of Covariates

Comorbidity

CVD and lower body osteoarthritis were selected for this analysis because they are highly prevalent in older populations and frequently co-occur. Also, biological pathways for OA and CVD may overlap (11) due to antecedent risk factors in common. Lower body OA (as opposed to total OA) was also chosen for its' significant effect on mobility (5).

CVD included nine categories (myocardial infarction, angina pectoralis, congestive heart failure, intermittent claudication, stroke, atrial fibrillation, deep vein thrombosis, heart catheterization). These measures derived from self-report of a doctor's diagnosis during the home visit interviews. Lower body OA was defined by self-report from an annual questionnaire. Participant was asked if a physician had told them they had arthritis in the hands, shoulder, hips, knees, and back. Positive responses to hips, knees, and back were coded as lower body.

We constructed a four-category, time-varying COM variable based on a subject's OA and cardiovascular status at each visit. The categories were as follows: no COM, lower body OA only, CVD only, and both. For example, an individual could have only CVD at one visit and acquire lower body OA at the next. In such circumstances, he/she would be "CVD only" at visit one and "Both" at visit 2. We did not allow for "backward" transitions from disease state to normal.

Covariates

Other covariates included age in years, nativity (Mexico or other country in Latin America vs United States), body mass index, waist circumference in inches, physical activity, education in years, and the presence or absence of health insurance. Additionally, we included diabetes (based on a doctor's report of diabetes, use of diabetes medication, or fasting glucose > 125), hypertension (based on a doctor's report of hypertension, use of any hypertension medication, or measured systolic blood pressure ≥ 140, or diastolic blood pressure ≥ 90). Others included any alcohol consumption, an acculturation score, and cognitive function measured by the Modified Mini-Mental State Exam. Physical activity was composed of a summary score for 17 items with a range of 0–51 (12). Walking pace was based on a question about the pace of walking outside (13). The Modified Mini-Mental State Exam is a global cognitive test ranging from 0 to 100 (14). A pain score was composed of eight questions regarding the presence or absence of pain in a musculoskeletal location (hands, feet, knees, hips, neck, back, shoulder, or other) for at least 6 months.

Outcome for Functional Status

IADL were measured at baseline and at each follow-up visit by self-report of the level of difficulty for a specific activity (15). IADL was the primary outcome in this analysis because it is widely used in studies of aging, impairment on IADL represents significant effects on quality of life, and it is predictive of major outcomes such as death. The participant was asked to rate the difficulty (none, some, a lot, cannot do without help, or equipment) of specific tasks. Fifteen IADL items summed to form a scale that ranged from 0 to 45 (low impairment to high; Supplementary Table 1).

Statistical Analysis

We assessed the association of changing patterns of COM (CVD and OA) with changes in IADL using mixed effects Poisson regression analysis. The models included time-varying COM status, time, and other covariates as predictors, as well as random intercepts to accommodate the repeated measures of IADL for each subject. The models also include interactions of time, COM group, and gender to allow for assessment in differences in IADL time trends by COM and gender. We assessed the statistical significance of the interactions using likelihood ratio tests.

We used indicator variables for the COM groups (none, CVD only, OA only, both). The COM group "None" was the reference. We tested whether there were gender differences in IADL change over time by including two-way interaction term (gender × time). We tested whether the association between each COM and IADL

varied over time with three two-way interactions (COM × time). We added a three-way interaction model (gender × COM × time) to test whether the association between COM and IADL change differed by gender. This result was not statistically significant (likelihood ratio = 4, *df* = 3, *p* = .26). We stratified analyses on gender.

To test the notion that CVD and OA are biologically related, in proportional hazards models, we examined the age- and gender-adjusted associations between baseline or time-dependent CVD and incident OA, and baseline or time-dependent OA and incident CVD. All analyses were performed using SAS version 9.4.

Results

Table 1 compares baseline covariates in relation to the four-category COM variable by gender.

Among men, age, body mass index, waist circumference, acculturation, physical activity score, and nativity did not differ across the COM groups. Lower education was associated with OA and with OA and CVD. Although more than 90% of the participants overall had health insurance, health insurance coverage was lower among men with neither condition and highest among men with both COM. Type II diabetes was more common in men with CVD and in men with both conditions. Hypertension was highest among men with CVD or with both conditions and lowest among men with neither condition or only with OA. Slow walking pace was more common in those with both COM compared to those with neither. At baseline, IADL 2+ limitations were highest among those with both conditions and lowest among those with neither condition. A baseline Modified Mini-Mental State Exam score <80 was lowest among those with both conditions and highest among those with only CVD.

Among women, those with both conditions were older and had higher body mass index and waist circumference. Mean education, acculturation scores, and physical activity were lowest. Mean pain scores and percent with health insurance coverage, diabetes, and hypertension were all highest among those with both conditions. Alcohol consumption was lowest among those with both OA and CVD and highest among those with neither condition. Slow walking pace was highest among women with both conditions. Both IADL with two or more limitations and baseline Modified Mini-Mental State Exam score <80 were highest among those with both conditions. Nativity was unrelated to COM. In sum for both men and women, those with both COM were less healthy, less educated, more likely to be obese, less physically active, and less likely to drink alcohol.

Figure 1 shows the composition of the four COM groups over time by gender. Among men, the prevalence of those with no COM declines from about 50% at baseline to 20% in year 6. The prevalence of those with only OA increases slightly from 15.7% to 20%; the prevalence of those with only CVD changes from about 24% to about 26%; and the prevalence of those with both conditions increases from nearly 10% to 32%. Among women, a similar pattern prevails. Notably, the co-occurrence of CVD and OA is higher at baseline in women (18.2%) than in men (9.9%) and increases more rapidly over time in women compared to men. At the last follow-up, 32% of men and 43% of women had both conditions.

Figure 2 and Table 2 show results for time-dependent IADL modeled using mixed effects Poisson models with random intercepts. As shown in model 1, interactions between time and the time-dependent COM groups are significant for both men and women such that those with OA, CVD, or both conditions develop more functional impairment over time compared to those with neither condition. As noted earlier, because the three-way interaction between COM × gender × time was not significant, the models in Table 2 are gender stratified.

Model 1

For both men and women, there are statistically significant interactions between each of the time-dependent COMs and time. Among men with OA, CVD, or both conditions, functional impairment accelerates more rapidly than among those with neither condition (IADL: CVD only = 1.15 greater impairment, OA only 1.12 more impairment, both CVD and OA = 1.26 more impairment). Among women with OA, CVD, or both conditions, functional impairment accelerates more rapidly over time than among those with neither condition (IADL count: CVD only = 1.36 more impairment, OA only = 1.35 more impairment, both CVD and OA = 1.26 more impairment).

Model 2: Adjustment for Covariates

To the models, we added adjustment for covariates identified in bivariate analyses. The results for men remain unchanged from model 1 by this addition of covariates. The results for women from model 1 are largely unchanged (compared to none, CVD only = 1.32 more impairment, OA = 1.34 more impairment, both = 1.26 more impairment). The interaction between time and OA for women is no longer significant. Figure 2 illustrates these gender-specific trajectories with specific covariate values set at the median or most prevalent condition as noted.

In separate gender-specific and age-adjusted proportional hazards models, baseline CVD was associated with incident OA (men: hazard ratio [HR] = 1.50, *p* = .006; women: HR = 1.37, *p* = .02). As well, time-dependent CVD was associated with incident OA (men: HR = 1.50, *p* = .0004; women: HR = 1.55, *p* = .0005).

In men, we found that neither baseline nor time-dependent OA was associated with incident CVD (HR = 0.96, *p* = .82; HR = 0.90, *p* = .48). However, in women, both baseline and time-dependent OA were associated with CVD incidence (HR baseline = 1.33, *p* = .04 and time-dependent HR = 1.39, *p* = .03). In men, adjustment of these models for physical activity and pain score had no influence on the association. In women, these adjustments attenuated the association (HR = 1.14, *p* = .42).

In the scientific literature in general, potential biological/behavioral links between CVD and OA have been identified (11) as physical activity, obesity, diabetes, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs). Adjustment for these risk factors (except NSAID use) had only minor effects on the associations of COM with change over time in IADL (Table 2).

Discussion

Our findings suggest that patterns of associations between these two COMs and functional decline vary by gender and COM group. Compared to men, women were more impaired at baseline and become impaired over time more rapidly, specifically in relation to CVD and combined CVD and OA but not for OA alone. The task-specific patterns of baseline impairment suggest that women were more impaired than men in tasks requiring physical effort but not in complex tasks such as writing or managing money. The joint presence of CVD and OA influences function in physical tasks more in men than in women. Only CVD or the combination of CVD and OA influenced complex tasks over time in women.

Table 1. Baseline Characteristics of the Study Cohort by Gender and COM Group

COM Group at Baseline	Men (*N* = 745)					Women (*N* = 1,044)				
	None, *N* = 376	Arthritis (LB), *N* = 117	CVD, *N* = 178	Both, *N* = 74	*p* Value	None, *N* = 404	Arthritis (LB), *N* = 233	CVD, *N* = 217	Both, *N* = 190	*p* Value
Baseline covariates										
Mean (*SD*)										
Age, y	70.0 (7)	70.0 (7)	71.0 (7)	71.0 (8)	ns	70 (7)	71 (8)	71 (8)	72 (7)	**
Body mass index, kg/m^2	28.8 (4.7)	30.2 (5.2)	29.4 (5.5)	29.7 (4.3)	ns	29.2 (6.4)	30.5 (5.6)	29.6 (7.2)	31.9 (6.4)	**
Waist circumference, inches	38.8 (4.8)	39.9 (4.5)	39.5 (4.9)	39.9 (4.3)	ns	36.4 (4.9)	37.8 (5.3)	37.1 (5.6)	38.8 (5.8)	**
Education, y	8 (6)	7 (5)	8 (6)	7 (6)	*	8 (5)	7 (5)	7 (5)	5 (5)	**
Acculturation score, 0–56	24 (13)	20 (12)	24 (13)	23 (12)	ns	22 (13)	21 (13)	21 (13)	18 (12)	†
Physical activity summary score, 0–40	16.2 (5.1)	16.3 (5.5)	15.6 (5.4)	15.6 (5.9)	ns	18.7 (5.2)	18.0 (5.4)	17.6 (5.3)	16.9 (5.8)	†
Pain score 0–8	0.8 (1.5)	2.8 (2.6)	1.0 (1.8)	3.1 (2.5)	**	1.1 (1.8)	3.6 (2.6)	1.5 (2.0)	4.0 (2.7)	**
% (*N*)										
Health insurance	89.7 (330)	95.7 (111)	94.9 (169)	98.7 (73)	†	85.8 (343)	91.9 (214)	88.4 (191)	94.2 (179)	*
Diabetes	25.5 (94)	32.5 (38)	45.5 (81)	55.4 (41)	**	24.4 (98)	29.2 (68)	36.9 (80)	45.3 (86)	**
Hypertension	61.7 (232)	62.4 (73)	79.2 (141)	86.5 (64)	**	58.2 (235)	65.7 (153)	72.8 (158)	80.0 (152)	**
Any alcohol consumption	70.2 (259)	65.0 (76)	61.2 (109)	54.1 (40)	*	51.5 (206)	46.4 (108)	37.5 (81)	34.7 (66)	**
Walking pace										
Slow	21.1 (75)	22.3 (25)	32.1 (53)	42.9 (30)	†	24.4 (92)	35.6 (80)	32.8 (65)	49.7 (92)	**
Medium	59.0 (210)	59.8 (67)	53.9 (89)	47.1 (33)		52.5 (198)	44.4 (100)	53.0 (105)	44.3 (82)	
Fast	19.9 (71)	17.9 (20)	13.9 (23)	10.0 (7)		23.1 (87)	20.0 (45)	14.1 (28)	6.0 (11)	
Nativity (Mexican)	50.7 (187)	51.3 (60)	46.6 (83)	40.5 (30)	ns	51.1 (205)	51.9 (121)	51.2 (111)	58.4 (111)	ns
Baseline IADL (2+ limitations)	46.2 (168)	68.7 (79)	59.9 (103)	82.2 (60)	**	58.9 (231)	83.8 (192)	73.2 (150)	89.3 (166)	**
Baseline ADL (1+ limitations)	5.5 (20)	7.8 (9)	17.5 (30)	17.8 (13)	**	7.4 (29)	18.3 (42)	15.1 (31)	27.8 (52)	**
Baseline 3MSE (<80 score)	21.4 (79)	19.7 (23)	31.5 (56)	13.5 (10)	†	21.8 (87)	22.3 (52)	26.7 (58)	36.3 (69)	†

*Notes:*3MSE = Modified Mini-Mental State Exam, ADL= Activities of Daily Living; COM, comorbidity; CVD = cardiovascular condition; IADL = Instrumental Activities of Daily Living; LB = lower body; ns = not significant; *SD* = standard deviation. *p* Values represent within-gender group differences. *$p < .05$, †$p < .01$, **$p < .001$.

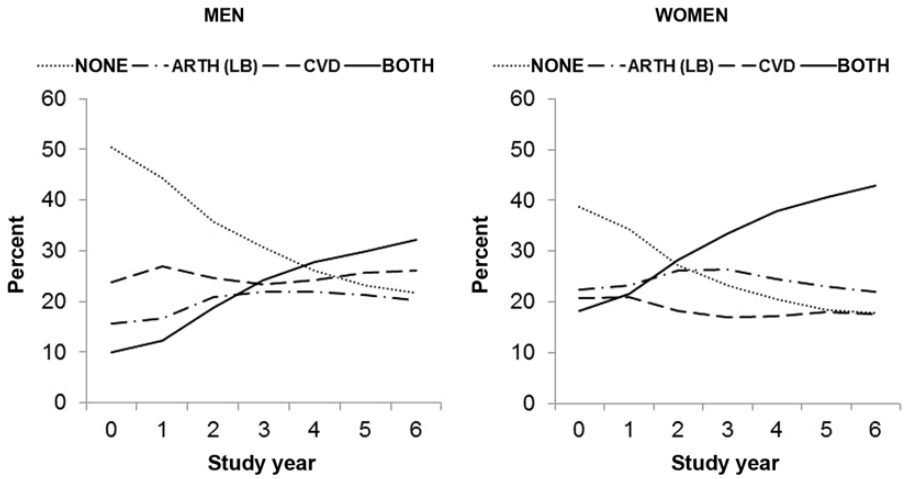

Figure 1. Prevalence of four comorbidity groups over time by gender.

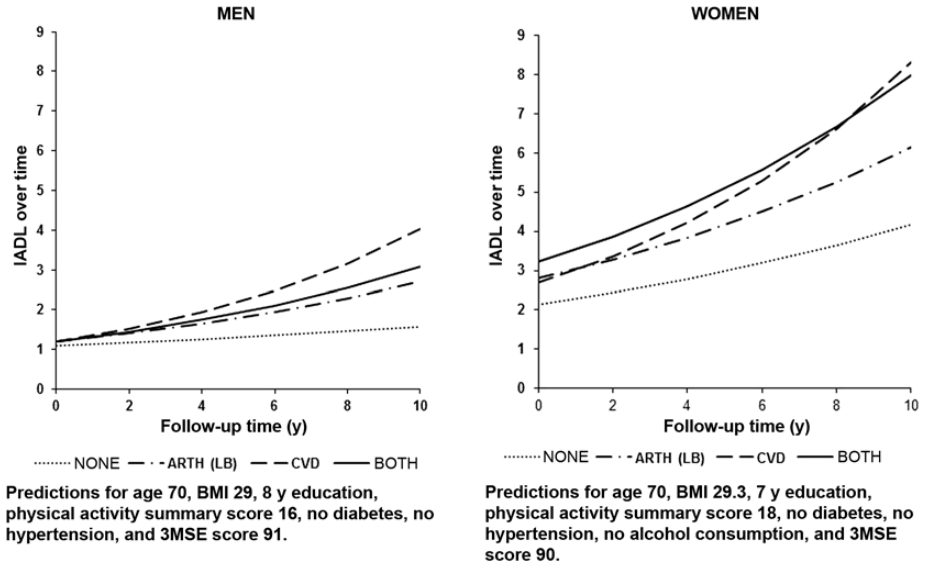

Figure 2. Association between time-dependent comorbidities and Instrumental Activities of Daily Living (IADL) counts over time by gender from a mixed effects Poisson model with random intercepts.

Grunau and coworkers (6) has suggested that disease-specific models perform better than a summary score when evaluating prognosis for a specific outcome. The intent of our analysis was to test whether the burden of COM on functional decline varies by gender over time, using COMs that are likely to affect physical functioning independently and in combination. Few studies of functional include time-dependent COMs or differences in joint effects (9). Our analysis allows us to disentangle the contributing roles of two commonly occurring COMs, CVD and lower body osteoarthritis, on the progression of functional impairments among older adults.

Other work (11) has suggested that baseline OA is associated with an increased risk of CVD. We found the opposite that CVD was a modest predictor of OA. As suggested by Rahman and coworkers (11), the association between OA and CVD may be explained by antecedent risk factors such as physical activity, obesity, type 2 diabetes, and the use of NSAIDs. In this analysis, we have adjusted for all of these risk factors except NSAIDs (due to lack of data).

This cohort was entirely Hispanic (95% Mexican ancestry). Few other studies have examined the constellation of COM and functional change in such a population. Work by Caskie and coworkers (16) based on the Hispanic Established Populations for Epidemiologic Study of the Elderly (EPESE) study has reported significant increases in IADL impairment over a 7-year period in older Hispanics, especially associated with hypertension. Also in the Hispanic EPESE data (17) suggested that IADLs limitations increased over 7 years from 2.1 to 4.0 average limitations, or approximately double from baseline. Similarly, Jones (18) reported that the number of COMs at baseline accelerated IADL impairment. The SALSA population differs from non-Hispanic White populations in important ways that might adversely affect the disablement process. Our participants had lower education (average 9 years), were more obese, more diabetic, and hypertensive than non-Hispanic White samples. Over 50% of the participants were born in Mexico.

The study has some limitations that are important to note: Both COMs were based on self-reports of a physician diagnosis.

Table 2. Association Between Comorbidity and Categories of Impairment in IADL, by Gender From a Mixed Effects Poisson Model With Random Intercepts

	Men		Women	
Model 1				
–2 log-likelihood	19,354		31,595	
Parameter	Estimate	95% CI	Estimate	95% CI
Neither condition	Reference			
Arthritis (LB)	0.08	(–0.02, 0.18)	0.28	(0.20, 0.35)**
CVD	0.18	(0.08, 0.28)**	0.24	(0.15, 0.33)**
Both	0.19	(0.08, 0.30)**	0.44	(0.36, 0.52)**
Time, y	0.07	(0.05, 0.09)**	0.06	(0.05, 0.08)**
Baseline age	0.09	(0.07, 0.10)**	0.07	(0.08, 0.08)**
Time × arthritis	0.03	(0.01, 0.06)*	0.02	(0.01, 0.04)*
Time × CVD	0.06	(0.04, 0.08)**	0.07	(0.05, 0.09)**
Time × both OA and CVD	0.04	(0.02, 0.07)**	0.03	(0.01, 0.05)**
Model 2				
–2 log-likelihood	16,970		28,407	
Parameter	Estimate	95% CI	Estimate	95% CI
Neither condition	Reference			
Arthritis (LB)	0.09	(–0.01, 0.20)	0.28	(0.20, 0.36)**
CVD	0.10	(–0.01, 0.20)	0.23	(0.14, 0.32)**
Both	0.10	(–0.014, 0.21)	0.42	(0.34,0.50)**
Time, y	0.04	(0.02, 0.06)**	0.07	(0.05, 0.08)**
Baseline age	0.07	(0.06, 0.09)**	0.05	(0.04, 0.06)**
Time × arthritis	0.05	(0.02, 0.07)**	0.01	(–0.01, 0.03)
Time × CVD	0.08	(0.06, 0.11)**	0.05	(0.02,0.07)**
Time × both OA and CVD	0.06	(0.03, 0.08)**	0.02	(0.01, 0.04)**
Body mass index	0.03	(0.01, 0.05)**	0.03	(0.02, 0.04)**
Education, y	–0.03	(–0.05, –0.01)**	–0.03	(–0.04, –0.01)**
Physical activity summary score	–0.05	(–0.07, –0.03)**	–0.05	(–0.06, –0.04)**
Diabetes	0.72	(0.51, 0.94)**	0.47	(0.34, 0.61)**
Hypertension	0.25	(0.02, 0.48)*	0.29	(0.15, 0.42)**
Any alcohol consumption†	NA	NA	–0.11	(–0.23, 0.02)
Time-dependent 3MSE score	–0.01	(–0.01, –0.01)**	–0.01	(–0.01, –0.01)**

Notes: CI = confidence interval; CVD = cardiovascular conditions; *df* = degrees of freedom; IADL = Instrumental Activities of Daily Living; LB = lower body; NA = not available; OA = osteoarthritis alone. Men: model 1 versus model 2, chi square = 2,384, *df* = 6, $p < .0001$; women: model 1 versus model 2, chi square = 3,188, *df* = 7, $p < .0001$. Estimate reflects a 1 unit change in IADL.

*$p < .05$, **$p < .01$.

†Not adjusted in models for men since it is not statistically significant.

This may have resulted in under reporting of less severe conditions. As well, we lack radiographic assessments of OA or clinical assessments of impairment that might contribute to functional impairment. However, pain scores were higher and physical activity lower in those reporting osteoarthritis with or without CVD (Table 1). This confers face validity on the associations with functional impairment.

The general concept in this article was to evaluate the joint and separate occurrences of COM and their influence of trajectories of functional status. We selected two COMs that are common in older people, differ by gender, and represent relatively distinct diagnoses. Type 2 diabetes is a common health problem in Mexican American populations but is more closely associated with CVD than OA and did not meet this criteria.

These results support the notion that women experience higher burdens of both COM and functional decline than do men. At the end of follow-up, women with CVD had twice the IADL impairment as men with CVD. Women with both conditions had nearly three times the impairment of men with both conditions. The reasons for these substantial differences are not clear but have important implications for health care of older women. Women are often primary caregivers for spouses and elderly parents. If they suffer impairment disproportionately, the burden of caring for others may add to their functional decline. There has been a lack of attention to what the combined effects of specific chronic diseases (in this case OA and CVD) might be on functional outcomes. This provides evidence for the concept that specific and unrelated COMs influence functional change and that this varies by gender.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

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