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Predictors of Combined Cognitive and Physical Decline

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OBJECTIVES: To determine the incidence and correlates of combined declines in cognitive and physical performance.

DESIGN: Cohort study of community-dwelling older women with moderate to severe disability.

SETTING: The community surrounding Baltimore, Maryland.

PARTICIPANTS: Participants in the Women's Health and Aging Study I with Mini-Mental State Examination (MMSE) score or 24 or greater and walking speed greater than 0.4 m/s at baseline.

MEASUREMENTS: Cognitive decline was defined as an MMSE score less than 24 and physical decline as a walking speed of 0.4 m/s or less in at least one of the three annual follow-up visits. Participants were stratified into groups based on cognitive or physical decline or both. Group characteristics were compared, and results were adjusted for age, race, education, and significant covariates.

RESULTS: Of 558 women that met the baseline MMSE and walking speed inclusion criteria, 21% developed physical decline, 12% developed cognitive decline, and 11% experienced combined cognitive and physical decline. After adjustment, physical decline was associated with age, nonwhite race, former smoking, baseline walking speed, and instrumental activities of daily living (IADL) impairment. Cognitive decline was associated with age and baseline MMSE score. Combined decline was associated with age, baseline walking speed, MMSE score, IADL impairment, as well as current smoking (odds ratio (OR) = 5.66, 95% confidence interval (CI) = 1.49–21.54) and hemoglobin level (OR = 0.68, 95% CI = 0.47–0.98).

CONCLUSION: Potential predictors of cognitive and physical performance decline were identified. The association between smoking and lower hemoglobin levels and combined cognitive and physical decline may represent potentially modifiable risk factors and should be confirmed in future studies. **J Am Geriatr Soc 53:1197–1202, 2005.**

Key words: cognitive; physical; function; decline; women

Cognitive and physical decline are important to the development of disability in older adults. Instrumental activities of daily living (IADLs) explicitly include physical and cognitive elements.[1] Activities of daily living (ADLs) are understood to be physical capabilities but are also affected by cognitive impairment.[2] Clinical and research findings have demonstrated that a variety of diseases affecting cognition are associated with deteriorating physical function.[3–7] Classification and assessment of the severity of cognitive impairment often depends on physical function status.[8] However, research for preventing disability in older adults has more often examined decline in the cognitive or physical domains individually. Identification of factors for combined cognitive and physical decline could point to targets for potential interventions, including risk factor modification or more aggressive treatment of comorbidities.

The use of self-reported physical function has generally limited prior studies examining the relationship between cognitive and physical function. It is likely that cognitive decline affects the self-perception of physical function.[9] Measures of physical performance, such as walking speed, have been demonstrated to predict functional dependence in persons with and without cognitive impairment.[10,11] Such measures may be more reliable and provide additional information on the process of combined cognitive and physical decline. Combined declines in physical and cognitive performance have been demonstrated in a high-functioning older population,[12] but these findings have never been extended to individuals with lower functional status. Further understanding of the interrelationship between cognitive and physical function is needed in frail populations because these individuals are at highest risk for functional dependence and major health-related events.[13] Additionally, frail individuals have more comorbid conditions than higher-functioning individuals, thus providing a greater number of potential predictors of decline to assess.

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The aim of the present study was to characterize combined declines in cognitive and physical performance in a lower-functioning population and to identify specific factors associated with this pattern of decline versus physical decline alone, cognitive decline alone, or no decline. The Women's Health and Aging Study (WHAS) I was a 3-year prospective study of older women established to study the course and causes of disability in moderate to severely disabled women and is therefore well suited for addressing these associations.

METHODS AND PARTICIPANTS

The WHAS I Population

The WHAS I was a prospective study of disability in 1,002 older women residing in the community surrounding Baltimore, Maryland. The design and characteristics of the cohort are described in more detail elsewhere.[14] Briefly, women with moderate to severe disability were enrolled and followed over 3 years with in-home study assessments by trained study nurses every 6 months. Basic inclusion criteria for the WHAS study consisted of having self-report difficulty in performing tasks in two or more of the following areas: basic self-care, higher-functioning tasks of daily living, upper extremity activities, and mobility. The research ethics committee of Johns Hopkins University approved WHAS I, and participants provided written informed consent upon enrollment.

For the present analyses, 558 participants with a Mini-Mental State Examination (MMSE)[15] score of 24 or greater and walking speed greater than 0.4 m/s at baseline were considered. Selected participants had at least one follow-up visit. A total of 367 participants did not meet inclusion MMSE and walking speed criteria. Additionally, 77 participants were excluded because data were not available beyond the baseline visit. Of those participants, 20 died during the first year, and of the remaining 57 participants, the most common reason for unavailability of data was refusal to participate in the interview and examination.

Cognitive and Physical Decline Measures

Cognition was assessed using the Folstein MMSE.[15] Cognitive decline was defined as a decrease in MMSE to less than 24, a generally accepted cutoff for abnormal cognition[16] recorded in at least one of the three annual follow-up visits.

Walking speed was calculated as the time to walk 4 m at usual pace. In fewer than 10% of the participants, a distance of 3 m was used because of space limitations in the home. Physical decline was defined as a decrease in walking speed to less than 0.4 m/s in at least one of the three annual follow-up visits. A walking speed lower than 0.42 m/s has been demonstrated to be predictive of functional dependence and is considered to represent severe walking disability.[17,18]

Participants were classified into four main groups according to changes in cognitive and physical performance over the three annual follow-up visits: no cognitive or physical decline, physical decline only, cognitive decline only, and combined cognitive and physical decline.

Covariates

The four groups were compared on the basis of sociodemographic characteristics and health habits (age, race, education, marital status, and smoking status), cognitive, affective, and functional measures (MMSE score, Geriatric Depression Scale (GDS) score,[19] ADL[2] and IADL[1] impairment, and walking speed), diseases (discussed below), and biological risk measures (body mass index, ankle brachial index (ABI), total cholesterol, high-density lipoprotein cholesterol, serum creatinine, hemoglobin level, and spirometry).

Sociodemographic characteristics and health habits were self-reported. Educational level was dichotomized as 8th grade or less or more than 8th grade, and current marital status was reported as married or not married. The number of ADLs and IADLs in which participants reported requiring assistance defined ADL and IADL disability. ADLs were transferring, bathing, using the toilet, dressing, and feeding oneself.[2] IADLs were shopping, doing light housework, preparing meals, managing money, using the telephone, and self-administering medications.[1]

The methods of disease ascertainment in WHAS have been extensively described elsewhere.[20] Briefly, the status of 17 chronic conditions were assessed on the basis of self-report, medical records, examinations, roentgenograms, medications, laboratory testing, and questionnaires sent to primary physicians. The presence of each disease was ascertained through application of data to standardized algorithms that were reviewed by trained clinicians. For these analyses, the total number of diseases and presence of eight diseases with strong relevance to cognitive or physical function were considered: coronary artery disease, peripheral arterial disease, congestive heart failure, stroke, diabetes mellitus, cancer, osteoarthritis, and pulmonary disease. Coronary artery disease, peripheral arterial disease, congestive heart failure, and stroke were combined into a single variable: cardiovascular disease. Only diseases classified as definite were included.

Biological risk measures were determined through physical assessments and laboratory work done at baseline. Body mass index was calculated as weight in kg divided by height in meters squared. Weight was measured on a calibrated digital scale placed on a firm surface with the participant standing wearing light house clothes and no shoes, and height was measured using a stadiometer. ABI was measured using a Doppler stethoscope (Parks model 841-A, Aloha, OR). Two blood pressures were assessed in the right brachial artery and in each of the posterior tibial arteries. The higher of the two pressures in each artery was used, and the ABI was calculated by dividing the lower of the right and left posterior tibial pressures by the brachial artery pressure. Total cholesterol, high-density lipoprotein cholesterol, serum creatinine concentrations (all in mg/dL), and hemoglobin level (in g/dL) were measured using standard methods. Spirometry measures include forced expiratory volume in the first second (FEV_1) and forced vital capacity (FVC), measured according to a standard protocol.[21,22] Results are reported for FEV_1 less than 80% of predicted value and calculated FEV_1/FVC ratio of less than 70% of predicted value for each participant.[22]

Statistical Methods

The relationship between cognitive and physical decline was tested for independence using a Pearson chi-square test. Physical and cognitive decline groups were compared using chi-square and analysis of variance tests for categorical and continuous variables, respectively. Three separate logistic regression analyses were performed comparing the physical, cognitive, and combined decline groups with the group with neither decline. Models were adjusted for age, race, education, and all covariates found using univariate analysis to be statistically significant ($P < .05$) to provide odds ratios (ORs) and 95% confidence intervals (CIs). SPSS version 10.1 software was used (SPSS Corp., Chicago, IL).

RESULTS

Women participating in WHAS I had a mean age of 78.0 ± 8.1 at baseline; 71% were white, and 43% had an 8th grade education or less. The mean MMSE score was 26.0 ± 3.0, and the mean number of IADLs and ADLs impaired were 1.3 ± 1.4 and 1.2 ± 1.4, respectively.

Of the 558 women who met the baseline MMSE and walking speed inclusion criteria, 318 (57%) developed no decline, 112 (21%) developed physical decline only, 68 (12%) developed cognitive decline only, and 60 (11%) experienced combined cognitive and physical decline. From the assessment of statistical independence of cognitive and physical decline, physical decliners were 1.98 times ($P < .001$) as likely to have cognitive decline as nonphysical decliners, and cognitive decliners were 1.80 times ($P < .001$) as likely to develop physical decline.

The timing and magnitude of declines below the cutoff levels for MMSE and walking speed were assessed. In individuals with cognitive decline (n = 128), a drop below the cutoff MMSE of 24 occurred in 8% at Year 1, 27% at Year 2, and 65% at Year 3. In those with physical decline (n = 172), a drop below the cutoff walking speed of 0.4 m/s occurred in 6% at Year 1, 18% at Year 2, and 76% at Year 3.

Comparing the 128 subjects who developed cognitive decline with the 430 not developing cognitive decline, more participants with cognitive decline had a baseline MMSE score of 24 or 25 (35% vs 10%), but participants developing cognitive decline showed significantly greater losses from baseline in MMSE points than did those without cognitive decline (Year 1: -2.5 vs -0.1; Year 2: -3.5 vs -0.1; Year 3: -4.6 vs -0.4, all $P < .001$).

Comparing the 172 subjects developing physical decline with the 386 not developing physical decline, more participants with physical decline had a baseline walking speed below 0.6 m/s (48% vs 17%). Participants developing physical decline had significantly greater losses in walking speed (in m/s) from baseline than those without physical decline (Year 1: -0.20 vs -0.03; Year 2: -0.33 vs -0.04; Year 3: -0.53 vs -0.05; all $P < .001$).

Characteristics of the groups of women with no decline, cognitive decline alone, physical decline alone, or combined decline were compared. Results are reported in Table 1. Women with physical, cognitive, or combined decline were more likely to be older and less likely to be married than those with no decline. Subjects with cognitive decline alone had a lower educational level, less pulmonary disease, and lower baseline MMSE scores than those with no decline or physical decline only. Subjects with cognitive decline alone had fewer diseases and a higher baseline walking speed than those with physical decline only. Additionally, women with cognitive decline only had less impairment in ADLs than those with no decline, physical decline only, or combined decline. Subjects with physical decline only and combined decline were more likely to have higher GDS scores than those with no decline.

In these unadjusted comparisons, women with combined decline were less likely to be white than those with no decline or physical decline only. Additionally, those with combined decline had a lower educational level, hemoglobin level, and mean baseline MMSE score than women with no decline or physical decline only. Participants with combined decline had lower baseline walking speed and more baseline impairments in IADLs than those with no decline or cognitive decline only. Participants with combined decline were also more likely to smoke than those with cognitive decline only.

Table 2 shows ORs and 95% CIs from three separate logistic regression models in which the reference group of participants with neither cognitive nor physical decline were compared with the groups with physical decline only, cognitive decline only, and combined decline. The models were adjusted for age, race, education, and covariates found to be statistically significant at the univariate analyses (smoking, education, number of diseases, pulmonary disease, hemoglobin, baseline walking speed, baseline MMSE, baseline IADL, baseline ADL). Age was significantly associated with all patterns of decline. Former smoking status was significantly associated with physical decline only, and white race was inversely associated with physical decline. Lower baseline walking speed and greater IADL impairment was associated with physical decline only and combined decline. Lower baseline MMSE was associated with cognitive decline and combined decline.

Current smoking (OR = 5.66, 95% CI = 1.49–21.54) and hemoglobin level (OR = 0.68, 95% CI = 0.47–0.98) were the strongest predictors of combined decline that were not also statistically significantly associated with isolated declines in physical or cognitive performance.

DISCUSSION

In this population of lower-functioning women, the occurrence of combined declines in cognition and physical performance was greater than expected based on the proportion of the cohort declining in either domain considered separately. This finding suggests that declines in the two domains may share underlying etiologies. This study also identified significant demographic, functional, health, and biological differences in women with combined cognitive and physical decline.

Several studies link cognitive and physical function, but all are limited in important ways in addressing combined cognitive and physical decline. Selection bias, prevalence/incidence bias, and bias due to selective survival limit cross-sectional studies.[3] Longitudinal studies have confirmed that baseline cognitive status and cognitive decline predict subsequent physical function status,[4–7] but they do not provide substantial insight into factors contributing to combined

Table 1. Baseline Characteristics of Participants Who Developed Cognitive, Physical, or Combined Decline During the Follow-Up (Mean, or %)

Characteristic	No Decline (n = 218)	Physical Decline (n = 112)	Cognitive Decline (n = 68)	Combined Decline (n = 60)
Age, mean ± SD	74.4 ± 6.4†‡§	78.5 ± 7.6*	78.9 ± 7.7*	79.4 ± 8.7*
White, %	82.7§	78.6§	72.1	61.7†*
Smoking, %				
Never	52.5§	48.2	50.0§	40.0*‡
Former	35.8‡	40.2	44.1*§	38.3‡
Current	11.6	11.6	5.9§	21.7‡
Education, %				
≤8th grade	28.6‡§	25.9‡§	55.9*†	56.7*†
>8th grade	71.4‡§	74.1‡§	44.1*†	43.3*†
Marital status, %				
Married	34.3†‡§	16.1*	14.7*	8.3*
Not married	65.7†‡§	83.9*	85.3*	91.7*
Geriatric Depression Scale score, mean ± SD	6.7 ± 4.9†§	7.8 ± 5.9*	7.2 ± 4.7	8.0 ± 5.1*
Number of diseases, mean ± SD	2.9 ± 1.5	3.2 ± 1.8‡	2.5 ± 1.7†	2.8 ± 1.8
Cardiovascular disease, %	43.4	53.6	42.6	46.7
Cancer, %	14.5	14.3	8.8	8.3
Diabetes mellitus, %	12.9	17.9	10.3	15.0
Osteoarthritis, %	80.8	80.4	70.6	75.0
Pulmonary disease, %	32.1‡	33.9‡	14.7*†	28.3
Body mass index, kg/m^2, mean ± SD	28.8 ± 6.2	29.2 ± 7.4	28.3 ± 5.5	29.5 ± 8.4
Ankle brachial index, mean ± SD	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2	1.0 ± 0.2
Albumin, mg/dL, mean ± SD	4.1 ± 0.3	4.0 ± 0.3	4.0 ± 0.2	4.0 ± 0.5
Total cholesterol, mg/dL, mean ± SD	227.8 ± 40.2	224.8 ± 43.7	225.5 ± 37.6	222.8 ± 36.5
High-density lipoprotein cholesterol, mg/dL, mean ± SD	54.7 ± 15.5	52.2 ± 14.7	51.9 ± 15.5	49.5 ± 14.6
Creatinine, mg/dL, mean ± SD	1.0 ± 0.3	1.1 ± 0.4	1.1 ± 0.2	1.3 ± 1.5
Hemoglobin, g/dL, mean ± SD	13.3 ± 1.2§	13.0 ± 1.5§	12.8 ± 1.1	12.3 ± 1.4*†
FEV_1 <80% predicted, %	44.1	48.6	40.4	45.0
FEV_1/forced vital capacity <70% predicted, %	43.2	40.0	23.4	42.5
Baseline Mini-Mental State Examination score, mean ± SD	28.1 ± 1.6‡§	27.8 ± 1.7‡§	26.5 ± 1.9*†	26.6 ± 1.7*†
Baseline walking speed, m/s, mean ± SD	0.83 ± 0.25†§	0.68 ± 0.25*‡	0.75 ± 0.16†§	0.62 ± 0.15*‡
Baseline instrumental activities of daily living, mean ± SD‖	0.5 ± 0.8†§	1.1 ± 1.1*‡	0.6 ± 0.7†§	1.5 ± 1.1*†‡
Baseline activities of daily living, mean ± SD‖	1.0 ± 1.1‡	1.2 ± 1.2‡	0.8 ± 1.0*†§	1.1 ± 1.2‡

Physical decline was defined as walking speed falling to 0.4 m/s or less and cognitive decline as Mini-Mental State Examination (MMSE) score falling to less than 24 in one of the three annual follow-up visits.

$P < .05$ compared with the group with * no decline; † physical decline; ‡ cognitive decline; § combined decline.

‖ Higher values indicate greater impairment.

SD = standard deviation; FEV_1 = forced expiratory volume in 1 second.

changes in cognition and physical function. The use of self- or proxy-reported information on physical function, which may be less reliable as individuals decline cognitively, also limit them.[9] The current study of lower-functioning women extends the findings of a recent longitudinal study of high-functioning, disability-free older adults in which objective physical performance declines were mapped to declines in global cognition over a 7-year follow-up.[12]

Of the differences noted in this study in patterns of decline, current tobacco smoking and lower hemoglobin levels appear to be uniquely associated with combined declines even after adjustment for potential confounders. It is possible that these factors are simply indicators of persons who are globally less healthy, but the observations are also consistent with current knowledge about the individual associations between smoking, anemia, and cognitive and physical status. Smoking has been shown to be associated with accelerated cognitive decline in a large cohort of non-demented elderly subjects.[23] In addition, smoking and sarcopenia were found to be related in two recent studies.[24,25] Chronic anemia has been demonstrated to be associated with declines in cognitive functioning in cancer patients,[26] and there is growing interest in the potential effects of anemia on cognitive performance in older people. Hemoglobin levels and anemia also appear to be related to muscle strength, muscle density, physical performance, and disability independent of disease status or inflammation.[27,28] In addition to these potential separate effects on the nervous system and muscles, it may also be that smoking (via effects on atherosclerosis and oxygenation) and lower hemoglobin

Table 2. Logistic Regression Models Assessing the Association Between Baseline Characteristics and Cognitive Decline Only, Physical Decline Only, or Combined Decline

Characteristic	Physical Decline (n = 112)	Cognitive Decline (n = 68)	Combined Decline (n = 60)
	Odds Ratio (95% Confidence Interval)		
Age	1.10 (1.05–1.16)	1.09 (1.03–1.16)	1.07 (1.00–1.15)
White	0.40 (0.19–0.86)	1.00 (0.37–2.71)	0.55 (0.19–1.56)
Smoking			
Never	1	1	1
Former	1.97 (1.02–3.80)	1.03 (0.43–2.46)	1.38 (0.48–4.00)
Current	2.16 (0.76–6.13)	1.19 (0.31–4.54)	5.66 (1.49–21.54)
Education ($\leq 8^{th}$ grade)	0.55 (0.27–1.15)	1.38 (0.60–3.19)	0.97 (0.36–2.57)
Number of diseases	1.17 (0.97–1.41)	0.94 (0.72–1.23)	0.75 (0.53–1.05)
Pulmonary disease	0.95 (0.49–1.83)	0.49 (0.17–1.33)	1.96 (0.69–5.56)
Hemoglobin, g/dL	0.97 (0.77–1.23)	0.86 (0.60–1.21)	0.68 (0.47–0.98)
Baseline walking speed (per SD increase[†])	0.70 (0.48–1.00)	0.99 (0.64–1.54)	0.46 (0.22–0.97)
Baseline Mini-Mental State Examination score	1.02 (0.85–1.23)	0.56 (0.44–0.70)	0.70 (0.54–0.92)
Baseline instrumental activities of daily living	2.04 (1.46–2.86)	1.40 (0.86–2.29)	2.58 (1.58–4.20)
Baseline activities of daily living	0.86 (0.65–1.12)	0.79 (0.55–1.12)	0.80 (0.53–1.20)

Note: Reference group: No physical or cognitive decline (n = 318). Analysis was performed using separate logistic regression models adjusted for age, race, smoking, education, number of diseases, pulmonary disease, hemoglobin, baseline walking speed, baseline Mini-Mental State Examination score, baseline instrumental activities of daily living, and baseline activities of daily living.

[†] Baseline walking speed standard deviation (SD) = 0.24 m/s.

concentrations (via decreased oxygen delivery) affect specific central nervous system processes associated with cognition and motor performance (frontal-subcortical circuits).[29]

The main strengths of this study are its use of data collected specifically for the purpose of understanding diseases and conditions contributing to disability in high-risk older women. Characterizing combined cognitive and physical decline in this group is particularly pertinent because it may lead to better understanding of the process of decline in the population most at risk for functional dependence.[13] This study also uses a performance-based measure of physical function to characterize physical decline. This approach offers distinct advantages over the use of self- or proxy-reports of disability to characterize decline, including increased sensitivity to change and less-explicit influence of language, culture, education, and cognition.[9]

There are also several limitations of this study. The dichotomization of outcomes to create groups with and without decline and the modest sample sizes of each declining group likely limited power to detect true differences. Despite these limitations, it was possible to detect significant predictors for the outcome variables that could be more deeply explored in specifically designed studies. It is also possible that some of the findings (e.g., the association between smoking and lower hemoglobin levels and combined decline) could be due to chance, a potential pitfall of multiple comparisons. Nonetheless, the findings seem consistent with other reports focusing on cognitive and physical function separately. Another limitation of the present study is the use of the MMSE, because it is not a sensitive means of detecting subtle declines in cognitive function in community-dwelling, cognitively intact persons.[30] Similarly, the definition of physical decline as falling to below a specific cutoff may have limited the detection of more subtle declines in physical performance. Another concern is that a substantial proportion of subjects with cognitive decline, physical decline, or combined decline were already close to the cutoff levels defining decline at baseline. However the assessment of the magnitude of decline indicated that individuals declining cognitively or physically had indeed declined to a significantly greater degree than those not declining. Although the definitions of cognitive and physical performance decline were chosen to be most sensitive to changes in status with the small sample size, some individuals who declined to below the cutoff points at any follow-up visit may have improved in performance at subsequent follow-up visits. However, as indicated by the assessment of the timing of decline, the majority of declines below cutoff levels occurred at the third follow-up visit. Additionally, by the design of these analyses, no direction of causality can be determined to explain combined cognitive and physical decline, and future studies are needed to examine this question. Finally, due to the nature of the sample, these findings are limited to older functionally impaired women.

In summary, these findings add support to an emerging body of evidence for the link between age-related cognitive and physical decline. The results also show that there are specific pathological associations with combined decline. Evidence that certain factors (tobacco smoking and lower hemoglobin levels) may be specific discriminators of individuals at risk for combined cognitive and physical decline may provide a basis for developing approaches to prevent or reduce disability in and institutionalization of these individuals.

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