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Functional Decline in Cognitive Impairment – The Relationship between Physical and Cognitive Function

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Key Words
Sarcopenia · Dementia · Cognition · Chinese elderly · Physical function · Muscle

Abstract
Background: Physical function decline is associated with dementia, which might either be mediated by the coexisting sarcopenia or directly related to the impaired cognition. Our objectives are to examine the relationship between cognitive function and performance-based physical function and to test the hypothesis that cognitive function is related to poor physical function independent of muscle mass. ***Methods:*** We measured muscle strength, performance-based physical function and muscle mass using dual-energy X-ray absorptiometry and cognitive function using the cognitive part of the Community Screening Instrument of Dementia (CSI-D) in 4,000 community-dwelling Chinese elderly aged >65 years. A CSI-D cognitive score of >28.40 was considered as cognitively impaired. The effect of cognitive impairment on muscle strength and physical function was analyzed by multivariate analysis with adjustment for age, appendicular skeletal mass (ASM), the Physical Activity Scale for the Elderly (PASE) and other comorbidities. ***Results:*** In both genders, the cognitively impaired (CSI-D cognitive score >28.40) group had a weaker grip strength (–5.10 kg, $p < 0.001$ in men; –1.08 kg in women, $p < 0.001$) and performed worse in the two physical function tests (in men, 6-meter walk speed, –0.13 m/s, $p < 0.001$, chair stand test, 1.42 s, $p < 0.001$; in women, 6-meter walk speed, –0.08 m/s, $p < 0.001$, chair stand test, 1.48 s, $p < 0.001$). After adjustment for age, ASM, PASE and other comorbidities, significant differences in grip strength (–2.60 kg, $p < 0.001$ in men; –0.49 kg, $p = 0.011$ in women) and the two physical function tests persisted between the cognitively impaired and nonimpaired group (in men, 6-meter walk speed, –0.072 m/s, $p < 0.001$, chair stand test, 0.80 s, $p = 0.045$; in women, 6-meter walk speed, –0.049 m/s, $p < 0.001$, chair stand test, 0.98 s, $p < 0.001$). ***Conclusions:*** Poor physical function and muscle strength coexisted with cognitive impairment. This relationship was independent of muscle mass. It is likely therefore that the functional decline in dementia might be related directly to factors resulting in cognitive impairment independently of the coexisting sarcopenia.

Introduction

The relationship between cognitive impairment and functional disability has been investigated in various cross-sectional surveys, which demonstrated that cogni-

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tive decline was associated with functional disability [1–5]. Lower cognitive function was also associated with poor physical performance in gait speed, standing balance and chair stand tests [6, 7]. Even those with only mild cognitive impairment exhibited more gait and balance impairment than cognitively normal subjects [8], and impaired equilibrium and limb coordination were clinically demonstrable in a series of patients suffering from mild cognitive impairment and mild Alzheimer's disease [9].

In a 3-year follow-up study, dementia was found to be the major cause of functional dependence in the elderly [10], and in a cohort of older Mexican Americans, Raji et al. [11] demonstrated that poor cognition was associated with a greater risk of incident disability in a 7-year period. More recently, Atkinson et al. [12] observed that global and executive functions predicted faster gait speed decline over 3 years.

However, the causal relationship between dementia and the development of functional decline could be bidirectional. Black and Rush [13] demonstrated that cognitive and functional decline appeared to influence the development of each other. Camicioli et al. [14] had revealed that motor slowing was evident prior to the development of cognitive impairment in a group of healthy older persons. Wang et al. [15] demonstrated that lower levels of performance-based physical function were associated with an increased risk of dementia and therefore suggested that poor physical function might in fact precede the onset of dementia. Similarly, weak handgrip strength at baseline was found to be associated with more rapid cognitive decline over a 7-year period [16]. Most recently in a prospective study, Inzitari et al. [17] observed that gait speed predicted decline in attention and psychomotor speed in older adults after 5 years.

On the other hand, Nourhashemi et al. [18] found that low cognitive function was associated with muscle loss in a group of over 7,000 community-dwelling older women. The occurrence of sarcopenia with aging is multifactorial, which may involve decreased exercise and activity, malnutrition, hormonal changes, oxidative stress and possibly an inflammatory process [19], of which some are also common in cognitive decline. It is possible that dementia and sarcopenia share certain mechanisms of pathogenesis. However, sarcopenia by itself has been demonstrated to be related to functional disability [20–23]. It seemed therefore that the apparent association between cognitive impairment and functional decline could have been mediated by coexisting sarcopenia in cognitively impaired persons. In fact Raji et al. [11] have demonstrated that older American Mexicans with poor cognition had a steeper decline in muscle strength over 7 years than those with good cognition. They postulated that sarcopenia might be the missing link between poor cognition and subsequent disability.

In the present study, we measured muscle mass by dual-energy X-ray absorptiometry (DEXA) and physical function by performance-based tests. The DEXA scan offered an objective measurement of muscle mass while the performance-based tests were less subjected to reporting bias than the self-reported disability questionnaires. To our knowledge, apart from the American Mexican cohort [11, 16], very few studies have examined the intertwining relationship between muscle, cognition and disability at the same time. We hypothesized that cognition affects physical function directly and not just indirectly through the coexisting muscle degeneration. Our objective was to examine the relationship between cognition and physical function by performance-based tests and to investigate whether this relationship persists after controlling for the coexisting muscle degeneration effect in cognitively impaired older persons.

Methods

Four thousand community-dwelling men and women aged 65 years or over were invited to attend a health check carried out in the School of Public Health of the Chinese University of Hong Kong between August 2001 and December 2003 by placing recruitment notices in community centers for the elderly and housing estates. This project was primarily examining the bone mineral density of older Chinese adults. Talks were also given at these centers explaining the purpose, procedures and investigations to be carried out. Written informed consents were obtained. Only ethnical Chinese subjects were recruited. We excluded those who (1) were unable to walk without assistance of another person, (2) had had a bilateral hip replacement because that would have affected the bone mineral density measurement, (3) were not competent to give informed consent, and (4) had medical conditions, in the judgment of the study physicians, which made it unlikely that they would survive the duration of the study (3 years). The sample was stratified so that approximately 33% were in each of the age groups: 65–69, 70–74 and 75 years and over. The study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong.

A questionnaire containing information regarding demographics, smoking habit, physical activity level (Physical Activity Scale for the Elderly, PASE, score) [24] and medical history including heart disease, diabetes mellitus, stroke and arthritis was administered by trained interviewers. Heart disease includes coronary heart disease, heart failure and history of myocardial infarction. The presence or absence of disease was based on the subjects' report of their physician's diagnoses, supplemented by the identification of drugs brought to the interviewers.

Table 1. Comparison of baseline characteristics between men and women

	Men (n = 2,000)	Women (n = 2,000)	p value
Age, years	72.3 ± 5.0	72.5 ± 5.3	0.26
Body weight, kg	62.4 ± 9.3	54.5 ± 8.4	<0.001
Body mass index	23.4 ± 3.1	23.9 ± 3.4	<0.001
Ex- or current smokers, %	63.8	9.5	<0.001
Years of education, %			<0.001
0 years	5.2	37.7	
1–6 years	55.2	45.2	
7–12 years	26.1	11.3	
>12 years	13.6	6.0	
PASE score	97.2 ± 50.2	85.3 ± 33.1	<0.001
CSI-D cognitive score ≥28.40, %	4.9	25.3	<0.001
MMSE score	26.9 ± 2.7	24.2 ± 3.9	<0.001
Whole-body muscle mass, kg	44.2 ± 5.4	33.83 ± 4.1	<0.001
ASM, kg	19.1 ± 2.6	13.81 ± 1.9	<0.001
Arthritis, %	24.3	21.8	0.067
Diabetes mellitus, %	14.7	14.3	0.753
Stroke, %	5.5	3.3	0.001
Heart disease, %	18.3	16.5	0.102

Values are expressed as means ± standard deviation or percentages. MMSE = Mini-Mental State Examination. Statistical comparison was made by unpaired Student t test for continuous variables and χ^2 test for categorical variables.

Table 2. Comparison between the cognitively impaired and nonimpaired groups

	Impaired group	Nonimpaired group	p value
Age, years			
Men	76.43 ± 0.59	72.18 ± 0.11	<0.001
Women	74.64 ± 0.26	71.87 ± 0.13	<0.001
Whole-body muscle mass, kg			
Men	42.14 ± 0.56	44.34 ± 0.12	<0.001
Women	33.69 ± 0.19	33.88 ± 0.12	0.350
ASM, kg			
Men	18.12 ± 0.27	19.23 ± 0.06	<0.001
Women	13.73 ± 0.08	13.84 ± 0.05	0.264
Grip strength, kg			
Men	26.36 ± 0.71	31.46 ± 0.14	<0.001
Women	19.44 ± 0.19	20.52 ± 0.11	<0.001
Six-meter walk speed, m/s			
Men	0.89 ± 0.024	1.02 ± 0.004	<0.001
Women	0.85 ± 0.009	0.93 ± 0.005	<0.001
Chair stand test, s			
Men	13.99 ± 0.45	12.57 ± 0.088	<0.001
Women	14.45 ± 0.27	13.07 ± 0.12	<0.001
PASE score			
Men	84.2 ± 5.60	97.9 ± 1.14	0.008
Women	79.4 ± 1.39	87.3 ± 0.86	<0.001

Values are expressed as means ± standard error. Statistical comparison was made by unpaired Student t test.

Cognitive function was assessed by trained interviewers using the cognitive score of the Chinese version of the Community Screening Instrument of Dementia (CSI-D), validated in different cultural and educational settings [25]. The cutoff point for probable dementia is 28.4 [25, 26]. The average grip strength was calculated using that of both hands (Jamar Hand dynamometer 5030 J1, Sammons Preston Inc., Bolingbrook, Ill., USA). Subjects were asked to stand up with folded arms from a chair 5 times, and the time required was recorded. The time to walk 6 m at normal pace was measured.

We measured muscle mass by DEXA using a Hologic QDR 2000 densitometer (Hologic, Waltham, Wash., USA). We measured both whole-body and appendicular muscle mass. In our subjects, appendicular skeletal mass (ASM) was calculated by the summation of muscle mass measured in the 4 limbs, with the operator adjusting the cut lines of the limbs according to specific anatomical landmarks as described by Heymsfield et al. [27]. All data used in the analysis were on participants who clearly fitted within the DEXA field of view. During the course of the study, the DEXA systems were regularly matched to quality assurance scans to ensure there was no drift.

Statistical Methods

Men and women were analyzed separately in all statistical tests. The cognitively impaired and nonimpaired subjects as defined by the CSI-D cognitive score were compared by Student's t test for the continuous variables and the χ^2 test for the categorical variables. The relationship between performance-based physical function and cognitive impairment was further examined by 3 separate multiple linear regression models. In each model, each of the three physical function results was taken as dependent variable, and cognitive impairment (CSI-D cognitive score >28.4), age, ASM, PASE score, arthritis, diabetes mellitus, stroke and any heart disease were entered as independent variables. To adjust for the effect of body build on muscle mass, the whole procedure was repeated with the covariate ASM replaced by ASM/body weight. All tests were 2-sided, and a p value of less than 0.05 was taken as statistically significant. The statistical analysis was conducted using SPSS version 13.0.

Results

We studied 2,000 men and 2,000 women aged 65 or older, with a mean age of 72.5 ± 5.2 years. All of them were independent in ambulation and community dwellers. The male subjects had a higher education level ($p < 0.001$), Mini Mental State Examination score ($p < 0.001$), PASE score ($p < 0.001$) and muscle mass ($p < 0.001$; ta-

Table 3. Multivariate analysis of performance-based physical function tests

Covariates	Mean ± SD/ %	Unit	Mean difference per unit change	
			Grip strength, kg	
			adjusted for ASM	adjusted for ASM/weight
Males				
Cognitive impairment	4.9	yes/no	–2.64 (–3.75, –1.53)*	–3.22 (–4.43, –2.01)*
Age, years	72.3 ± 5.0	5.0	–1.52 (–1.78, –1.27)*	–2.05 (–2.32, –1.79)*
PASE score	97.2 ± 50.2	50.2	0.46 (0.22, 0.7)*	0.53 (0.27, 0.8)*
Diabetes	14.7	yes/no	–1.15 (–1.83, –0.48)*	–0.32 (–1.06, 0.42)
Stroke	5.5	yes/no	–1.91 (–2.96, –0.87)*	–1.69 (–2.83, –0.55)*
Heart disease	18.3	yes/no	–0.36 (–0.98, 0.26)	0.17 (–0.51, 0.85)
Arthritis	24.3	yes/no	–0.84 (–1.4, –0.29)*	–0.22 (–0.83, 0.38)
ASM, kg	19.1 ± 2.6	2.6	2.53 (2.28, 2.77)*	–
ASM/weight	0.31 ± 0.02	0.02	–	0.61 (0.39, 0.83)*
Females				
Cognitive impairment	25.3	yes/no	–0.47 (–0.85, –0.09)*	–0.4 (–0.81, 0.01)
Age, years	72.5 ± 5.3	5.3	–0.81 (–0.98, –0.64)*	–1.15 (–1.33, –0.97)*
PASE score	85.3 ± 33.1	33.1	0.30 (0.13, 0.47)*	0.37 (0.19, 0.56)*
Diabetes	14.3	yes/no	–0.77 (–1.23, –0.31)*	–0.54 (–1.03, –0.04)*
Stroke	3.3	yes/no	–0.78 (–1.68, 0.13)	–1.07 (–2.04, –0.1)*
Heart disease	16.5	yes/no	–0.36 (–0.79, 0.08)	–0.01 (–0.49, 0.46)
Arthritis	21.8	yes/no	–0.70 (–1.1, –0.31)*	–0.27 (–0.69, 0.16)
ASM, kg	13.81 ± 1.9	1.9	1.59 (1.42, 1.75)*	–
ASM/weight	0.26 ± 0.02	0.02	–	0.41 (0.27, 0.55)*

95% confidence limits are given in parentheses. * $p < 0.05$.

ble 1). Therefore all subsequent analyses were done separately for men and women. In both genders, the cognitively impaired group had a weaker grip strength (–5.10 kg in men, $p < 0.001$; –1.08 kg in women, $p < 0.001$) and performed worse in the two physical function tests (in men, 6-meter walk speed, –0.13 m/s, $p < 0.001$, chair stand test, 1.42 s, $p < 0.001$; in women, 6-meter walk speed, –0.08 m/s, $p < 0.001$, chair stand test, 1.48 s, $p < 0.001$; table 2). The relationship between physical function and cognitive impairment was further examined by multiple linear regression with adjustment for other covariates. The results were tabulated for men and women in table 3. After adjustment for age, ASM, PASE score and 4 comorbid conditions (heart disease, arthritis, diabetes mellitus and past stroke) that could adversely affect the performance-based tests, cognitively impaired subjects of both genders performed consistently worse in all the 3 tests. Repeating the regression by replacing ASM with ASM/body weight only slightly altered the results. The adjusted and unadjusted differences in the physical function test in both genders were tabulated in table 4.

Discussion

We found that poorer physical function coexisted with cognitive impairment, which is compatible with previous observations [1–9]. After the adjustment for muscle mass and other possible confounding factors, the difference in physical function performance between the cognitively impaired and nonimpaired groups persisted though the difference had narrowed considerably, illustrating the residual confounding effect of the covariates entered into the regression model, namely muscle mass, age, comorbidities and physical activity level. These adjusted differences in physical function performance, though statistically significant, were relatively modest and may not be translated into meaningful clinical outcomes. Past studies have demonstrated that physical function disturbances might precede the onset of dementia [14–17]. Based on our results, we propose that impaired physical function such as walking and getting up from a chair in the cognitively impaired might contribute directly to later disabilities, independently of any muscle degeneration as-

Covariates	Mean difference per unit change			
	Walking speed, m/s		Chair stand test, s	
	adjusted for ASM	adjusted for ASM/weight	adjusted for ASM	adjusted for ASM/weight
Males				
Cognitive impairment	–0.07 (–0.11, –0.03)*	–0.08 (–0.12, –0.03)*	0.80 (0.01, 1.58)*	0.81 (0.03, 1.6)*
Age, years	–0.06 (–0.07, –0.05)*	–0.06 (–0.07, –0.05)*	0.63 (0.45, 0.8)*	0.62 (0.45, 0.79)*
PASE score	0.03 (0.02, 0.04)*	0.03 (0.02, 0.04)*	–0.36 (–0.53, –0.19)*	–0.35 (–0.52, –0.17)*
Diabetes	–0.02 (–0.04, 0.01)	–0.01 (–0.04, 0.02)	0.23 (–0.25, 0.71)	0.19 (–0.29, 0.66)
Stroke	–0.09 (–0.13, –0.05)*	–0.09 (–0.13, –0.05)*	1.03 (0.29, 1.78)*	1.00 (0.26, 1.75)*
Heart disease	–0.03 (–0.05, –0.003)*	–0.02 (–0.04, 0.002)	0.53 (0.09, 0.97)*	0.48 (0.04, 0.92)*
Arthritis	–0.02 (–0.04, –0.003)*	–0.02 (–0.04, 0.002)	0.41 (0.02, 0.81)*	0.38 (–0.01, 0.77)
ASM, kg	0.02 (0.01, 0.03)*	–	–0.03 (–0.2, 0.14)	–
ASM/weight	–	0.01 (0.002, 0.02)*	–	–0.13 (–0.27, 0.01)
Females				
Cognitive impairment	–0.05 (–0.07, –0.03)*	–0.05 (–0.07, –0.03)*	0.99 (0.47, 1.5)*	1.00 (0.49, 1.52)*
Age, years	–0.05 (–0.06, –0.04)*	–0.05 (–0.06, –0.04)*	0.68 (0.44, 0.91)*	0.63 (0.4, 0.86)*
PASE score	0.03 (0.02, 0.04)*	0.03 (0.02, 0.04)*	–0.38 (–0.61, –0.15)*	–0.35 (–0.58, –0.12)*
Diabetes	–0.02 (–0.04, 0.004)	–0.02 (–0.05, 0)	0.59 (–0.03, 1.21)	0.64 (0.01, 1.26)*
Stroke	–0.04 (–0.09, 0.01)	–0.04 (–0.09, 0.01)	0.92 (–0.31, 2.14)	0.87 (–0.35, 2.1)
Heart disease	–0.02 (–0.04, 0.01)	–0.01 (–0.04, 0.01)	0.22 (–0.37, 0.81)	0.23 (–0.37, 0.82)
Arthritis	–0.05 (–0.07, –0.03)*	–0.05 (–0.07, –0.03)*	1.36 (0.83, 1.89)*	1.39 (0.86, 1.92)*
ASM, kg	0.00 (–0.01, 0.01)	–	0.24 (0.02, 0.47)*	–
ASM/weight	–	0.01 (–0.0001, 0.01)	–	–0.07 (–0.24, 0.11)

sociated with dementia. However, it is also possible that the cognitively impaired had difficulty in understanding the instruction of the 3 tests and therefore their performance was adversely affected.

In the present study, over 25% of female subjects were classified as cognitively impaired by the CSI-D cognitive score, which was much higher than the 4.95% in the male counterpart. These results are comparable with two previous surveys conducted in elderly Hong Kong Chinese [28, 29]. The lower education in elderly Hong Kong Chinese women partly explained the discrepancy in prevalence between the genders. Hence, in this study, separate analysis for males and females was performed in order to avoid any confounding effect of the considerable difference in education level.

Although the CSI-D has been used as an instrument to screen for 'probable dementia', over 25% prevalence in women might suggest overclassification in the absence of a clinician-based diagnostic process. This might have resulted in a heterogeneous group of women subjects who might not have dementia [29]. As such, we have chosen

Table 4. Adjusted and unadjusted physical function test results of the cognitively impaired as compared to the nonimpaired

	Unadjusted difference (p value)	Adjusted difference[1] (p value)	Adjusted difference[2] (p value)
Grip strength, kg			
Men	–5.10 (<0.001)	–2.64 (<0.001)	–3.21 (<0.001)
Women	–1.08 (<0.001)	–0.49 (0.011)	–0.42 (0.044)
Six-meter walk speed, m/s			
Men	–0.13 (<0.001)	–0.072 (0.001)	–0.076 (<0.001)
Women	–0.08 (<0.001)	–0.049 (<0.001)	–0.050 (<0.001)
Chair stand test, s			
Men	1.42 (<0.001)	0.80 (0.045)	0.82 (0.041)
Women	1.48 (<0.001)	0.98 (<0.001)	1.00 (<0.001)

Statistical adjustment was made by multiple linear regression. Figures in parentheses are p values.

[1] Adjusted for age, ASM, PASE score, arthritis, diabetes mellitus, stroke and any heart disease.

[2] Adjusted for age, ASM/body weight, PASE score, arthritis, diabetes mellitus, stroke and any heart disease.

the term 'cognitive impairment' rather than 'probable dementia' to describe our subjects. The CSI-D has been developed and tested to be a culturally and educationally unbiased screening tool for dementia with 87% sensitivity and 83% specificity [30] but has not been used as a measure of the severity of cognitive impairment [25, 26]. Therefore, the validated cutoff point was employed in the present study to define cognitive impairment [26]. Nevertheless, the use of a screening tool instead of a clinical diagnosis was a major limitation in this survey.

As to whether reduced physical activity in the cognitively impaired could account for poorer physical function due to deconditioning, we have attempted to eliminate the confounding effect of daily physical activities by adjusting for the PASE score in the multivariate analysis. Our results suggested that impaired muscle strength and physical function were directly related to poor cognition independent of comorbidities, inactivity and muscle mass.

Good physical function preserves muscle mass and prevents cognitive deterioration, as has been revealed by several previous studies [31–33]. Being cross-sectional, our results were unable to establish the directionality of the interrelationship among cognition, muscle loss and function. Although we have hypothesized that cognition affects physical function directly and indirectly via muscle degeneration, the results could be interpreted otherwise. It is possible that the interrelationship is even more complex, such as a bidirectional cause-effect relationship or shared etiological pathogenesis in sarcopenia and dementia via sex hormone decline [34–36] or cytokine activation [37, 38].

Our sample is the largest reported in older Chinese adults. However, our study was limited by the subjects being recruited by walk-in voluntary participation via recruitment in community centers. As the subjects were more likely to be physically capable and health conscious than the general elderly population, this would affect the generalizability of the findings to the general elderly population.

Conclusion

Poor physical function and muscle strength coexisted with cognitive impairment, independently of muscle mass. It is likely, therefore, that the functional decline in dementia might be related directly to factors resulting in cognitive impairment independently of the coexisting sarcopenia.

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