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The Effect of Depression and Cognitive Impairment on 7-year Cardiorespiratory Fitness in Chinese Aged 65 and Older

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Abstract

Objective: To examine the influence of depression and cognitive impairment at baseline on the subsequent levels of cardiorespiratory fitness as measured with maximal oxygen uptake (VO_{2max}), the distance walked in the 6-minute walk test (6MWD) at 7 years and to compare VO_{2max}, 6MWD, and self-reported physical activity in relation to depression and cognitive impairment.

Methods: A total of 1,179 Chinese older adults aged 65 and above who participated in the MrOs (Hong Kong) and MsOs (Hong Kong) study during 2001-2003 were re-assessed after 7 years of follow-up. Baseline information on depression, cognitive function and a number of health-related variables were obtained through interview. The outcome variables were cardiorespiratory fitness as measured by VO_{2max}, 6MWD, and physical activity as measured with the Physical Activity Scale of the Elderly (PASE) at 7 years.

Results: Subjects with depression at baseline were associated with lower VO_{2max} during a follow-up period of approximately 7 years and this relationship remained significant after adjustment for physical activity, gait speed, and other potential confounders for men only ($P<0.05$) but not for women. Cognitive impairment at baseline was also associated with shorter 6MWD during the follow-up ($P<0.05$); however, the association was eliminated in sex-stratified analyses. There was no relationship between baseline depression and cognitive impairment with the subsequent levels of physical activity.

Conclusions: Among older men, baseline depression was associated with lower VO_{2max} but not 6MWD or PASE score over 7 years. Our findings reinforce that VO_{2max} is better than 6MWD or self-reported physical activity as a measurement of cardiorespiratory fitness in relation to depression in elderly population.

Keywords Depression; Cognitive impairment; Cardiorespiratory fitness; VO_{2max}; 6-minute walk distance; Elderly

Introduction

A decline in cardiorespiratory fitness is an important physiological change that occurs during the ageing process because of its influence on functional independence [1] and quality of life [2]. Although age per se is thought to contribute to this decline, increase in fat mass and decline in lean body mass or muscle mass [3,4] and possibly changes in muscle aerobic capacity with age [3], as well as the age-related decrease in physical activity [4] also contribute to the age-related decline process.

Accumulating evidence suggested that higher cardiorespiratory fitness (as quantified by exercise test duration or walking distance) is associated with lower risk of incident depressive symptoms in middle-aged and older adults [5-7]. It also seems that depressive symptoms are related to the decline in various measures of cardiorespiratory fitness, including exercise test duration, oxygen consumption (VO_2), and oxygen uptake efficiency slope in older women [8] via reduced physical activity [9]. A bidirectional prospective association between depressive symptoms and gait speed (a surrogate measure of cardiorespiratory fitness) has also been observed at older ages [10], but another prospective study has failed to demonstrate such an association [11]. To date, however, there are relatively few studies that are available to examine the role of depression on the subsequent levels of maximal oxygen uptake (VO_{2max}), the widely accepted "gold standard" measure of cardiorespiratory fitness [12], particularly in older adults.

In parallel, cognitive impairment may occur as a consequence of poor cardiorespiratory fitness or as a risk factor for the decline in cardiorespiratory fitness. A number of cross-sectional studies have linked higher cardiorespiratory fitness with better cognition, especially measures of attention or executive function [13,14] and visuospatial function [15]. However, the cross-sectional design of these studies precludes determination of the direction of the association. Longitudinally, a previous study of older adults found a positive association between baseline peak VO_2 and follow-up cognitive function. However, the absence of most of the cognitive measures at baseline limited conclusions regarding cognitive change over time [16]. Another study among older adults has also demonstrated that lower baseline VO_{2max} was associated with accelerated memory

decline over time [17]. However, there are few studies that have prospectively explored the role of cognitive impairment on the subsequent levels of VO_{2max} in older adults.

Using data from the MrOs (Hong Kong) and MsOs (Hong Kong) cohort of elderly Chinese aged 65 years and above, we examined the influence of depression and cognitive impairment at baseline on the subsequent levels of cardiorespiratory fitness as measured with VO_{2max} and the distance walked in the 6-minute walk test (6MWD), a surrogate measure of fitness level and disability [18], over 7 years. We also compared VO_{2max}, 6MWD and self-reported physical activity in relation to depression and cognitive impairment.

Methods

Study population

Subjects for this study came from the MrOs (Hong Kong) and MsOs (Hong Kong) studies, the first large-scale prospective studies on bone health that has followed a cohort of 4,000 Chinese men and women aged 65 years and above in Hong Kong since 2001. The method of recruitment consisted of notices placed in housing estates and community centers all over Hong Kong. Stratified sampling was adopted in the study in order to achieve approximately 33% of subjects in each of the three age groups: 65-69, 70-74 and ≥75 years. Details of the study population have been reported elsewhere [19]. Written informed consent was obtained from each subject and the study was approved by the Clinical Research Ethics Committees of the Chinese University of Hong Kong.

Procedures

Information regarding demographics, education level, medical history (the presence or absence of disease based on subjects' report of diagnosis by their doctor), smoking habit, physical activity level, depression, and cognitive impairment was obtained as part of a questionnaire administered by an interviewer. Physical activity level was assessed using the Physical Activity Scale of the Elderly (PASE). This is a 12-item scale measuring the average number of hours per day spent in leisure, household and occupational physical activities over the previous 7-day period. Activity weights for each item were determined based on the amount of energy expended, and each item score was calculated by multiplying the activity weight by the activity daily frequency. A summary score of all the items reflects the daily physical activity level [20]. Depression was diagnosed by a trained interviewer during face-to-face interviews, using a validated 15-item Chinese version of the Geriatric Depression Scale (GDS-15), with depression being defined as a cut-off of 8 or above [21,22]. The GDS-15 was found to be highly reliable (reliability coefficient of 0.90) and valid screening device (sensitivity of 96.3% and 87.5% specific) for assessing geriatric depression in Hong Kong Chinese [22]. Cognitive function was assessed using the cognitive score of the Community Screening Instrument for Dementia (CSI-D), the validity of which had been examined elsewhere. The cutoff point for probable dementia is ≤ 28.4 [23,24].

Body weight was measured with subjects wearing a light gown using the Physician Balance Beam Scale (Healthometer, Illinois, USA). Height was measured by the Holtain Harpenden standiometer (Holtain Ltd, Crosswell, UK). Body mass index was documented.

Between 2005 and 2007, the original cohort was invited to re-attend for repeat questionnaire interviews and physical examinations. 2,861 of the original 4,000 subjects returned (71.5%). Between 2008 and 2010, the cohort was further invited for repeat interview and examination as well as to take part in the VO_{2max} assessment and the 6-minute walk test (6MWT) which were not included in the previous examinations. The inclusion criteria for the VO_{2max} assessment were based on: (1) ambulant without assistance from another person; (2) self-report of no leg pain, no pacemaker implanted, or were not taking blood thinning medications; and (3) no evidence of abnormal resting or exercise electrocardiogram. Of those who returned, 1,180 participated in both the VO_{2max} assessment and the 6MWT, 65 participated in the VO_{2max} assessment only, 600 performed the 6MWT only, and the remaining 31 subjects did not participate in any tests. Nonparticipation in each fitness test was due to either an inability to perform the task or refusal to perform it.

VO_{2max} was assessed with a symptom-limited maximal exercise test on an electrically braked bicycle ergometer (Ergoline 900, Ergoline GmbH, Lindenstrasse, Bitz, Germany). Subjects were instructed to abstain from any strenuous exercise on the day before testing. Each subject was connected to a calibrated respiratory gas analyzer (Fitmate, COSMED Srl, Italy) for gas analysis using a face mask. The respiratory gas analyzer was calibrated before each test. Blood pressure was monitored throughout the exercise test. The test started with a 3-min warm up at a workload of 20 W and continued with 10 W increments every minute, until the subject was exhausted or was not able to maintain the required pedaling frequency of 50 rpm. Subjects were verbally encouraged to reach their maximum. The test was terminated when the subject reached VO_{2max} [25,26] or showed any symptoms that indicated termination of exercise based on the guidelines of the American College of Sports Medicine [27].

The 6MWT was performed on a level hallway (flat hard) surface with a length of 18 meter according to a standardized protocol [28]. Subjects were instructed to sit and rest on a chair, located near the starting position, for at least 10 minutes before the test starts. Subjects were then instructed to walk at their own pace but to cover as much ground as possible in 6 minutes and were allowed to set the pace of ambulation with rest stops as needed. Standardized encouragement, "You are doing well" or "Keep up the good work" were offered at 2 and 4 minute. The total distance ambulated in meters during the 6MWD and the number of rest stops during the test was also recorded. As we did not carry out the 6MWT at baseline but only measured the gait speed (using the average time in seconds to complete a walk along a straight line 6 meter long), the latter was used as a surrogate of cardiorespiratory fitness at baseline and was controlled for in statistical analysis.

For the present analysis, data evaluated at baseline and at 7 years was used. Moreover, only subjects with complete data of VO_{2max} and 6MWD were included. Therefore, the analytical sample consists of 1,179 subjects (Figure 1).
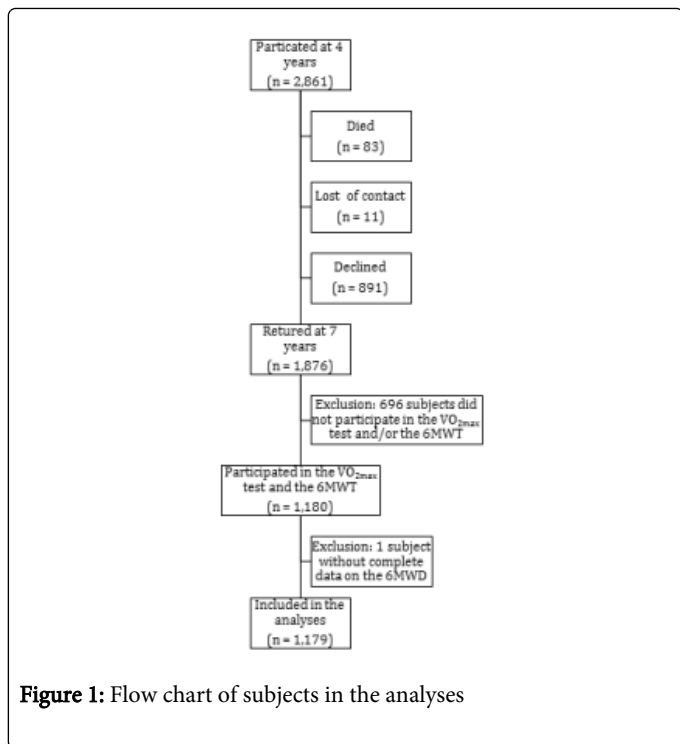
Figure 1: Flow chart of subjects in the analyses

Statistical analysis

Student t-tests were used to compare the marginal distribution of continuous variables while chi-square tests were used to compare the proportions between those who did and did not participate in the fitness assessments; between men and women, and between those with and without depression or cognitive impairment at baseline. As baseline analysis on this cohort has shown a preponderance of cognitive function in women, the present analyses were stratified by sex to investigate the potential gender differences in the outcome measurements. Because the GDS had been validated in subjects without cognitive impairment, subjects with cognitive impairment (CSI-D score ≤ 28.4) were excluded from the GDS assessment. Furthermore, as depression may be associated with cognitive impairment, in the analysis of cognitive impairment and outcome variables, GDS was adjusted for as a confounding factor. In the analysis for depression, CSI-D score was adjusted for as a confounding factor. The relationships of depression and cognitive impairment at baseline with VO_{2max}, 6MWD and PASE score at 7 year were examined by ANCOVA, with adjustment for age, education level, BMI, smoking, medical history, and CSI-D / GDS score. To adjust for the possible effect of physical activity on VO_{2max} and 6MWD, the models for VO_{2max} and 6MWD were further adjusted for physical activity. To control for the pre-existing cardiorespiratory capacity, adjustments were also made for baseline gait speed. All analyses were carried out using the Window-based SPSS Statistical Package (version 17.0; SPSS Inc., Chicago, IL), and P values less than 0.05 were considered statistically significant.

Results

Baseline characteristics of subjects who did or did not participate in the VO_{2max} assessment / the 6MWT at 7 years are shown in Table 1. Subjects who participated in the VO_{2max} assessment were younger, more often male, with higher education level, lower BMI, more likely to be ever smokers and had a lower prevalence of comorbidities. In contrast, with the exception of age, gender and hypertension, there were no differences in characteristics between subjects who participated in the 6MWT and those who did not.

	VO_{2max} test			6-minute walk test		
Characteristic	No (n = 600)	Yes (n = 1,245)	P[1]	No (n = 65)	Yes (n = 1,780)	P[1]
Age, years	71.5 ± 4.3	70.4 ± 4.2	<0.001	71.8 ± 4.6	70.8 ± 4.2	0.047
Gender, % women	64.7	39.2	<0.001	29.2	48.1	0.003
Education, % primary school or above	41.7	57.6	<0.001	58.5	52.2	0.320
BMI, kg/m²	24.5 ± 3.3	23.4 ± 2.9	<0.001	23.7 ± 3.5	23.8 ± 3.1	0.892
Ever smokers, %	27.2	36.2	<0.001	40.0	33.0	0.242
Medical histories						
Diabetes, %	15.5	11.6	0.021	10.8	13.0	0.602
Hypertension, %	45.7	37.1	<0.001	27.7	40.3	0.041
Stroke, %	4.0	3.5	0.619	1.5	3.8	0.350
Heart attack/coronary/myocardial infarction %	13.7	6.4	<0.001	9.2	8.8	0.896
Angina, %	12.5	6.5	<0.001	6.2	8.5	0.497
Congestive heart disease, %	5.8	2.5	<0.001	1.5	3.7	0.368

BMI, body mass index; VO_{2max}, Maximal oxygen uptake

Data expressed as mean ± SD for continuous variables or percentage for dichotomous variables.

[1]P values were obtained from two-sample t tests for continuous and x^2 tests for dichotomous variables.

Table 1: Baseline characteristics of subjects who participated in the VO_{2max} test / 6-minute walk test at 7-year compared with those who did not

Baseline characteristics of subjects by sex are shown in Table 2. Men had a statistically significant higher level of education and proportion of ever smokers compared to their female counterparts. Men also had a lower prevalence of cognitive impairment.

	Men	Women	
Characteristic	(n = 710)	(n = 469)	P1
Age, years	70.5 ± 4.1	70.2 ± 4.2	0.300
Education, % primary school or above	66.9	43.3	<0.001
BMI, kg/m^2	23.4 ± 2.8	23.5 ± 3.1	0.668
Ever smokers, %	55.5	6.6	<0.001
Medical histories			
Diabetes, %	12.1	11.1	0.592
Hypertension, %	37.2	38.4	0.678
Stroke, %	4.4	2.6	0.105
Heart attack/coronary/myocardial infarction, %	6.6	5.8	0.550
Angina, %	7.6	4.9	0.066
Congestive heart disease, %	2.4	2.8	0.687
Depression, GDS ≥ 8, %	5.1	5.1	0.971
Cognitive impairment, CSI-D ≤ 28.4, %	2.3	14.9	<0.001

BMI, body mass index; CSI-D, Community Screening Instrument for Dementia; GDS, Geriatric Depression Scale.

Data expressed as mean ± SD for continuous variables or percentage for dichotomous variables.

[1]P values were obtained from two-sample t tests for continuous and x^2 tests for dichotomous variables.

Table 2: Baseline characteristics between men and women (n = 1,179)

Baseline characteristics of subjects by GDS score and CSI-D score are shown in Table 3. Subjects with depression (GDS ≥ 8) were younger. Those who were cognitive impaired (CSI-D ≤ 28.4) were older, more often female, less educated and less likely to be ever smokers than those with normal cognition.

	Depression*			Cognitive function		
	Normal (GDS < 8)	Depressed (GDS ≥ 8)		Normal (CSI-D > 28.4)	Cognitively impaired (CSI-D ≤ 28.4)	
Characteristic	(n = 1,039)	(n = 54)	P[1]	(n = 1,093)	(n = 86)	P[1]
Age, years	70.3 ± 4.1	69.1 ± 3.7	0.042	70.2 ± 4.1	71.9 ± 4.7	0.002
Gender, % female	36.6	35.2	0.836	36.5	81.4	<0.001
Education, % primary school or above	61.0	50.0	0.106	60.5	19.8	<0.001
BMI, kg/m^2	23.4 ± 2.9	22.9 ± 2.8	0.190	23.4 ± 2.9	23.5 ± 2.9	0.644
Ever smokers, %	37.2	44.4	0.287	37.6	16.3	<0.001
Medical histories						
Diabetes, %	11.6	11.1	0.905	11.6	12.8	0.745

Hypertension, %	37.3	33.3	0.552	37.1	44.2	0.194	
Stroke, %	3.8	1.9	0.451	3.8	2.3	0.497	
Heart attack/coronary/myocardial infarction, %	6.6	1.9	0.161	6.4	4.7	0.519	
Angina, %	6.6	7.4	0.826	6.7	4.7	0.464	
Congestive heart disease, %	2.5	1.9	0.764	2.5	3.5	0.564	

BMI, body mass index; CSI-D, Community Screening Instrument for Dementia; GDS, Geriatric Depression Scale

Data expressed as mean ± SD for continuous variables or percentage for dichotomous variables.

*Subjects with cognitive impairment were excluded.

[1]P values were obtained from two-sample t tests for continuous and x^2 tests for dichotomous variables.

Table 3: Baseline characteristics according to GDS score and CSI-D score (n = 1,179)

The mean value of VO_{2max}, 6MWD and PASE score at 7 year by GDS score and CSI-D score are shown in Table 4. In both gender, subjects with depression at baseline had significantly lower VO_{2max} over the 7-year study period than non-depressed subjects, even after adjusting for age, education level, physical activity, and other confounding factors (P<0.05). Further adjustment for gait speed did not alter the results (data not shown). However, when the sample was stratified by sex, the observed association remained in men only. No significant differences in 6MWD and PASE score were found between depressed and non-depression subjects.

Characteristic	Depression*					Cognitive function				
	Normal (GDS < 8)	Depressed (GDS ≥ 8)	P[1]	P[2]	P[3]	Normal (CSI-D > 28.4)	Cognitively Impaired (CSI-D ≤ 28.4)	P[1]	P[4]	P[5]
Total	(n = 1,039)	(n = 54)				(n = 1,093)	(n = 86)			
VO_{2max}, ml/kg/min	21.1 ± 4.5	20.4 ± 4.7	0.240	0.030	0.024	21.1 ± 4.5	19.0 ± 4.0	<0.001	0.061	0.083
6MWD, m	440.4 ± 80.2	434.7 ± 91.8	0.615	0.309	0.270	440.1 ± 80.7	393.4 ± 70.8	<0.001	0.029	0.040
PASE score	106.4 ± 42.9	104.3 ± 37.6	0.723	0.393	--	106.3 ± 42.6	107.0 ± 44.1	0.892	0.560	--
Men	(n = 659)	(n = 35)				(n = 694)	(n = 16)			
VO_{2max}, ml/kg/min	22.1 ± 4.5	21.3 ± 5.0	0.278	0.062	0.043	22.1 ± 4.5	21.6 ± 5.1	0.657	0.961	0.965
6MWD, m	457.5 ± 81.7	449.2 ± 95.2	0.559	0.354	0.246	457.1 ± 82.4	431.7 ± 74.8	0.223	0.743	0.735
PASE score	108.6 ± 46.8	106.8 ± 43.6	0.825	0.513		108.5 ± 46.7	122.2 ± 43.9	0.245	0.261	--
Women	(n = 380)	(n = 19)				(n = 399)	(n = 70)			
VO_{2max}, ml/kg/min	19.4 ± 3.9	18.8 ± 3.8	0.487	0.228	0.260	19.4 ± 3.9	18.4 ± 3.5	0.042	0.637	0.687
6MWD, m	410.7 ± 68.0	408.1 ± 80.9	0.872	0.708	0.725	410.5 ± 68.5	384.6 ± 67.4	0.004	0.449	0.464
PASE score	102.6 ± 34.8	99.6 ± 23.0	0.715	0.779	--	102.4 ± 34.3	103.5 ± 43.7	0.849	0.597	--

6MWT, six-minute walk test; CSI-D, Community Screening Instrument for Dementia; GDS, Geriatric Depression Scale; PASE, Physical Activity Scale for Elderly; VO_{2max}, Maximal oxygen uptake.

Data expressed as mean ± SD.

*Subjects with cognitive impairment (CSI-D ≤ 28.4) were excluded.

[1]P values were obtained from two-sample t tests.

[2]P values were obtained from ANCOVA testes adjusted for age, education levels (No completed primary school vs. completed primary school), BMI, smoking (Non-smokers vs. ex- and current smokers), medical history of diabetes mellitus, hypertension, stroke, heart attack/coronary/myocardial infarction, angina, congested heart failure, and CSI-D score.

[3]P values were obtained from ANCOVA testes adjusted for age, education levels (No completed primary school vs. completed primary school), BMI, smoking (Non-smokers vs. ex- and current smokers), medical history of diabetes mellitus, hypertension, stroke, heart attack/coronary/myocardial infarction, angina, congested heart failure, CSI-D score, and physical activity categories (PASE score < 95 vs. ≥ 95).

[4]P values were obtained from ANCOVA testes adjusted for age, education levels (No completed primary school vs. completed primary school), BMI, smoking (Non-smokers vs. ex- and current smokers), medical history of diabetes mellitus, hypertension, stroke, heart attack/coronary/myocardial infarction, angina, congested heart failure, and GDS score.

[5]P values were obtained from ANCOVA testes adjusted for age, education levels (No completed primary school vs. completed primary school), BMI, smoking (Non-smokers vs. ex- and current smokers), medical history of diabetes mellitus, hypertension, stroke, heart attack/coronary/myocardial infarction, angina, congested heart failure, GDS score, and physical activity categories (PASE score < 95 vs. ≥ 95).

Table 4: VO_{2max}, 6MWD and PASE score at 7 year by baseline GDS score and CSI-D score (n = 1,179)

Similarly, subjects with cognitive impairment at baseline had significantly lower VO_{2max} than those who were cognitively normal. Adjustment for age, education level, physical activity, and other confounding factors weaken the association. Cognitive impairment at baseline was also associated with a significant shorter 6MWD over the 7-year study period after adjustment for confounding factors (P<0.05). However, when the sample was stratified by sex, the observed associations were eliminated. No significant differences in PASE score were found between the cognitively impaired and the cognitively intact subjects.

Discussion

Few studies have examined depression and cognitive impairment in relation to measures of cardiorespiratory fitness. This study showed that older adults with depression at baseline were associated with lower VO_{2max} during a follow-up period of approximately 7 years. After adjustment for physical activity, gait speed, and other potential confounders, the relationship remained significant for men only, but not for women. Cognitive impairment at baseline was also associated with shorter 6MWD during the follow-up; however, the association was eliminated in sex-stratified analyses. There was no relationship between baseline depression and cognitive impairment with the subsequent levels of physical activity as measured with PASE.

Several prospective cohort studies about the effect of cardiorespiratory fitness on depression have found a protective association [5-7], whereas others have suggested the possibility of reverse causality in which depression predicts cardiorespiratory fitness. Hollenberg *et al.* [8] found that depressive symptoms were associated with lower levels of exercise duration, peak VO_2 and oxygen uptake efficiency slope in a group of older women and that depressed women did report less leisure time physical activity, thus suggesting that physical inactivity may partially mediate the relationship. A recent review of longitudinal studies also showed that baseline depression might lead to a sedentary lifestyle or to a decreased level of physical exercise [9]. Results of another study of community-dwelling people aged 60 years and older also found that depressive symptoms were associated with slower gait speed (a surrogate measure of cardiorespiratory fitness) [10]. However, the association between depression and VO_{2max} in our study could not be explained by PASE score, suggesting that factors other than physical activity may contribute to the lower VO_{2max}. We also found that the association remained significant in men but not in women. The lack of statistically significant association in women may reflect a lack of power owing to the relatively small number of cases of depression. Furthermore, older women consistently have lower cardiorespiratory fitness than their male counterparts [29]. This discrepancy may be partly explained by the physiological variations between genders, including higher adiposity and less muscle mass in women than men [30]. As such, this might be one of the explanations for the gender differences seen in the association between depression and VO_{2max} in the present study. Our findings also showed that baseline depression was not associated with

6MWD over 7 years, suggesting that 6MWD may not be an adequate measure of cardiorespiratory fitness in relation to depression.

The mechanisms mediating the attenuating effect of depression on VO_{2max} are not completely understood but neurohormonal system may be involved. Several studies have observed increased cortisol levels among depressed subjects [31,32], where chronic exposure to elevated levels of cortisol is known to magnify its catabolic effects [33], stimulate degradation and inhibit synthesis of muscle proteins, and leading to loss of muscle mass [34] and thus lower VO_{2max}. In support to this notion, one study among middle-aged and older men also found that cortisol levels were inversely associated with muscle strength of the knee extensor [35]. Future research is necessary to reveal whether there is a relationship between cortisol and VO_{2max}.

Another objective of this study was to determine whether cognitive impairment was associated with lower cardiorespiratory fitness, as people with cognitive decline consistently exhibit reduced gait speed [36] and variability [37] compared to their healthy counterparts. Studies examining the effect of cognitive impairment on the levels of cardiorespiratory fitness have been relatively few compared with depression, although one previous study in a population of older people with chronic heart failure found significant positive association between cognitive function as measured with the Mini-Mental State Examination (MMSE) score and 6MWD [38]. However, this study was cross-sectional in design and included only patient population. Our study therefore extends the results of this study by longitudinally examining a sample of community-dwelling older adults in Hong Kong. We found that cognitive impairment was independently associated with shorter 6MWD but not with lower VO_{2max}. However, when the sample was stratified by sex, the association between cognitive impairment and 6MWD was eliminated. The attenuation of the association suggests that gender remains an important confounding factor of the observed relationship. In the present study, 14.9% of women were classified as cognitively impaired, which was much higher than the 2.3% in their men counterparts. As previously demonstrated [39], these results are comparable with two previous surveys conducted in elderly Hong Kong Chinese [40,41]. The discrepancy in prevalence between the genders may be partly explained by the lower education in elderly Hong Kong Chinese women.

The presence of cognitive impairment at baseline was not associated with VO_{2max} at 7 year. It is possible that gait and balance were not measured in the VO_{2max} tests which have been associated with cognitive processing; however, these parameters would probably affect the 6MWT performance. In addition, subjects participated in the 6MWT have to control their pace and the termination of the test which would be affected by the cognitive status; by contrast, constant verbal encouragement and reminders were provided during the VO_{2max} test, and thus the test can be deemed as a passive measure of cardiorespiratory fitness without much immediate effect of cognitive function.

In contrast to previous studies in elderly population [42,43], we did not observe any association of baseline depression or cognitive impairment with the subsequent levels of physical activity during follow-up. It is possible that associations might be apparent with only a wide variation in physical activity levels in the study population; in that our subjects could have a fairly low level of physical activity. Alternatively, subjects with chronic diseases were mostly excluded in the VO_{2max} assessment and thus our study population may be biased toward the healthier sector of the population, which may contribute to the non-significant results. Our findings also suggested that physical activity estimated from the self-reported physical activity questionnaire may not be a good surrogate of cardiorespiratory fitness in our study population. Although we observed significant age- and BMI-adjusted correlations of PASE score with VO_{2max} ($r = 0.2$, $P<0.01$) and 6MWD ($r = 0.2$, $P<0.01$), the magnitude of the relationships were modest (data not shown).

There are some limitations in this study. The first issue concerns the nature of our data. Because baseline data of VO_{2max} and 6MWD were not available, the reported associations may be confounded by pre-existing cardiorespiratory capacity. Nevertheless, we have attempted to validate the associations by adjusting baseline physical activity and gait speed (a surrogate measure of cardiorespiratory fitness) where results did not alter. The instruments used for depression and cognitive impairment are screening instruments only and the findings may not represent the situation in subjects with clinically diagnosed disease. The measurement of depression and cognitive function were based on single questionnaire interview at baseline that may not have been representative of chronic exposure over the long term. The number of cases of depression was small, particularly among women; therefore, the relationship between depression and fitness variables may not have achieved statistical significance. Furthermore, our cohort is more educated and more physically active than the general elderly population in Hong Kong; therefore, findings should not be generalized to those who are institutionalized or frailer, or with lower educational level. Also, there was a possibility of selection bias as the subjects participated in the VO_{2max} assessment were relatively healthier. The strengths of the study lies in the large sample, the use of screening instruments validated in Hong Kong Chinese, the direct measurement of cardiorespiratory fitness, and the comprehensive range of confounding factors covered.

In conclusion, this study demonstrated that among older men, baseline depression was associated with lower VO_{2max} but not 6MWD or PASE score over 7 years. Our findings reinforce that the objective measures of VO_{2max} is better than 6MWD or self-reported physical activity as a measurement of cardiorespiratory fitness in relation to depression in elderly population. Further work is needed to determine the role of depression in preventing the age-related cardiorespiratory fitness decline, and thereby reduce the risk of disability and improve quality of life in the Chinese elderly.

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