Beneficial Effects of Weekly Walking Activity on Vascular Hypertensive Mediated Organ Damage in Community-dwelling Elderly Chinese: Northern Shanghai Study

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Abstract

Background: The value of exercise is well-established for health promotion. Walking as the most common campaign in older people, is recommended to improve their cardiovascular health. However, the direct association between weekly walking activity and asymptomatic hypertensive mediated organ damage (HMOD) remains unclear.

Methods: 2830 community-dwelling elderly subjects (over 65 years) in northern Shanghai were recruited from June 2014 to June 2018. Weekly walking activity was evaluated by standard questionnaire based on the International Physical Activity Questionnaires-short form (including walking duration per time and walking days per week). Within the framework of comprehensive cardiovascular examinations, HMOD, including left ventricular mass index (LVMI), peak transmitral pulsed Doppler velocity/early diastolic tissue Doppler velocity (E/Ea), carotid intima-media thickness (CIMT), arterial plaque, creatinine clearance rate (CCR), urinary albumin-creatinine ratio (UACR), carotid-femoral pulse wave velocity (cf-PWV) and ankle-brachial index (ABI), were all evaluated.

Results: 1862 (65.8%) participants were enrolled in weekly walking activity, with 56.8 ± 36.8 min/day and a median of 6.71 days/week walking. Young elderly, fewer smokers, lower CIMT, lower cf-PWV, fewer abnormal ABI, lower prevalence of hypertension and coronary heart disease were observed in walking activity group. Similarly, pearson's correlation analysis revealed that weekly walking activity was significantly correlated with elderly (age ≥ 70 years) and smoker. After adjusting for cardiovascular risk factors, weekly walking activity was only significantly associated with peripheral artery diseases in logistic regression analysis. Finally, only walking duration more than 30 min per time was related to arterial plaque in subgroup analysis of weekly walking activity (OR: 1.048, 95% CI: 1.002-1.095, $P = 0.038$).

Conclusions: In the community-dwelling elderly Chinese, weekly walking activity seemed to be a way to encourage a healthy lifestyle for HMOD prevention and management, especially for vascular HMOD, irrespective of walking duration per time and walking days per week.

Clinical Trial Registration: NCT02368938 (clinicaltrials.gov)

Introduction

Hypertension is the leading cause of cardiovascular disease and premature death worldwide [1]. Owing to the ageing of the population, the prevalence of hypertension is increasing globally (31.3%, 1.39 billion in 2010), especially in low/middle-income countries (31.5%, 1.04 billion) [2]. Despite awareness and treatment of hypertension improved, control rates of hypertension remain extremely low, resulting in the increase of mortality and economic burden of the society [2, 3]. Therefore, effective therapies to manage hypertension and hypertensive mediated organ damage (HMOD) are needed at a population level, especially in the elderly. Apart from treatment with anti-hypertensive medicine, exercise also plays an

important role in the prevention and control of high blood pressure, such as walking, morning exercise, square dancing, Yoga, *etc* [4].

Exercise (including low, medium and high intensity exercise) has multi-system anti-aging effects and prevents cardiovascular diseases (CVD) [5-7]. Notably, elderly with hypertension presents a challenge to achieve medium/high intensity exercise [8]. Walking as a low intensity exercise is regarded as the most feasible and accessible exercise in the elderly [9, 10]. Numerous studies indicated the positive effects of walking activity on improving cardiovascular (CV) risk factors, for instance, diabetes, hypertension, stroke, *etc* [9, 11, 12]. However, to our knowledge, no study has examined the direct association of weekly walking activity with asymptomatic HMOD among hypertensive elderly Chinese. Considering asymptomatic HMOD as critical prodromes of CV events and mortality, we investigated whether weekly walking activity was directly associated and HMOD (cardiac HMOD, renal HMOD and vascular HMOD) within the framework of CV risk assessment in a community-dwelling elderly.

Methods

Study design

The Northern Shanghai Study is a prospective, on-going and multistage study, and aims to investigate the CV risk assessment system in the elderly Chinese, as previously described [13, 14]. We recruited residents from urban communities in the north of Shanghai (aged 65 years or more), who are also available for long-term follow-up. Subjects with severe cardiac disease (NYHA IV) or end-stage renal disease (CKD > 4), or malignant tumor with life expectancy less than 5 years, or stroke history within 3 months were excluded. Finally, 2830 participants (91.5%) were enrolled from June 2014 to May 2018. The study was approved by the Ethics Committee of Shanghai Tenth People's Hospital, and written informed consent was obtained from all participants.

Definition of weekly walking activity

Weekly walking activity was evaluated by standard questionnaire based on the International Physical Activity Questionnaires-short form (including how many days spent on walking at least 10 minutes at a time and walking duration time) [15, 16]. In subgroup analysis, walking duration per day was classified into two categories: over 30 min/day and over 1 h/day, and walking days per week were categorized into < 4 and ≥ 4 days/week.

Social, clinical and biological parameters

We obtained social and clinical information from standard questionnaire, including gender, age, weight, smoking habits, history of hypertension / diabetes mellitus / coronary heart diseases, and usage of medications, *etc* [13].

As to biological markers, venous blood samples and urine samples were obtained from subjects after an overnight fast. Biological markers were measured in the Department of Laboratory Medicine of Shanghai

Tenth People's Hospital, including fasting plasma glucose, plasma low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, plasma creatinine, urinary microalbumin and creatinine, *etc.* We respectively calculated creatinine clearance rate (CCR) and urinary albumin-creatinine ratio (UACR) based on the modified MDRD formula for Chinese and urinary microalbumin divided by urinary creatinine [14].

Measurement of blood pressure, ankle-brachial index and carotid-femoral pulse wave velocity

Specialized physicians measured the blood pressure (BP) of each subject in the morning by the electronic device three times after at least 10 minutes of rest in the sitting position. The average of the three BP readings was used in the subsequent statistical analysis.

Bilateral brachial and ankle blood pressures were measured and ankle-brachial index (ABI, calculated as ankle systolic BP divided by brachial systolic BP) was automatically calculated via the VP1000 system (Omron, Japan). Lower ABI was used for analysis in the present study.

Carotid-femoral pulse wave velocity (Cf-PWV) was measured using SphygmoCor system (AtCor Medical, Australia) to assess the arterial stiffness. Briefly, after a 10-minute rest, peripheral BP was recorded twice with an interval of 3 minutes, and measurements of the superficial distance directly from the carotid to the femoral artery were performed. Subsequently, pressure waveforms in the right carotid and right femoral arteries were recorded, and transit time for each artery was automatically calculated via ECG data. Finally, cf-PWV was calculated by travelling distance divided by travelling time. An operator index greater than 80% indicated a high-quality waveform.

Ultrasonography

All ultrasonographic measurements were performed by a single experienced sonographer. Arterial plaque and common carotid artery intima-media thickness (CIMT) was assayed by the MyLab 30 Gold CV system (ESAOTE SpA, Genoa, Italy). The presence or absence of plaques in the left and right carotid arteries was recorded. CIMT was measured on the left common carotid artery (always on plaque-free arterial segments), 2 cm from the bifurcation, as previously described [14]. The average value of three CIMT measurements was used for further analysis.

Furthermore, M-mode and 2-dimensional echocardiography were performed using the same device, according to the guidelines of the American Society of Echocardiography (ASE). From the parasternal view, we measured left ventricular end-diastolic diameter (LVEDd), interventricular septal (IVSd) and posterior wall thickness at end-diastole (PWTd), and then calculated left ventricular mass index (LVMI). Simultaneously, peak transmitral pulsed Doppler velocity / early diastolic tissue Doppler velocity (E/Ea) was calculated for the evaluation of LV diastolic function. Additionally, left atrial volume index (LAVI) was calculated using model formula, as previously described [13].

Definition of asymptomatic hypertensive mediated organ damage

Asymptomatic HMOD included cardiac, renal and vascular HMOD. Left ventricular hypertrophy was defined as LVMI ≥ 115 g/m² (male) or LVMI ≥ 95 g/m² (female). LV diastolic dysfunction was defined as E/Ea ≥ 15 , or $15 > E/Ea > 8$ with any of the follows (LAVI > 40 ml/m² or LVMI > 149 g/m² (male) or LVMI ≥ 122 g/m² (female)). Chronic kidney diseases (CCR < 60 ml/min/1.73m²) and microalbuminuria (UACR > 30) represented renal HMOD, while vascular HMOD included the presence of arterial plaque, increased CIMT (CIMT > 900 μ m), arterial stiffness (cf-PWV ≥ 12 m/s) and peripheral artery disease (ABI < 0.9).

Statistical analysis

Data were presented as means $\pm$ standard deviation or the percentage by Student's *t*-test or Chi-squared test, respectively. Pearson's correlation analysis was applied to investigate the correlation of cardiovascular risk factors with walking activity. Logistic regressions were conducted to investigate the association of weekly walking activity with HMOD, together with cardiovascular risk factors. In subgroup analysis, pearson's correlation analysis and logistic regressions were performed to investigate walking days per week and walking duration per day in association with vascular HMOD. Statistical analysis was performed using SAS software, version 9.3 (SAS Institute, Cary, NC, USA). *P* < 0.05 was considered statistically significant.

Results

Characteristics of study participants

There were 1862 (65.8%) participants enrolled in weekly walking activity, with 56.8 ± 36.8 min/day and a median of 6.71 days/week walking. Detailed characteristics of participants by walking activity are presented in Table 1, including cardiovascular risk factors, HMOD, and concomitant diseases. The 2830 participants included 1258 (44.5%) male, 722 (25.5%) current smokers, 1530 (54.1%) participants with hypertension, 566 (20.0%) participants with diabetes mellitus, and 937 (33.1%) participants with coronary heart disease. Further, participants with walking activity, compared with non-walking activity, were younger (71.23 ± 6.04 vs 72.12 ± 6.60 years, *P* < 0.001), and had fewer current smokers (24.2% vs 27.9%, *P* < 0.032). Interestingly, there was no significant difference between participants with and without walking activity in cardiac and renal HMOD (*P* > 0.05). As to vascular HMOD, participants with walking activity had significant lower cf-PWV (9.39 ± 2.23 vs 9.68 ± 2.50 m/s, *P* = 0.004), lower CIMT (631.1 ± 156.8 vs 650.8 ± 162.8 μ m, *P* = 0.002), lower percentage of participants with arterial stiffness (12.4% vs 16.1%, *P* = 0.008), increased CIMT (5.3% vs 7.4%, *P* = 0.021), and peripheral artery disease (12.1% vs 16.3%, *P* = 0.003). In addition, participants with walking activity also had a lower percentage of concomitant diseases, including hypertension and coronary heart disease (52.3% vs 57.8%, *P* = 0.005; 31.5% vs 36.6%, *P* = 0.006, respectively).

Correlation of cardiovascular risk factor with weekly walking activity

Spearman's correlation analysis was performed to investigate the correlation of cardiovascular risk factors with weekly walking activity. As shown in Table 2, weekly walking activity is correlated with

Elderly (age ≥ 70 years) (correlation coefficient: -0.043, $P = 0.024$) and smoker (correlation coefficient: -0.040, $P = 0.032$).

Association of weekly walking activity with asymptomatic HMOD

To investigate the association of weekly walking activity with asymptomatic HMOD, logistic regressions was conducted, together with conventional cardiovascular risk factors. Similarly, weekly walking activity was only associated with peripheral artery disease (OR = 0.777, 95% CI 0.613-0.984, $P = 0.037$), but not cardiac and renal HMOD (Table 3, Figure 1).

Association of walking duration and frequency of walking activity with vascular HMOD

To further examine the association of walking duration and walking days per week with vascular HMOD, subgroup analysis was conducted. First, pearson's correlation analysis was performed to investigate the association of walking days per week with vascular HMOD in the different subgroups of walking duration per day. Interestingly, in the subgroup of walking duration ≥ 30 min/day or ≥ 1 h/day, there was no significant difference of vascular HMOD between walking activity < 4 days/week and ≥ 4 days/week (Table 4). Moreover, logistic regressions were conducted to investigate the association of walking duration per day (≥ 30 min/day or ≥ 1 h/day) with vascular HMOD. Only walking duration more than 30 min/day was related to arterial plaque (OR: 1.048, 95% CI: 1.002-1.095, $P < 0.038$) (Figure 2).

Discussion

The present study had two major findings. First, weekly walking activity was significantly associated with a lower risk of vascular HMOD, but not cardiac or renal HMOD. Second, beneficial effects of walking activity on vascular HMOD seem not to be related with walking duration per day or frequency of weekly walking activity in the study of community-dwelling elderly.

Increased exercise is a recommended lifestyle modification for hypertension management. The American College of Sports Medicine recommends that most adults participate in moderate intensity cardiorespiratory exercise training for 30 min/d on 5 days/week, high intensity exercise training for 20 min/d on 3 days/week, or a combination of moderate and high intensity exercise to consume up to 500-1000 MET·min/week of energy [17]. Fan *et al.* indicated that, in a Chinese hypertensive population, not only moderate and high intensity exercise, but also low intensity exercise reduces CV mortality in a 7.1-year follow-up study [7]. Notably, the exercise intensity among elderly tend to decrease along with age, and exercise may increase the risk of mortality. Therefore, walking, as a low intensity exercise with a lower risk of injury than running or sport participation, is easily accessible [18]. Population-wide walking campaigns has been recommended for health promotion across the lifespan. However, whether weekly walking activity could affect asymptomatic cardiac / renal / vascular HMOD in hypertensive elderly population remains unclear. Our study identified that walking activity played a protective role against vascular HMOD, but not cardiac HMOD and renal HMOD. The main reason might be that vascular

function and structure was influenced more than cardiac / renal function and structure during walking activity.

Walking not only increases lower extremity muscle strength, improve balance performance and psychological conditions [10], but also exerts beneficial effects on reduction of CV risk, blood pressure, cardiac capacity, and quality of life in hypertensive patients with concomitant diseases [9, 19, 20]. In the present study, walking activity was significantly correlated with aging and smoking, but not overweight and high blood pressure, which might partly due to different intensity exercise and inclusive criteria. In the future, more randomized clinical trials were consequently warranted to evaluate the correlation of walking activity and CV risk factors.

Subsequently, subgroup analysis was conducted to evaluate association of walking duration and frequency of weekly walking activity with vascular HMOD. Importantly, almost no significant differences were observed in the subgroup analysis regarding the effects of walking duration and frequency of weekly walking activity. These findings indicated that the superior effects of weekly walking activity on vascular HMOD might not be related with walking duration per day and frequency of weekly walking activity. To the best of our knowledge, this is the first study to investigate the relationship of self-reported weekly walking activity and asymptomatic HMOD in the elderly population, based on walking duration and frequency of walking activity. From the viewpoint of organ-protection-driven exercise management, weekly walking activity may be a way to help Chinese elderly for asymptomatic hypertensive HMOD prevention and management, especially for those who suffered from the vascular abnormalities.

Limitations

Our results should be interpreted within the limitations. First, weekly walking activity was only evaluated by questionnaires in the cross-sectional study, but without precise measurement. With ongoing follow-up studies, target heart rate or exercise intensity will provide more accurate data in the future. Second, we could not adjust for the influence of medicine, especially anti-hypertensive medication.

Conclusions

In the community-dwelling elderly Chinese, weekly walking activity seems to play a protective role in HMOD, especially vascular HMOD, irrespective of walking duration per time and walking days per week.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Shanghai Tenth People's Hospital, and written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

Competing interests

None.

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Authors' contributions

Y.Z. and Y.X. designed research; Y.L., S.Y., C.C., J.T., and H.J. performed research; Y.L., Y.Z. and Y.X. analyzed the data; Y.L., Y.Z. and Y.X. wrote the paper. All authors reviewed the manuscript.

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Tables

Table 1. Characteristics of participants by walking activity.

	Overall (n=2830)	Walking activity (n=1862)	Non-Walking activity (n=959)	P
Cardiovascular risk factors				
Age (years)	71.53±6.25	71.23±6.04	72.12±6.60	0.001
Male gender, n (%)	1258 (44.5)	836 (44.9)	417 (43.5)	0.488
Smoker, n (%)	722 (25.5)	451 (24.2)	268 (27.9)	0.032
Body mass index (kg/m ²)	24.02±3.64	23.97±3.54	24.10±3.84	0.385
Systolic blood pressure (mmHg)	135.1±17.4	134.7±17.4	135.9±17.3	0.087
Hypertensive mediated organ damage				
Left ventricular mass index (g/m ²)	90.4±28.9	90.4±28.2	90.4±30.3	0.971
Left ventricular hypertrophy, n (%)	754 (26.9)	491 (26.6)	263 (27.6)	0.556
E/Ea	9.67±3.91	9.59±3.83	9.82±4.05	0.150
Diastolic dysfunction, n (%)	369 (13.5)	240 (13.2)	129 (14.0)	0.585
Creatinine clearance rate (ml/min/1.73m ²)	93.2±24.3	93.7±24.7	92.3±23.5	0.145
Chronic kidney diseases, n (%)	170 (6.1)	101 (5.5)	69 (7.4)	0.054
Urinary albumin-creatinine ratio (mg/g)	65.3±153.5	64.5±172.5	67.0±108.0	0.642
Microalbuminuria, n (%)	1593 (57.9)	1035 (57.0)	558 (59.9)	0.144
Carotid-femoral pulse wave velocity (m/s)	9.49±2.33	9.39±2.23	9.68±2.50	0.004
Arterial stiffness, n (%)	370 (13.6)	223 (12.4)	147 (16.1)	0.008
Carotid intima-medium thickness (µm)	638.1±159.1	631.1±156.8	650.8±162.8	0.002
Increased carotid intima-medium thickness, n (%)	168 (6.0)	97 (5.3)	71 (7.4)	0.021
Arterial plaque, n (%)	1780 (63.6)	1166 (63.1)	614 (64.5)	0.477
Ankle-brachial index	1.02±0.13	1.03±0.12	1.00±0.14	<0.001
Peripheral artery disease, n (%)	358 (13.5)	212 (12.1)	146 (16.3)	0.003
Concomitant diseases				
Hypertension, n (%)	1530 (54.1)	973 (52.3)	554 (57.8)	0.005

Diabetes mellitus, n (%)	566 (20.0)	381 (20.5)	184 (19.2)	0.423
Coronary heart disease, n (%)	937 (33.1)	586 (31.5)	351 (36.6)	0.006

Data are means $\pm$ standard deviation or numbers with percentages in parenthesis. Student's t-test and Chi-squared test were conducted to compare the differences between men and women for quantitative and qualitative variables, respectively. Creatinine clearance rate was calculated with modified MDRD formula for Chinese. Abbreviations: E/Ea, peak transmitral pulsed Doppler velocity/early diastolic tissue Doppler velocity.

Table 2. Correlation of cardiovascular risk factors with walking activity.

Cardiovascular risk factors	r	P
Gender (male)	0.013	0.488
Elderly (age $\geq$ 70 years)	-0.043	0.024
Smoker	-0.040	0.032
Overweight (BMI $\geq$ 24 kg/m ²)	0.034	0.072
High blood pressure (SBP $\geq$ 140 mmHg)	-0.030	0.108

Pearson's correlation analysis was conducted to investigate the correlation of cardiovascular risk factors with walking activity. Abbreviations: BMI, body mass index; SBP, systolic blood pressure.

Table 3. Association of walking activity with hypertensive mediated organ damage analyzed by logistic analysis.

Hypertensive mediated organ damage		OR (95% CI)	P
Cardiac HMOD	Left ventricular hypertrophy	1.003 (0.832-1.208)	0.978
	Diastolic dysfunction	1.022 (0.804-1.299)	0.858
Renal HMOD	Chronic kidney diseases	0.861 (0.618-1.200)	0.376
	Microalbuminuria	0.932 (0.790-1.099)	0.402
Vascular HMOD	Arterial stiffness	0.804 (0.632-1.023)	0.075
	Increased intima-medium thickness	0.751 (0.543-1.041)	0.085
	Arterial plaque	1.020 (0.862-1.208)	0.814
	Peripheral artery disease	0.777 (0.613-0.984)	0.037

Logistic regressions were conducted to investigate the association of walking activity with hypertensive mediated organ damage, together with cardiovascular risk factors. Abbreviations: HMOD, hypertensive mediated organ damage.

Table 4. Correlation of walking days per week with vascular hypertensive mediated organ damage.

Prevalence of HMOD (%)	Walking duration ≥ 30 min/day		P	Walking duration ≥ 1 h/day		P
	< 4 days/week	≥ 4 days/week		< 4 days/week	≥ 4 days/week	
Arterial stiffness	11.39	12.75	0.507	13.84	11.22	0.092
Increased intima-medium thickness	5.85	5.14	0.606	4.58	5.93	0.192
Arterial plaque	59.57	63.83	0.149	61.46	64.66	0.154
Peripheral artery disease	12.58	11.90	0.738	13.36	10.71	0.087

Pearson's correlation analysis was conducted to investigate the association of walking days per week with vascular hypertensive mediated organ damage in different subgroups of walking duration per day. Abbreviations: HMOD, hypertensive mediated organ damage.

Figures

Figure 1

Association of weekly walking activity with hypertensive mediated organ damage. Odds ratios of walking activity were presented after adjustments for confounders using logistic regressions. Abbreviations: CIMT, carotid intima-medium thickness; HMOD, hypertensive mediated organ damage.

Figure 2

Association of walking duration per time with vascular hypertensive mediated organ damage. Odds ratios of walking duration per time (≥ 30 min/day or ≥ 1 h/day) were presented after adjustments for confounders using logistic regressions. Abbreviations: CIMT, carotid intima-medium thickness.