

1 **Walking, but not other physical activity at a higher intensity, is associated with**
2 **improved kidney function: a cross-sectional health survey of general adult**
3 **population**

4 **Running head:** ambulation and renal function

5

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Abstract

Background: Chronic kidney disease is common and brings significant health burden. This study was to investigate the relationship between physical activity and kidney function.

Methods: This was a cross-sectional study set in the Nanjing Community Cardiovascular Risk Survey, using random cluster sampling. Questionnaires were completed, wherever possible, through face-to-face interviews. Age, sex, BMI, weekly physical activity and kidney function were collected. Physical activity was measured by the metabolic equivalent of task × minutes per week, and grouped into “walking”, “moderate” and “vigorous” according to intensity. Kidney function was measured by the estimated glomerular filtration rate (eGFR, mL/min/1.73 m²). Regression modelling was used to investigate the proposed relationship with adjustment for other confounding factors.

Results: 5,824 participants included, with an average age of 52 years. 44% were males. The eGFR in average was 76, with 19%≥90, 67% between 60-89, and 14%<60. In average the total physical activity during a week was 3,644. Moderate activity contributed 64% of the total activity, followed by walking (23%) and vigorous activity (13%). Overall, the total activity was weakly associated with eGFR (p=0.039). However, in stratified analysis, only walking-related activity was associated with eGFR (p<0.0001), after confounding adjustment.

Conclusions: Walking is associated with improved kidney function.

51 **Introduction**

52 Chronic kidney disease (CKD) is one of the major health burdens worldwide,¹ with
53 an estimated prevalence more than 10% in the general population.²⁻⁶ It is the
54 progressive deterioration of ability of kidney to remove fluid and nitrogenous waste
55 from the body over a period of months or years. Hypertension and diabetes are the
56 most common risk factors of CKD,⁷ and moderate to severe CKD is associated with
57 higher risks of cardiovascular disease (CVD), and CVD-related and all-cause
58 mortality.⁸⁻¹⁰ CKD may lead to renal failure (end-stage renal disease), the complete
59 loss of kidney function. When it happens, dialysis or transplant is the only option for
60 those patients.

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62 In order to reduce the disease burden, it is essential to identify modifiable and
63 promotable factors which may help to prevent CKD or the progression of disease.
64 Physical activity has shown to be effective in prevention of certain conditions
65 including hypertension and diabetes.^{11,12} However, only a few studies have
66 investigated the relationship between physical activity and CKD or kidney function in
67 the general population, with contradictory findings.¹³⁻¹⁵ Physical activity can be
68 divided into various types according to intensity (e.g. low, moderate, vigorous).
69 Whether all physical activity or only a certain subtype plays a role in association with
70 kidney function is unclear.

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72 The purpose of this study was to investigate whether physical activity was
73 associated with kidney function in a health survey of general adult population. The
74 analysis was further stratified by type of physical activity according to intensity.

75

76 Materials and Methods*77 Population*

78 The Nanjing Community Cardiovascular Risk Survey was carried out, using random
79 cluster sampling, between 2011 and 2013 among the residents of 6 communities in
80 Nanjing, Jiangsu Province, China (population 0.7 million-1.3 million). In each
81 community, one street district or township was randomly selected. All households
82 (n=6,445) in the selected street or town were included with only one participant aged
83 ≥ 20 years selected from each household, without replacement. Overall, 5,824
84 residents completed the survey and examination (with a response rate of 90%).
85 Questionnaires were completed, wherever possible, through face-to-face interviews
86 by trained research staff. Questions included age, sex, and physical activities. Body
87 measurements including body height and weight were taken three times using a
88 standardized methodology and the mean of the two closest recordings was used.
89 Body mass index (BMI) was calculated based on the obtained body height and
90 weight using kg/m^2 . Fasting blood specimens were processed at the examination
91 centre. Creatinine levels were measured by Olympus AU600 automated analyser
92 according to manufacturer's instructions (Olympus Optical, Tokyo, Japan).

93

94 Physical activity

95 Physical activity during a (usual) week (last week including weekdays and weekends)
96 was collected by the long form International Physical Activity Questionnaire (IPAQ),¹⁶
97 and was calculated as a sum of occupation, transportation, housework and
98 recreational activity reported in metabolic equivalents of task (MET) \times minutes per
99 week. Physical activity with a period less than 10 minutes was not included as per
100 the IPAQ guidelines.¹⁶ MET is a physiological measure expressing the energy cost

101 of physical activities and is defined as the ratio of metabolic rate (and therefore the
102 rate of energy consumption) during a specific physical activity to a reference
103 metabolic rate.¹⁷ Physical activity in specific settings was summarised into groups
104 based on the intensity of activity (Table 1). Stratified physical activity scores,
105 including “walking”, “moderate” and “vigorous”, were obtained. In descriptive
106 statistics, the total and intensity-stratified physical activity was categorised into “none”
107 (0 MET × minutes per week), “not meeting” (1 - 599) or “meeting” (≥ 600) the current
108 WHO physical activity guideline for people aged 18 – 64 years old.¹⁸ 600 MET ×
109 minutes per week, equivalent to 150 minutes per week of moderate activity, was the
110 lower limit for the recommended volume of physical activity.^{18,19}

111

112 *Measure of kidney function*

113 Glomerular filtration rate is a measure of ability of kidney to clear plasma of
114 nitrogenous wastes over a specific amount of time. At present, it was regarded as
115 the best way to exam kidney function. The estimated glomerular filtration rate (eGFR,
116 in mL/min/1.73 m²) was calculated from serum creatinine using the Chronic Kidney
117 Disease Epidemiology Collaboration (CKD-EPI) equation.²⁰

118

119 *Comorbidity*

120 Type 2 diabetes and hypertension were the common risk factors of CKD. Plasma
121 glucose was measured by the Olympus automated analyser. Type 2 diabetes was
122 defined using the WHO criteria or by self-reported if previously diagnosed.²¹ The
123 blood pressure was taken three times using a standardized methodology and the
124 mean of the two closest recordings was used.²² Hypertension was recorded based
125 on the WHO criteria or by self-reported if previously diagnosed.²³

126

127 *Statistical analysis*

128 The demographic, physical activity and kidney function characteristics of the
129 participants at the survey were first described. Using continuous variable, robust
130 linear regression modelling was applied to assess the effect of physical activity (total
131 and stratified by different intensity, measured by MET × minutes per week) on kidney
132 function (measured by eGFR in mL/min/1.73 m²), with adjustment for age, sex BMI,
133 type 2 diabetes and hypertension. Robust regression is designed to reduce the effect
134 by possible violation of assumption in linear regression models. Furthermore, to
135 investigate the association of walking as a usual activity (walking MET × minutes per
136 week > 0 vs. 0) with healthy kidney function (eGFR ≥ 90 vs. < 90), relevant
137 measurements were grouped into binary variables. Logistic regression modelling
138 then was used to analyse the effect of association, reported by odds ratio.
139 A sensitivity analysis which excluded participants whose eGFR < 60 was carried out.
140 All statistical analysis was performed using STATA 12.

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142 *Approval and consent*

143 This study was approved by the Institutional Review Board of Jiangsu Province
144 Hospital on Integration of Chinese and Western Medicine (11–006). Signed,
145 informed consent was obtained from all participants in the survey.

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147 **Results:**

148 A total of 5,824 participants were included, with an average age of 52 years. 56%
149 were females. Average body weight, height and BMI were 63 kg, 1.6 m and 24 kg/m²,
150 respectively (Table 2). The average eGFR among the participants was 76

151 mL/min/1.73 m², with 19% ≥ 90, 67% between 60 and 89, and 14% < 60 (Table 2). In
152 average, the total physical activity during a week was 3,644 MET × minutes per
153 week in the survey population (Table 2). Moderate activity contributed 64% of the
154 total physical activity, followed by walking (23%) and vigorous activity (13%). 80% of
155 the survey population reached the lower limit of the WHO's weekly recommendation
156 on total physical activity (Table 3).

157

158 The total physical activity was weakly associated with eGFR ($p = 0.039$; see Table 4
159 model 1). However, in stratified analysis, only walking-related activity was associated
160 with eGFR ($p < 0.0001$; see Table 4 model 2). In a linear regression model
161 containing walking, moderate and vigorous activities together as independent
162 variables and eGFR as dependent variable, the association of walking-related
163 activity and eGFR remained ($p < 0.0001$, see Table 5). Logistic regression analysis
164 showed that walking was associated with healthy kidney function with an OR of 2.23
165 (95% CI 1.91, 2.60), after adjustment for age, sex, BMI, type 2 diabetes and
166 hypertension (Table 6).

167

168 Sensitivity analysis only showed similar results (data not shown).

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170 **Discussion:**

171 In this large population survey, weekly physical activity (quantified by MET × minutes
172 per week) of residents from urban communities in China was described. The kidney
173 function in such participants estimated by eGFR was also determined. Only about 1
174 in 5 of the survey population had an eGFR ≥ 90 mL/min/1.73 m² considered as
175 healthy kidney function, whereas there was 14% who showed clear evidence of

176 reduced function in kidney (eGFR < 60). Benefit to the random sampling of survey
177 and the high response rate, this estimate of kidney function may be representative to
178 the urban residents in Nanjing (a large modern city in east China) if not to all the city
179 populations across the country. Our data reflects the potential burden of kidney
180 disease in China, and it should be raised as a public concern.

181

182 There is a disagreement in the literature as to whether higher physical activity is
183 associated with better kidney function. In patients with CKD, higher physical activity
184 level was associated with slower rate of eGFR loss,²⁴ whereas physical inactivity
185 was associated with increased mortality.¹⁴ However, the picture is not clear in the
186 population without established kidney disease. In a study using the National Health
187 and Nutrition Examination Survey data, it was shown that increased total and light
188 physical activities were associated with improved kidney function (measured by
189 eGFR), while moderate-vigorous physical activity was not significantly associated
190 after adjustment for other confounding factors.¹³ It is in line with our results showing
191 that the increased total physical activity overall was associated with improved kidney
192 function, but the actual positive effect was from walking-related activity. For the
193 moderate and vigorous-related activity, although not significant the effect showed
194 negative direction i.e. higher moderate/vigorous activity was related to reduced
195 kidney function. In contrast, a recent longitudinal study demonstrated there was no
196 association of physical activity with kidney function in participants aged 26 to 65
197 years from the Doetinchem Cohort study.¹⁵ It has a better study design as it
198 investigated the relationship between 5-year changes in physical activity and eGFR
199 using time-lagged generalized estimating equation analysis. However, the study only
200 reported the total activity while did not analyse the effects of subsets of physical

201 activity according to intensity. In our study, the association of total physical activity
202 with kidney function was only weak. Several studies showed that sedentary
203 behaviour was associated with reduced renal function in different types of
204 population.^{13,25,26} However, we didn't investigate this relationship in the current study.

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206 This study was firstly limited by its cross-sectional design, so no formal attempt with
207 regard to causality would be discussed. However, our observation that higher
208 moderate/vigorous physical activity was related to reduced kidney function
209 (insignificant finding) implied the association of more walking with improved kidney
210 function may be not due to the assumption that people with reduced kidney function
211 tended to walk less. A sensitivity analysis which excluded participants with obviously
212 reduced kidney function generated the same results. Secondly, data from
213 questionnaire (self-reported records) can be biased due to many reasons such as
214 response bias. However, thanks to the high response rate, such systematic error
215 was not likely to be large. Although the study population was carefully selected using
216 random cluster sampling and the survey tool was validated, the generalizability of
217 study results has yet to be supported.

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219 Walking is the most common aerobic activity, and it has been associated with
220 reduced risk of many diseases such as heart disease, type 2 diabetes and asthma.
221 However, it is one of many light physical activities, and the survey did not investigate
222 other light activities. Aerobic activity, rather than anaerobic activity, may be
223 associated with better kidney function and may explain the mechanism behind the
224 current findings. Other limitations included that the data distribution of primary
225 independent variable (i.e. physical activity in MET × minutes per week) was not

226 optimal. To address this, we used robust regression modelling to reduce the effect
227 by possible violation of assumption in linear regression models and used logistic
228 regression modelling to estimate the relationship between walking as a usual activity
229 and healthy kidney function.

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231 In conclusion, our study for the first time has shown that walking, but not other
232 physical activity at a higher intensity, is associated with improved kidney function.
233 Regular walking can be promoted and performed easily, a low cost strategy in
234 maintaining kidney health as well as other benefits.

235

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239 the development of study. Y Chen and D Yu managed and analysed the data, and
240 takes responsibility for the integrity of the data and the accuracy of the data analysis.
241 Y Chen, T Chen and D Yu drafted the initial manuscript, and all authors contributed
242 to the interpretation of the data and approved the final version of the manuscript
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351 Table 1 IPAQ questions on physical activity grouped by activity intensity

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IPAQ items	By intensity
For heavy physical activity at work	Vigorous
For moderate physical activity at work	Moderate
For walking as part of your work	Walking
For bicycle to go from place to place	Moderate
For walking to go from place to place	Walking
For heavy physical activity in the garden or yard	Vigorous
For moderate physical activity in the garden or yard	Moderate
For moderate physical activity inside your home	Moderate
For walking during your leisure time	Walking
For heavy physical activity in your leisure time	Vigorous
For moderate physical activity in your leisure time	Moderate

353 IPAQ, International Physical Activity Questionnaire.

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370 Table 2 Participant characteristics on demographics, physical activity, comorbid condition
 371 and renal function

Characteristics	Participants (n = 5,824) Mean (SD) or n (%)
Demographics	
Age, year	51.7 (9.9)
Male, %	2,546 (43.7)
Weight, kg*	62.8 (12.2)
Height, cm*	160.2 (7.8)
BMI, kg/m ² *	24.4 (4.1)
Comorbidity	
Type 2 diabetes, %	472 (8.1)
Hypertension, %	2,259 (38.8)
Physical activity (during a normal week)	
Total MET × minutes per week	3,644 (4,934)
MET × minutes per week by activity intensity	
Walking	833 (1,554)
Moderate	2,324 (3,266)
Vigorous	488 (2,771)
Renal function	
eGFR (in mL/min/1.73 m ²)*	76.3 (16.9)
eGFR group*	
≥ 90	1,117 (19.2)
60 - 89	3,886 (66.8)
30 - 59	812 (14.0)
< 30	6 (0.1)

372 BMI, the body mass index; MET, the metabolic equivalent of task; eGFR, the estimated
 373 glomerular filtration rate; *Weight on 5,762 subjects; Height on 5,741 subjects; BMI on
 374 5,739 subjects; eGFR on 5,821 subjects.

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381 Table 3 Physical activity in the study population, measured by MET × minutes per week and
 382 stratified by activity intensity

Activity group (MET × minutes per week)	Walking, n (%)	Moderate, n (%)	Vigorous, n (%)	Total, n (%)
0	2,183 (37.5)	714 (12.3)	5,274 (90.6)	370 (6.4)
1 – 599	1,655 (28.4)	1,234 (21.2)	178 (3.1)	772 (13.3)
≥ 600	1,986 (34.1)	3,876 (66.6)	372 (6.4)	4,682 (80.4)

383 MET, the metabolic equivalent of task.

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402 Table 4 The relationship of total and intensity-stratified physical activity with eGFR in
 403 separate models
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Independent variable	Regression coefficients (95% CI)	p value
Model 1, total activity	0.00008 (0.000004, 0.00015)	0.039
Model 2, walking-related activity	0.0012 (0.0010, 0.0015)	< 0.0001
Model 3, moderate-related activity	0.00002 (-0.00009, 0.00013)	0.72
Model 4, vigorous-related activity	-0.00008 (-0.00022, 0.00005)	0.22

405 eGFR, the estimated glomerular filtration rate; CI, confidence interval; Robust regression
 406 analysis: Dependent variable, eGFR; Adjusted for age, gender, BMI, type 2 diabetes and
 407 hypertension; Participants in the model n = 5,736.
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427 Table 5 The relationship between intensity-stratified physical activity and eGFR within one
 428 model

Independent variable	Regression coefficients (95% CI)	p value
Walking-related activity	0.0013 (0.0010, 0.0015)	< 0.0001
Moderate-related activity	-0.00007 (-0.00018, 0.00005)	0.24
Vigorous-related activity	-0.00012 (-0.00025, 0.00002)	0.09
Age	-0.60 (-0.64, -0.56)	< 0.0001
Male	6.32 (5.57, 7.08)	< 0.0001
BMI	-0.31 (-0.41, -0.22)	< 0.0001
Type 2 diabetes	-3.05 (-1.67, -4.43)	< 0.0001
Hypertension	-0.54 (-1.37, 0.28)	0.20

429 eGFR, the estimated glomerular filtration rate; CI, confidence interval; Robust regression
 430 analysis: Dependent variable, eGFR; Participants in the model n = 5,736.

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445 Table 6 The association of walking with healthy kidney function

Healthy kidney function	
Independent variable	OR (95% CI)
Walking	2.23 (1.91, 2.60)
Age	0.96 (0.95, 0.96)
Male	1.48 (1.29, 1.70)
BMI	0.96 (0.94, 0.98)
Type 2 diabetes	0.60 (0.47, 0.67)
Hypertension	0.87 (0.74, 1.02)

446 eGFR, the estimated glomerular filtration rate; OR, odds ratio; CI, confidence interval;
 447 Logistic regression analysis: Dependent variable, healthy kidney function (eGFR \geq 90
 448 mL/min/1.73 m² vs. < 90); Participants in the model n = 5,736.

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