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Physical activity and liver health among urban and rural Chinese adults: results from two independent surveys

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A B S T R A C T

Background: Increased physical activity has been associated with reduced risks of various physical and mental conditions. However, the association between physical activity and liver health in the Chinese general adult population is not clear. This study investigated whether physical activity, stratified by intensity (i.e. walking (light), moderate-to-vigorous), was associated with alanine aminotransferase (ALT) level in middle-aged and older Chinese adults.

Methods: Two independent surveys of urban (n = 5,824, males 44%, mean (standard deviation) age 52 (10) years) and rural populations (n = 20,269, males 41%, mean (standard deviation) age 51 (10) years) were undertaken. Physical activity was measured using the International Physical Activity Questionnaire, and in metabolic equivalents of task (MET) × minutes. Elevated serum level of ALT, a clinical surrogate of abnormal liver function, was defined as >40 IU/L (males) and >30 IU/L (females). Multivariable regression models were used.

Results: Amount of moderate-to-vigorous activity was inversely associated with serum level of ALT ($\beta = -0.147$ per 1k MET-minutes, $p < 0.001$), whereas walking was not associated. People who reached the lower limit of WHO recommendation (≥600 MET-minutes per week) had a reduced odds of ALT elevation, compared to those who did not (adjusted odds ratio: 0.85 95%CI (0.76, 0.95)).

Conclusions: Meeting the moderate-to-vigorous recommendations for physical activity in adults may be associated with decreased likelihood of abnormal liver function both in Chinese urban and rural populations. Promoting such activities could be a low-cost strategy in maintaining liver health as well as providing many other health-related benefits.

Introduction

Liver disease is a significant burden of public health because of its high prevalence worldwide and its association with poor clinical outcome including early mortality. In China, new cases of hepatitis B virus and hepatitis C virus infections have been largely prevented since 1990s. However, the prevalence of alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD) has dramatically increased recently probably due to altered lifestyles including physical inactivity, diet and sleep characteristics.[1–3] These two diseases are now the leading sources of chronic liver diseases, with NAFLD patients contributing to half of all Chinese people with a liver condition.[4] To date there is no approved effective pharmacologic therapy for NAFLD, therefore in order to reduce the disease burden it is essential to identify modifiable and promotable factors, which when intervened on, may assist to prevent the disease or the progression of disease.

Physical activity plays an important role in daily life. Increased physical activity levels have been associated with reduced risks of various physical (e.g. cardiovascular, metabolic, certain types of

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cancer) and mental (e.g. depression, anxiety) conditions,[5–14] whereas physical inactivity has been identified as the 4th leading risk factor globally for early mortality.[15] Recent systematic reviews have demonstrated a therapeutic effect of increased physical activity on liver health.[16–18] However, large population-level research is lacking..

Alanine aminotransferase (ALT), largely produced from damaged liver cells, is considered a surrogate marker of liver health in adults. Elevated serum level of ALT has been regarded as a reliable clinical indicator for an ongoing liver disease, particularly NAFLD.[19] Here, we aimed to investigate the relationship between physical activity and liver health status measured by serum level of ALT in two health surveys of general adult population in China.

Methods

Data setting

The study used two independent surveys of urban and rural Chinese people. The urban Chinese population data were derived from the Nanjing Community Cardiovascular Risk Survey, a random cluster sample of residents from 6 communities in Nanjing, Jiangsu Province, China between 2011 and 2013.,[11]. In each community, one street district or township was randomly selected. All households (n = 6445) in the selected street or town were included with only one participant aged ≥35 years selected from each household, without replacement. Overall, 5824 residents completed the survey and examination (response rate of 90%). The rural Chinese population data were derived from the Hefei Community Cardiovascular Risk Survey, using a random cluster sampling of residents from 10 rural towns in Hefei, Anhui Province, China, between 2012 and 2013.[11] In each rural area, one township was randomly selected. All households (n = 22,032) in the selected town were included with only one participant aged ≥35 years selected from each household, without replacement. Overall, 20,269 residents completed the survey and examination (response rate of 92%).

Questionnaires were completed in both surveys, wherever possible, through face-to-face interviews by trained research staff. Age, sex, and physical activity were self-reported. The two surveys were approved by the Institutional Review Board of Jiangsu Province Hospital on Integration of Chinese and Western Medicine (11–006). Signed consent was obtained from all participants. This study was carried out in accordance with the Declaration of Helsinki.

Measure of anthropometric variable

Body measurements (i.e. body height, weight) were taken three times using a standardized methodology and the mean of the two closest recordings was used. Body mass index (BMI) was calculated based on the obtained body height and weight using kg/m.[2]

Measure of physical activity

Self-reported data on physical activity during a whole week (from Monday to Sunday) prior to health survey were collected via the long form International Physical Activity Questionnaire (IPAQ).[20] Data were collected from specific settings across several domains including occupation, transportation, housework and recreational activity, and were reported in metabolic equivalents of task (MET) × minutes per week. Physical activity with a period less than 10 min was not included according to the IPAQ guidelines.[20] MET is a physiological measure expressing the energy cost of physical activities, and is defined as the ratio of metabolic rate (and therefore the rate of energy consumption) during a specific physical activity to a reference metabolic rate.[21] Physical activity in specific settings (IPAQ items) was categorised into two groups (i.e. walking (light), moderate-to-vigorous) based on activity intensity (Table 1).

The total and intensity-stratified physical activities were categorised into “none” (0 MET × minutes per week), “not meeting” (1–599), or “meeting” (≥600) the current WHO physical activity guideline for individuals aged 18–64 years old 21. The 600 MET × minutes per week was the lower limit for the recommended volume of physical activity.[22,23]

Measure of alanine aminotransferase (ALT)

Fasting blood specimens were processed at the examination centre of each survey. Serum levels of ALT were measured on each study participant by Olympus AU600 automated analyser according to manufacturer’s instructions (Olympus Optical, Tokyo, Japan). Elevated serum ALT, suggesting potential liver damage, was defined as >40 IU/L (males) and >30 IU/L (females).[24] ALT level was categorised into normal (<40 IU/L and <30 IU/L for males and females, respectively) or elevated status (≥40 IU/L and ≥30 IU/L for males and females, respectively) for each participant.

Statistical analysis

Descriptive statistics for participants’ demographic, physical activity, and ALT characteristics were presented in individual and combined surveys. Linear regression modelling was carried out to assess the associations of walking (light) and moderate-to-vigorous activities (both as continuous variables measured by MET-minutes per week) with serum level of ALT (IU/L), with adjustment for age, gender, BMI and geographic location (study site) (Hefei vs. Nanjing). The adjustment for geographic location was to take any systematic difference between the two studies into consideration such as conception of intensity of activity, equipment to measure the level of ALT, staff to carry out the survey and unmeasured participant characteristics. Once the association of certain types of physical activity with serum level of ALT was established, using logistic regression analysis we further quantified the magnitude of association between the WHO recommended volume of physical activity (none vs. 1–599 vs. ≥600 MET-minutes per week) and the status of ALT (normal vs. elevated). Association of statistical significance was set at $p < 0.05$, two-tailed. All analyses were performed using STATA (STATA SE 13.0 StataCorp, College Station, TX, USA).

Results

Overall 26,093 participants were included (Nanjing N = 5824 and Hefei N = 20,269), where 42% were males. The mean age was 51 (standard deviation (SD) 10) years old, and BMI 25 (SD 4) kg/m^2.

Table 1
IPAQ questions on physical activity.

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

IPAQ, International Physical Activity Questionnaire.

Characteristics of participants in each individual survey are also shown in Table 2. The amount of total physical activity (measured by MET-minutes per week) was less in urban (Nanjing) participants compared to those from rural (Hefei) (mean 3645 vs. 4002), apparently due to less walking activity (mean 833 vs. 1327 MET-minutes per week). Survey participants in Nanjing however did slightly more moderate-to-vigorous activity (mean 2812 vs. 2675 MET-minutes per week) (Table 2). Serum level of ALT was lower in Nanjing participants (mean 18 vs. 23 IU/L). Elevated ALT was recorded in 8.5% of participants in Nanjing and 15.3% in Hefei (Table 2).

In the pooled population, 49% of people reached WHO lower limit for the recommended volume of physical activity (600 MET-minutes per week) solely through walking, 69% solely through moderate-to-vigorous activity, and 84% through the total activities (walking plus moderate-to-vigorous) (Table 3).Six percent of people self-reported as physically inactive (total MET-minutes per week = 0) (Table 3).

A higher level of moderate-to-vigorous physical activity was associated with a lower serum level of ALT ($\beta = -0.15$ per 1k MET-minutes, $p < 0.001$) in each survey and the combined population (Table 4). Other significantly associated factors with a lower level of ALT included a younger age, being females and a smaller BMI (Table 4). However, walking was not significantly associated (Table 4).

Based on the combined population, people who reached the lower limit for the recommended volume of physical activity through doing moderate-to-vigorous activities were associated with a lower risk of elevated ALT in serum (OR 0.85 (95% CI 0.76, 0.95)), compared to those who did not perform any moderate-to-vigorous activity (Table 5).

Discussion

This study, which consisted of over 26,000 general adult population from two large health surveys, demonstrated a weak, significant association between higher levels of moderate-to-vigorous physical activity and lower levels of liver damage. Previous research has shown that physical activity on different intensity levels may contribute differently to certain health outcomes, independent of cumulative amounts.[25–28] In the present study, the results suggest that walking, the most commonly performed light physical activity, was not significantly associated with liver damage. We assessed whether the risks of liver damage were different between people who reached the lower limit of WHO physical activity guideline for the weekly recommendation and who did not, based on their moderate-to-vigorous physical activity volume. We found that those who achieved the lower limit of recommended volume of moderate to vigorous physical activity had a significantly lower risk of elevated ALT.

Potential liver damage, measured by elevated serum level of ALT (male >40 IU/L, female >30 IU/L),[24] was estimated in our survey participants. It was shown that although demographic characteristics were similar between urban and rural participants, the proportion of elevated ALT differed (9% vs. 15%). It is not clear whether such difference is due to systematic bias (e.g. equipment, assay kit, personnel) or reflects the diversity across different cities in China. In the combined population, 14% of participants at the mean age of 42 years old presented with an indication of potential liver damage, which suggests a high health burden and should be raised as a public concern. We found that urban (Nanjing) adults did more moderate-to-vigorous physical activity, yet less overall physical activity compared to their rural counterparts (Hefei).It may be due to that rural adults actually perform higher intensity physical activity compared to urban adults but they may have perceived it to be lower in intensity. This is could be a bias for the analysis of the combined population. However, the association was consistent between the two populations and in the multivariable analysis the influence of geographical location (study site) was statistically adjusted. Our estimates were benefited from the random sampling and high response rate of both surveys, however, its

Table 2
Participant characteristics on demographics, physical activity, and serum level of alanine aminotransferase (ALT).

Characteristics	Nanjing (urban) (N = 5824)	Hefei (rural) (N = 20,269)	p value[b]	Combined (N = 26,093)
	Mean (SD) or n (%)	Mean (SD) or n (%)		Mean (SD) or n (%)
Demographics				
Age, year	51.7 (9.9)	51.1 (9.9)	<0.001	51.2 (9.9)
Male, %	2546 (43.7)	8364 (41.3)	0.001	10,910 (41.8)
Weight, kg[a]	62.8 (12.2)	65.0 (12.2)	<0.001	64.5 (12.3)
Height, cm[a]	160.2 (7.8)	161.6 (8.3)	<0.001	161.3 (8.2)
BMI, kg/m^2[a]	24.4 (4.1)	24.8 (4.0)	<0.001	24.7 (4.0)
BMI, category			<0.001	
BMI < 25, kg/m^2 (normal)	3483 (60.7)	11,082 (55.2)		14,565 (56.7)
BMI ≥ 25 & < 30, kg/m^2 (overweight)	1907 (33.2)	7332 (36.7)		9239 (36.0)
BMI ≥ 30, kg/m^2 (obese)	349 (6.1)	1547 (7.8)		1896 (7.4)
Physical activity (during a week)				
Total MET-minutes per week	3645 (4934)	4002 (4780)	<0.001	3922 (4817)
MET-minutes per week by activity intensity				
Walking (light)	833 (1554)	1327 (1836)	<0.001	1217 (1788)
Moderate-to-vigorous	2812 (4469)	2675 (4176)	0.031	2706 (4243)
Liver enzyme				
ALT, IU/L[a]	17.7 (14.9)	22.7 (19.7)	<0.001	21.6 (18.9)
ALT category, %			<0.001	
Normal (male ≤ 40 IU/L, female ≤ 30 IU/L)	5328 (91.5)	17,166 (84.7)		22,494 (86.2)
Elevated (male > 40 IU/L, female > 30 IU/L)	495 (8.5)	3101 (15.3)		3596 (13.8)

BMI, the body mass index; MET, the metabolic equivalent of task. ALT, alanine aminotransferase.
[a] Weight on 5762 subjects of Nanjing survey, and 20,011 Hefei survey, Nanjing; Height on 5741 subjects of Nanjing survey, and 19,967 Hefei survey; BMI on 5739 subjects of Nanjing survey, and 19,961 Hefei survey; ALT on 5823 subjects of Nanjing survey and 20,267 Hefei survey; The missing data is due to that body height, body weight or ALT level was not measured in certain proportion of participants.
[b] p values for univariate analyses (e.g. T-test or Chi-squared test where appropriate) for the difference between Nanjing (the urban) and Hefei (the rural) populations.

Table 3
Stratification of the populations by physical activity intensity and WHO weekly amount guideline.

Activity type by intensity	Nanjing (urban) Group of weekly activity amount (MET-minutes per week)			Hefei (rural) Group of weekly activity amount (MET-minutes per week)			Combined Group of weekly activity amount (MET-minutes per week)		
	0	1–599	≥600	0	1–599	≥600	0	1–599	≥600
Walking (light), n (%)	2183 (37.5)	1655 (28.4)	1986 (34.1)	4329 (21.4)	5063 (25.0)	10,877 (53.7)	6512 (25.0)	6718 (25.8)	12,863 (49.3)
Moderate-to-vigorous, n (%)	700 (12.0)	1165 (20.0)	3959 (68.0)	2658 (13.1)	3547 (17.5)	14,064 (69.4)	3358 (12.9)	4712 (18.1)	18,023 (69.1)
Total, n (%)	370 (6.4)	772 (13.3)	4682 (80.4)	1222 (6.0)	1876 (9.3)	17,171 (84.7)	1592 (6.1)	2648 (10.2)	21,853 (83.8)

MET, metabolic equivalent of task.

Table 4
Associations of walking and moderate to vigorous physical activity, age, sex and BMI with ALT level.

Independent variable	Nanjing (urban)		Hefei (rural)		Combined	
	Coefficient (β)	p value	Coefficient (β)	p value	Coefficient (β)	p value
Walking (light), per 1k MET-minutes	0.03	0.79	−0.01	0.86	−0.006	0.93
Moderate-to-vigorous activity, per 1k MET-minutes	−0.14	0.002	−0.15	<0.001	−0.15	<0.001
Age, per year	−0.07	<0.001	−0.13	<0.001	−0.12	<0.001
Male	−3.28	<0.001	−4.85	<0.001	−04.50	<0.001
BMI, per kg/m2	0.64	<0.001	0.58	<0.001	0.60	<0.001
Geographic location[a]	–	–	–	–	4.80	<0.001

Linear regression analyses where serum ALT level as the dependent variable.
[a] Hefei vs. Nanjing (as referent). Total number in the regression models: Nanjing 5,738, Heifei 19,959, combined 25,697.

Table 5
Protective relationship between WHO recommended weekly amount of physical activity and liver function measured by ALT compared to inactivity.

Independent variable	Nanjing (urban)	Hefei (rural)	Combined
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Moderate-to-vigorous activity (categorical)			
0 MET-minutes per week	1.0 (referent)	1.0 (referent)	1.0 (referent)
1–599 MET-minutes per week	0.92 (0.66, 1.28)	0.96 (0.84, 1.10)	0.95 (0.84, 1.08)
≥600 MET-minutes per week	0.85 (0.64, 1.14)	0.85 (0.76, 0.95)	0.85 (0.76, 0.95)
Age, per year	0.98 (0.98, 0.99)	0.99 (0.98, 0.99)	0.99 (0.98, 0.99)
Male	0.68 (0.55, 0.82)	0.81 (0.75, 0.88)	0.79 (0.73, 0.85)
BMI, per kg/m2	1.08 (1.06, 1.10)	1.07 (1.06, 1.08)	1.07 (1.07, 1.08)
Geographic location[a]	–	–	1.90 (1.72, 2.11)

Logistic regression analysis.
[a] Hefei vs. Nanjing (as referent). Total number in the regression models: Nanjing 5,738, Heifei 19,959, combined 25,697.

generalizability to the entire Chinese population is unclear.

Increased physical activity has therapeutic effects on NAFLD by reducing hepatic fat,[16,17] but the effect on circulating aminotransferases remains unclear.[17] In a population of British women aged 60–79 years (n = 3789), although an inverse association between frequencies of physical activity and ALT level as observed, the association was attenuated towards the null after adjustment of BMI and waist/hip ratio.[29] In our study, though waist/hip ratio was not available, the observed association was independent of BMI. In an adolescent population (n = 718), Ruiz and colleagues demonstrated that increased moderate-to-vigorous physical activity was not associated with serum level of ALT, but with aspartate aminotransferase (AST) level and AST/ALT ratio.[25] Loprinzi, using the cohort of the National Health and Nutrition Examination Survey (2003–2006, n = 5030), reported a significant association between serum ALT and muscle strengthening activity, but not with moderate-to-vigorous physical activity.[30] Thus, the current literature is limited, with inconclusive findings.

This study was limited by its cross-sectional design, therefore causality could not be inferred. Self-reported data can be biased due to many reasons including response bias. However, thanks to the high response rates in both surveys such systematic error was not likely to be large. As previously mentioned, there may be potential systematic bias between the two surveys, such as equipment, assay kit and personnel, on the measurement of ALT level. However, the patterns of association between physical activity and elevated ALT level in each survey were highly consistent. In the combined population, the association results were further adjusted for geographic location in order to remove any such bias. ALT levels are influenced by many factors including diseases and lifestyle variables. Unfortunately, detailed morbidity and lifestyle (e.g. alcohol consumption) was not available, resulting a large limitation. Although walking in this paper was categorised as a light physical activity, it may reach to an intensity level of moderate or even vigorous activity. So, miscategorization may occur, which serves as another study limitation. In addition, although walking is the most common light activity, it is one of many light activities. Our survey did not investigate other light activities. In both surveys, populations were residents from the communities in east China, highlighting the need to investigate other parts of China to improve the generalizability of findings.

Conclusion

In conclusion, our study, for the first time using Chinese general adult populations, showed that increased moderate-to-vigorous physical activity was significantly associated with reduced liver damage. Moderate-to-vigorous physical activity through exercise and sports should be easily promoted and performed on a regular basis and it is a low-cost strategy in maintaining liver health as well as providing many other health-related benefits.

Author contributions

Yan Chen, Ying Chen, Feng Bai, Dahai Yu: Conceptualization, Methodology. Yan Chen, Ying Chen, Rui Qin, Yamei Cai, Dahai Yu, Feng Bai: Data curation, Writing- Original draft preparation. Baohua Geng, Yong Zhang, Rui Qin, Yamei Cai: Visualization, Investigation. Feng Bai, Rui Qin: Supervision Ying Chen, Yamei Cai: Software, Validation. Yan Chen, Ying Chen, Baohua Geng, Yong Zhang, Rui Qin, Yamei Cai, Feng Bai, Dahai Yu: Reviewing and Editing

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Declaration of competing interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jesf.2020.07.004.

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