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Different levels of physical activity and risk of developing type 2 diabetes among adults with prediabetes: a population-based cohort study

Wenchang Yang^{1†}, Yuntao Wu^{2†}, Yue Chen¹, Shuohua Chen², Xiang Gao¹, Shouling Wu^{2*} and Liang Sun^{1*}

Abstract

Objectives This study aimed to evaluate the association between different levels of physical activity and risk of developing type 2 diabetes (T2D) mellitus among adults with prediabetes in Chinese population.

Methods This prospective population-based cohort study included 12,424 participants (mean [SD] age, 52.8 [16.8] years; 82.2% men) with prediabetes at 2014 survey of the Kailuan study. Physical activity information was collected through the International Physical Activity Questionnaire-Short Form and categorized by metabolic equivalent (MET) of task as low, moderate, and high. Cox regression models were built to estimate hazard ratios (HRs) and 95% confidence intervals (Cls) for associations between physical activity levels and incident T2D.

Results During a median follow-up of 3.6 years, 2,207 (17.8%) participants developed T2D. The incident rate of T2D were 55.83/1000, 35.14/1000, and 39.61/1000 person-years in the low, moderate, and high physical activity level group, respectively. Both moderate (HR 0.57, 95% CI 0.49 to 0.67) and high (HR 0.76, 95% CI 0.66 to 0.89) physical activity levels were associated with lower risks of developing T2D compared to low physical activity level (P for trend < 0.001). The association between high physical activity level and T2D was primarily observed in participants without metabolic syndrome (P for interaction < 0.001). Moreover, participants with moderate or high levels of physical activity had significantly decreased fasting blood glucose levels during follow-up when compared to those with low level (P group*time < 0.001).

Conclusion This study suggested that individuals with prediabetes might benefit from moderate and high levels of physical activity.

Keywords Prospective study, Physical activity, Type 2 diabetes, Prediabetes

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Introduction

Prediabetes, a stage before diabetes, is characterized by moderately elevated blood glucose levels and, without intervention, approximately 70% of individuals at this state will progress to T2D [1–3]. The number of adults aged 20–79 years with prediabetes currently stands at approximately 762 million globally, and an estimated 1 billion people will be affected by 2045 [4, 5]. Prediabetes is also linked with a higher risk of developing cardiovascular diseases and all causes mortality [4, 6]. Fortunately, the prediabetic stage is manageable, and lifestyle modification including physical activity can effectively slow the progression from prediabetes to T2D [7].

Regular physical activity has been showed to improve blood glucose level and overall well-being in population with diabetes [8–11]. A review included 28 prospective studies on leisure-time physical activity or total physical activity and risk of T2D had indicated physical activity to be the primary approach for preventing and controlling T2D [12]. A meta-analysis of 6 studies found that better diet and physical activity were associated with a 53% higher possibility of returning to normal glucose levels in prediabetes participants [13]. Intervention studies like the Da Qing study, Finnish diabetes study, the American Diabetes Prevention Program, and the India Diabetes Prevention Program also indicated that moderate to vigorous physical activity could reduce the risk of developing T2D in high-risk individuals [14–19]. Korean Genome and Epidemiology study and Taiwan MJ cohort study found that prediabetes participants with higher physical activity were more likely to achieve normoglycemia and had lower risks of T2D progression and death compared to those with lower activity levels [20, 21]. However, it's worth noting that most of those studies incorporated interventions combined physical activity with diet, making it challengeable to explore the distinct impact of physical activity alone. Furthermore, there is limited evidence regarding the association between different levels or intensities of physical activity and the risk of T2D, especially among individuals at the prediabetes stage. Hence, we aimed to investigate the association between different levels of physical activity and the risk of developing T2D in a cohort of approximately 12,400 adults with prediabetes.

Methods

Study design and participants

In this analysis, participants were derived from the ongoing Kailuan Study, which was a population-based prospective cohort study conducted in the Kailuan community of Tangshan, China. The study design has been described in previous publications [22–24]. In brief, the study enrolled 101,510 adult participants (81,110 men and 20,400 women) during 2006 to 2007. Furthermore,

between 2008 and 2009, an additional 24,540 adult participants (19,356 men and 5,184 women) were enrolled. Participants completed questionnaires, and underwent physical measurements, clinical evaluations, and lab tests were performed in a single measurement at baseline. Subsequently, same assessments were conducted biennially. The study obtained approval from the ethics committees of Kailuan General Hospital, and all participants provided written informed consent.

This study investigated the relationship between physical activity levels and risk of T2D in the prediabetes population. Physical activity and other covariates of participants were collected from the 2014 survey (as baseline of this study) of the Kailuan Study. Participants included in present analyses were followed until December 31 2018, the average follow up time was 3.6 years. The fasting blood glucose (FBG) values were collected twice, at 2014 survey and end of the follow up period. In 2014, out of 101,588 participants, 1,718 lacked fasting plasma glucose data, 31,567 had no physical activity data, 52,626 did not meet the prediabetes criteria for FBG levels, 2,649 were lost to follow-up, and 604 deaths were excluded (Supplementary Fig. 1). Finally, a total of 12,424 participants were eligible for analysis.

Assessment of physical activity

Physical activity information of participants was collected once during 2006-2009 by using the International Physical Activity Questionnaire-Short Form [25]. Participants were asked how many days per week they did exercise; what kind of physical activity they performed; and how long each exercise session lasted (<30 min; 30-60 min; ≥60 min). We categorize MET intensity into three levels: high (8 METs), moderate (4 METs), and low (3.3 METs). The formula is: weekly exercise days × daily exercise duration (minutes) × MET intensity=weekly total MET minutes. Add up all weekly MET minutes to get the total MET value. After collecting frequency and intensity of the weekly physical activity, participants were categorized into three groups based on their weekly MET value: low (<600 MET-minutes per week), moderate (600–3000 MET-minutes per week), and high (≥3000 MET-minutes per week). These categories represented different levels of physical activity engagement, as detailed elsewhere [26, 27].

Assessment of prediabetics, T2D, changes of FBG, and metabolic syndrome

The primary outcome of our study is the incidence of T2D among prediabetic participants during the follow-up period. Prediabetes is defined as FBG level range between 5.6 and 6.9 mmol/L according to the guidelines of American Diabetes Association [28]. T2D is defined as meeting any of the following criteria: FBG \geq 7.0 mmol/L, a

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self-reported physician diagnosis, or self-reported use of anti-diabetic medication. The secondary outcome is the change in FBG levels between the baseline (2014 resurvey) and final FBG tests (2016 or 2018 resurvey) among participants from different physical activity groups. Metabolic syndrome was diagnosed by three or more of the following criteria: $TG \ge 150$ mg/dl (1.7 mmol/L), HDL-C<40 mg/dl (1.03 mmol/L) in men and <50 mg/dl (1.29 mmol/L) in women, fasting glucose ≥ 100 mg/dl (5.6 mmol/L) or previously diagnosed with type 2 diabetes, blood pressure $\ge 130/85$ mmHg or on antihypertensive medication, and central obesity (defined as waist circumference ≥ 90 cm in men and ≥ 80 cm in women, according to the ethnic criteria for Asians) [29, 30].

Data collection and definition

Demographic information (e.g., age, sex), socioeconomic status (e.g., income), family history of diabetes, and lifestyle factors (e.g., smoking status, alcohol consumption, sleep duration, physical activity, and dietary intake) were collected through a structured questionnaire. Education level was categorized as middle school and below, high school, or college and above. Average monthly income of each family member was classified as <1,000 Yuan, 1,000-3,000 Yuan and $\geq 3,000$ Yuan. Smoking status was defined as either a current smoker or never having smoked. Alcohol consumption was defined as either a current drinker or never having drunk.

Height and weight measurements were taken by trained nurses under standardized conditions, with participants wearing light clothes and being barefoot. Heights were measured to the nearest 0.1 cm, and weights were measured to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist circumference was also measured at standing position. Blood pressure was measured in the seated position and the average of three readings was recorded as systolic blood pressure (SBP) and diastolic blood pressure (DBP). Hypertension was defined as SBP≥140 mm Hg or DBP≥90 mm Hg, the use of antihypertensive medication, or a self-reported history of hypertension. Blood samples were collected after an 8 to 12-hours fasting period. FBG levels were measured using the Hexokinase/Glucose-6-phosphate dehydrogenase method (Mind Bioengineering Co., Ltd., Shanghai, China), with an upper detection limit of 30.07 mmol/L. Triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), and high-density lipoprotein-cholesterol (HDL-C) levels were measured by automatic analyzer (Hitachi 747, Hitachi, Tokyo, Japan).

Statistical analysis

Continuous, normally distributed data were summarized as mean and standard deviations; while categorical data

were summarized as the numbers and percentages. For 12,424 prediabetes participants included in the analysis, their demographic information (sex, age, education, income, marital status), behavioral status (smoking status, sleep duration, TV hours), and biochemical characteristics (FBG, DBP, and SBP) were described according to three levels of physical activity. For each individual, the person-time of follow-up was calculated from the 2014 survey date until the occurrence of T2D, being lost to follow-up, death or end of follow-up (December 31, 2018), whichever happened first. Supplementary Table 1 shows baseline characteristics for all participants and participants with prediabetes in the 2014 resurvey.

Cox proportional hazard models were utilized to determine hazard ratios (HR) and 95% confidence intervals (CIs) for the incidence of T2D in the three physical activity groups (low, moderate, and high), using the low physical activity group as reference. According to Schoenfeld residuals, our models satisfied the proportional assumption criteria. In Model 1, age and sex (men, women) were adjusted as covariates. Model 2 was further adjusted for smoking status (current or never), alcohol consumption (current drinker or never drink), sleep hours (<5, 5-7, or ≥ 7 h/day), TV time (<2, 2–3, or ≥ 4 h/day), central obesity (yes or no), family history of diabetes (yes or no), education level (middle school and below, high school, or college and above), average monthly income of each family member (<1000, 1000-3000, or ≥3000 Yuan), marital status (married or single), dietary approaches to stop hypertension (DASH) diet score (≤ 25 , 26–30, or ≥31 points), and BMI categories (<24, 24≤BMI<28, or ≥28 kg/m²). In model 3, systolic blood pressure, LDL-C, and TG were further adjusted for as the full model. Supplementary Table 2 indicated how DASH score was classified. Sensitivity analyses were conducted after excluding participants with conditions such as cancer, cerebral hemorrhage, cerebral infraction, subarachnoid rainbow, ankylosing spondylitis, rheumatoid joint disease, gout, and Parkinson's disease to test the consistency and stability of the results. Stratified analyses were performed based on sex, age, BMI, smoking status, alcohol consumption, nighttime sleeping hours, metabolic syndrome, hypertension, and DASH diet score. A likelihood ratio test was applied to examine the significance of interactions.

For FBG changes, mixed-effects liner models were used to analyze the effect of group (physical activity levels), time, and group by time interaction with adjusting for age, sex, and baseline FBG. In the analysis, individual participant was treated as random effects, while the group, times, and their interaction were considered as fixed effects. Statistical analysis was performed using R software (version 4.2.2) and SAS version 9.4 (SAS)

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Table 1 Baseline characteristics according to physical activity levels

Variable	Total N = 12,424	Low N=8,202	Moderate $N = 2,150$	High N=2,072
Men	10,084 (82.2)	6,494 (79.2)	1,806 (84.0)	1,784 (86.1)
Age, years	52.7 ± 16.7	55.0 ± 13.2	52.1 ± 23.2	51.2 ± 13.9
Education				
Middle School	6,648 (70.1)	4,499	1,157	992 (60.2)
&below		(73.8)	(66.8)	
High School	1,815 (19.1)	967 (15.9)	391 (22.6)	457 (27.7)
College & above	1,019 (10.7)	634 (10.4)	185 (10.7)	200 (12.1)
Income, CNY				
< 1,000	1,484 (30.8)	968 (27.7)	278 (34.5)	238 (45.8)
1,000-3,000	902 (18.7)	711 (20.4)	83 (10.3)	108 (20.8)
≥3,000	2,430 (50.5)	1,811 (51.9)	445 (55.2)	174 (33.5)
Married	9,279 (97.7)	6,026 (99.7)	1,659 (95.5)	1,594 (96.4)
Current smoker	4,716 (41.6)	2,851 (40.0)	934 (43.5)	931 (45.0)
Current drinker	5,376 (45.7)	3,475 (45.9)	985 (46.2)	916 (44.4)
With family his- tory of diabetes	370 (4.6)	291 (4.6)	37 (4.4)	42 (4.1)
Nighttime sleep- ing duration, h/ day	6.80 ± 1.10	6.90 ± 1.20	6.80±1.10	6.80 ± 1.10
Nap duration, h/ day	1.00 ± 1.10	1.02 ± 1.06	0.87 ± 1.00	0.97 ± 1.27
TV hours, h/day	2.50 ± 1.60	2.23 ± 1.80	2.51 ± 1.50	2.71 ± 1.60
Total DASH score	27.9 ± 4.10	28.4±3.90	26.7 ± 4.20	27.3 ± 4.30
Body mass index, Kg/m ²	25.2 ± 3.20	25.3 ± 3.30	25.2 ± 3.20	25.2 ± 3.10
Waist circumfer- ence, cm				
Men	89.6 (8.6)	89.6 (8.6)	89.3 (8.5)	89.7 (8.2)
Women	85.0 (9.3)	85.0 (9.3)	84.3 (9.3)	83.8 (7.4)
Systolic blood	141 ± 19.0	140 ± 19.8	140 ± 18.9	142±18.3
pressure, mmHg				
Diastolic blood pressure, mmHg	83.9±1.8	83.5 ± 10.8	84.1 ± 11.1	84.1 ± 10.6
High density lipo- proteins, mmol/L	1.36±0.50	1.40 ± 0.60	1.30 ± 0.40	1.40 ± 0.40
Low density lipo- proteins, mmol/L	3.00 ± 0.90	2.90 ± 0.90	3.10 ± 0.90	3.10 ± 0.80
Total cholesterol, mmol/L	5.30 ± 1.20	5.40 ± 1.20	5.30 ± 0.40	5.20 ± 1.60
Triglyceride, mmol/L	1.70 ± 1.50	1.80 ± 1.80	1.70 ± 1.30	1.60 ± 1.40
Fasting blood glucose, mmol/L	6.10 ± 0.40	6.10 ± 0.40	6.10 ± 0.40	6.00 ± 0.30

Values are presented as number (%) or mean $\pm\,\text{SD}$

Abbreviations: CNY, China Yuan; DASH, Dietary Approach to Stop Hypertension; TV, Television

Table 2 Association between physical activity and risk of incident type 2 diabetes (n = 12,424)

	Physical Activity levels					
Variables	Low	Moderate	High	P for trend		
No of cases	1,647	279	281	-		
Incidence rate ^a	55.83	35.14	39.61	-		
Model 1	1.00 [reference]	0.61 (0.53–0.69)	0.77 (0.68– 0.88)	< 0.001		
Model 2	1.00 [reference]	0.57 (0.49–0.66)	0.76 (0.66– 0.88)	< 0.001		
Model 3	1.00 [reference]	0.57 (0.49–0.67)	0.76 (0.66– 0.89)	< 0.001		

^aIncidence rate was calculated per 1000 person years

Model 1 adjusted for sex (men or women) and age (continuous variable, years); Model 2 further adjusted for smoking status (current or never), alcohol consumption (current or never), nighttime sleeping hours (<5, 5–7, or \geq 7 h/day), TV-time (<2, 2–4, or \geq 4 h/day), abdominal obesity (yes or no), family history of diabetes (yes or no), education (middle school &below, high school, or college & above), average monthly income of each family member(<1,000, 1,000–3,000, or \geq 3,000 Yuan), marital status(married or single), DASH diet score (\leq 25, 26–30, or \geq 31 points), and body mass index (<24, 24 \leq BMI<28, or \geq 28 kg/m²);

Model 3 further adjusted for systolic blood pressure, low density lipoprotein, and triglyceride

Institute, Cary, NC, USA). The level of significance was taken as two-sided P<0.05.

Results

Characteristics of the study participants

The characteristics of the study population at the 2014 resurvey, grouped according to different levels of physical activity, were presented in Table 1. Among the 12,424 participants enrolled in this study, 66% were categorized as having a low level of physical activity, 17.3% as having a moderate level, and 16.7% as having a high level. The participants had an average age of 52.7 years with a standard deviation of 16.7 years, and 82.2% of them were men. Compared with participants in groups of moderate and high physical activity level, those in low physical activity level group tended to be older, had longer sleep duration, and higher levels of BMI, TC, and TG.

The association between physical activity levels and T2D

During an average follow-up period of 3.6 years [(IQR 2.4–4.4); total cumulative follow-up was 44,563 person years] among the 12,424 participants, 2,207 (17.8%) developed T2D. Concurrently, 5,638 (45.37%) remained prediabetic, while 4,579 (36.86%) returned to a normoglycemic state.

As shown in Table 2, both moderate and high physical activity levels were linked to a lower risk of developing T2D compared to low physical activity level. In the full model, the moderate and high physical activity groups had a 43% and 24% lower risk of T2D, respectively.

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Figure 1 presents the Kaplan-Meier curves, which reveals that the group with moderate activity levels exhibited the lowest risk for T2D, while the group engaged in low physical activity had the highest risk (*P* for log-rank test < 0.001).

Sensitivity analyses were conducted by excluding participants with cancer, cerebral hemorrhage, cerebral infraction, subarachnoid rainbow, ankylosing spondylitis, rheumatoid joint disease, gout, and Parkinson disease. Both groups of moderate and high physical activity levels remained significantly associated with lower risk of T2D (HR 0.56, 95% CI 0.48 to 0.68 and HR 0.75, 95% CI 0.66 to 0.88, respectively) compared with low physical activity group in fully adjusted model (Supplementary Table 3).

In the stratified analysis presented in Table 3, the relationship between different physical activity levels and the risk of T2D remained consistent across different strata, including sex, BMI, smoking status, alcohol consumption, nighttime sleeping hours, hypertension, and the DASH score (all P value for interaction \geq 0.05). However, the association between high physical activity level and T2D was primarily observed in participants without metabolic syndrome (P value for interaction < 0.001). Figure 2 visually depicts a marked difference between participants with and without metabolic syndrome. A similar interaction was observed in the age-stratified group, indicating

that the association between physical activity level and risk of T2D was stronger in young participants (Table 3, P value for interaction 0.02). A J-shaped relationship between physical activity and the risk of T2D was observed, which reached a nadir at 1100–1500 MET minutes/week (*P* for non-linear<0.001, Supplementary Fig. 2).

Mixed-effects linear model

Supplementary Table 4 presents data on how different levels of physical activity were associated with FBG change in this cohort. All three physical activity groups had a similar average baseline FBG level. During the follow-up period, the low physical activity group experienced an average increase in FBG of 0.20 mmol/L (95% CI, 0.15 to 0.26) compared to their baseline level. Conversely, participants in both the moderate and high physical activity groups exhibited average reductions in their FBG values compared to baseline levels (-0.27 mmol/L, 95% CI, -0.38 to -0.16 in moderate group and -0.18 mmol/L,95% CI, -0.30 to -0.07 in high level group, respectively). In the mixed-effects linear model, we observed a significant interaction of group × time (*P* group*time<0.001) on FBG.

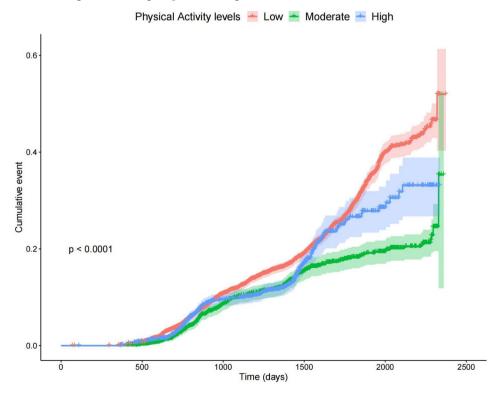


Fig. 1 Physical activity and risk of incident T2D. Kaplan-Meier estimation of association between physical activity and risk of incident T2D. Red, green, and blue lines represent for low (< 600 metablic equivalent-minutes per week), moderate (600−3000 metablic equivalent-minutes per week), and high (≥ 3000 metablic equivalent-minutes per week). Logrank P < 0.001 stands for observed differences between type 2 diabetes incidence between low, moderate and high physical activity groups were highly significant

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Table 3 Association between physical activity and risk of incident type 2 diabetes in stratified analysis

Variable Variable	N %	Low	Moderate HR(95%CI)	High HR(95%CI)	P for interaction
Sex					
Men	81.2	1.00 [Reference]	0.58 (0.49-0.69)	0.75 (0.64-0.88)	0.68
Women	18.8	1.00 [Reference]	0.60 (0.38-0.91)	0.92 (0.59-1.42)	
Age, years					
< 50	34.0	1.00 [Reference]	0.51 (0.40-0.66)	0.65 (0.52-0.82)	0.02
50-59	28.0	1.00 [Reference]	0.68 (0.51-0.90)	0.90 (0.69-1.17)	
≥60	38.0	1.00 [Reference]	0.74 (0.57-0.97)	1.03 (0.75-1.42)	
BMI, kg/m ²					
<24	34.0	1.00 [Reference]	0.61 (0.45-0.82)	0.81 (0.59-1.10)	0.90
24–28	47.3	1.00 [Reference]	0.58 (0.46-0.70)	0.80 (0.66-0.98)	
≥28	18.7	1.00 [Reference]	0.54 (0.40-0.73)	0.66 (0.48-0.89)	
Smoking Status					
Current smoker	41.6	1.00 [Reference]	0.59 (0.47-0.74)	0.72 (0.58-0.89)	0.83
Nonsmoker	58.4	1.00 [Reference]	0.57 (0.47-0.70)	0.81 (0.66-0.98)	
Alcohol Consumption					
Current drinker	45.7	1.00 [Reference]	0.63 (0.50-0.78)	0.76 (0.61-0.94)	0.23
Nondrinker	54.3	1.00 [Reference]	0.54 (0.43-0.66)	0.75 (0.62-0.92)	
Nighttime sleeping hours (hours/day)					
<5	7.9	1.00 [Reference]	0.56 (0.34-0.92)	0.65 (0.38-1.10)	0.77
5–7	24.7	1.00 [Reference]	0.61 (0.45-0.82)	0.72 (0.52-0.98)	
≥7	67.4	1.00 [Reference]	0.58 (0.48-0.69)	0.81 (0.68-0.97)	
Metabolic Syndrome					
Yes	53.1	1.00 [Reference]	0.54 (0.44-0.66)	0.85 (0.70-1.02)	< 0.001
No	46.9	1.00 [Reference]	0.65 (0.51-0.82)	0.69 (0.54-0.88)	
Hypertension					
Yes	70.5	1.00 [Reference]	0.59 (0.50-0.71)	0.84 (0.71-0.98)	0.08
No	29.5	1.00 [Reference]	0.57 (0.42-0.76)	0.57 (0.40-0.80)	
DASH diet score					
≤25	35.9	1.00 [Reference]	0.47 (0.44-0.68)	0.47 (0.44-0.68)	0.16
26-30	35.1	1.00 [Reference]	0.69 (0.53-0.89)	0.69 (0.53-0.89)	
≥31	29.0	1.00 [Reference]	0.65 (0.47-0.90)	0.65 (0.47-0.90)	

Abbreviations: BMI, body mass index; DASH, Dietary Approaches to Stop Hypertension; HDL, High density lipoproteins and the state of the properties of the

Adjusted model: model adjusted for sex (men or women) and age (continuous variable, years), smoking status (current or never), alcohol consumption (current or never), nighttime sleeping hours (<5, 5-7, or ≥ 7 h/day), TV-time (<2, 2-4, or ≥ 4 h/day), central obesity (yes or no), family history of diabetes (yes or no), education (middle school &below, high school, or college & above), average monthly income of each family member(<1,000, 1,000-3,000, or $\geq 3,000$ Yuan), marital status(married or single), DASH diet score (<25, 26-30, or <21 points), and body mass index (<24, $24\leq$ BMI <28, or <28 kg/m²), systolic blood pressure, low density lipoprotein, and triglyceride, except for the stratified factors

Discussion

In our prospective cohort study conducted in the Kailuan community, we investigated the association between three distinct levels of physical activity and the risk of developing T2D, specifically among individuals with prediabetes. Our findings suggest that moderate and high levels of physical activity were associated with lower risk of developing T2D, relative to low physical activity level. Moreover, the association between high physical activity level and incident T2D is primarily observed among participants without metabolic syndrome. During followup, a reduction of FBG value was observed in individuals with moderate and high physical activity levels, while an average increase of 0.2 mmol/L of FBG was found in

the low physical activity level group. The results of our study provided further evidence to support the potential benefits of physical activity on risk of T2D particularly in participants with prediabetes, which contributes to our understanding of T2D prevention.

Majority studies to date have focused on the relationship of dietary habits, physical activity, and sedentary behavior with risk of T2D [31–33]. The investigation into how varying levels of physical activity is related to the risk of T2D is scare, particularly for population at the prediabetes stage. Researches had emphasized the influence of physical activity on life quality or change of glycemic markers rather than T2D risks. For instance, a cross-sectional study involving 232 Northern Alberta

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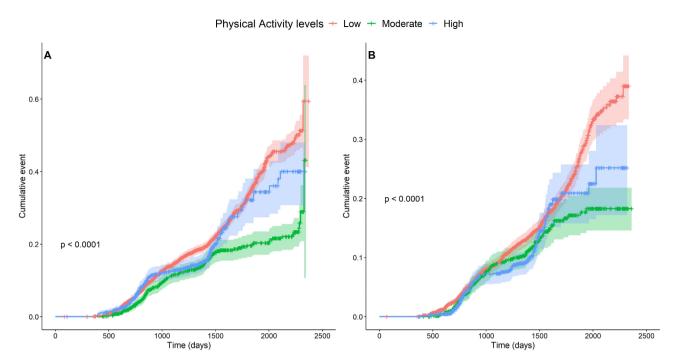


Fig. 2 Physical activity and risk of incident T2D stratified by metabolic syndrome status. Kaplan-Meier estimation of association between physical activity and risk of incident T2D stratified by metabolic syndrome status. **A** represents participants with metabolic syndrome and **B** represents individuals free of metabolic syndrome. Red, green, and blue lines represent for low (< 600 metablic equivalent-minutes per week), moderate (600−3000 metablic equivalent-minutes per week), and high (≥ 3000 metablic equivalent-minutes per week). Logrank P < 0.001 stands for observed differences between type 2 diabetes incidence between low, moderate and high physical activity groups were highly significant

residents with prediabetes revealed that those with higher levels of physical activity had an enhanced quality of life in comparison to their inactive counterparts [34, 35]. In the cohort of 10,308 British civil servants (Whitehall II study), 957 participants with prediabetes were followed up for 5 years [35], and moderate-to-vigorous physical activity was associated with better insulin sensitivity and β -cell function. Moreover, a RCT tested the individual and combined effects of physical activities and metformin on insulin sensitivity in 32 participants with prediabetes, exhibiting improved insulin sensitivity in exercise training with or without adding metformin [36]. Our study was focused on the relationship between physical activity and risk of T2D in the prediabetes population, providing more evidence for the prevention strategies of this high-risk population.

Our study showed that participants with moderate and high physical activity had 43% and 24% lower T2D incidence than those with low activity levels. The findings are consistent with a previous cohort study, demonstrating that participating in physical activity was associated with lower risk of T2D [37]. However, the previous cohort study of 8,796 prediabetic Spanish workers has identified physical activity as one of the key factors influencing prediabetes persistence and progression to T2D, but didn't compute MET values into different physical activity levels [38]. For general population, in a meta-analysis

including 28 prospective cohort studies, physical activity level was converted into MET h/week or marginal MET (MMET) h/week for the analysis [12]. The results revealed that higher level of leisure-time physical activity, specifically exceeding 11.25 MET-hours per week, was linked to a 26% lower incidence of T2D. However, most cohorts in the meta-analysis were not designed to solely access physical activity level, making it challengeable to explore the specific impact of physical activity on risk of T2D. Our study has linked different levels of physical activity with risk of developing T2D among participants with prediabetes, supporting the recommendation of physical activity for this specific population.

Remarkably, we found that the association between high physical activity and the incidence of T2D was observed primarily in participants without metabolic syndrome (*P* value for interaction < 0.001). Metabolic syndrome refers to the pathological state related symptoms such as obesity, hypertension, dyslipidemia, and hyperglycemia, and significantly increases T2D risk [9]. The underlying mechanism was not fully understood but might be due to several reasons. First, the higher level of physical activity is often accompanied by increased blood flow and elevated blood pressure, which may pose a potential long-term risk for participants with unstable blood glucose [38]. Second, intense workouts can stimulate the release of stress hormones, including adrenaline,

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which can stimulate the liver to release glucose [39]. Third, the moderate physical activity may bring more benefits than high level physical activity. A recent systematic review and meta-analysis of 126 studies, including 8 focusing on prediabetics, identified a J-shaped relationship between physical activity and HbA_{1c} levels [40]. For prediabetes, the optimal physical activity level was found to be 1,100 MET-minutes per week, achieving a reduction in HbA_{1c} of -0.38% to -0.24%. This optimal physical activity level aligns with the moderate physical activity level defined in our study (600-3000 MET-minutes per week). These factors highlight potential concerns for individuals with unstable blood glucose during high level physical activity [39]. Although more evidence is needed for optimal physical activity level to improve glycemic control in prediabetics, American College of Sports Medicine often recommend a moderate level of physical activity for individuals with chronic diseases [41].

Our results indicated that the moderate physical activity group had lowest risk of T2D. After the physical activity level exceeded 4000 MET minutes/week, protective effects of physical activity against T2D diminished (Supplementary Fig. 2). Our finding suggests the existence of an "optimal range" where moderate levels of physical activity could benefit metabolic health without the potential stress or negative effects associated with very high levels of physical activity. A systematic review and meta-analysis of eight studies focusing on prediabetic individuals identified a J-shaped relationship between physical activity and HbA1c levels, which is consistent with our findings [42]. The underlying mechanisms, though not fully understand, might be multifaceted. Aerobic and resistance exercises, as major forms of moderate physical activity, have been shown to enhance insulin sensitivity in skeletal muscles and improve glucose transport, thereby demonstrating their effectiveness in controlling blood glucose levels [43]. However, prolonged high-intensity physical activity may increase the production of pro-inflammatory cytokines, leading to elevated muscle oxidative stress, which may create a vicious cycle that further escalates inflammation [44], thereafter increases the risk of T2D. In contrast, moderate intensity activities may be more sustainable for longterm adherence and less likely to cause hypoglycemia or other stress responses in the body [45]. Therefore, promoting and sustaining physical activity are essential priorities for managing blood glucose levels and improving overall health in individuals with prediabetes.

Limitations

Our study has several strengths such as its large sample size which allows for robust statistical analysis and capture of a relatively large number of T2D incident events. However, this study also has several limitations that should be acknowledged. First, physical activity was assessed once at baseline, which limits the possibility to analyze long-term patterns and changes in physical activity over time. Second, the physical activity data was acquired from questionnaires, and misclassification bias introduced by self-reported information were inevitable. Third, participants with prediabetes were defined by FBG measurement at baseline, which might be underestimated without including HbA1c and/or 2 h blood glucose after glucose tolerance test in the diagnostic criteria. Lastly, the mean follow-up duration of 3.6 years is relatively short; however, reverse causality bias is unlikely in our study since we excluded individuals with existing T2D or taking anti-diabetic medication at baseline and included only the first episode of T2D after baseline.

Conclusion

In summary, our study provides compelling evidence that engagement in physical activity holds a pivotal role in mitigating the occurrence of T2D among individuals classified as prediabetes based on FBG criteria. These results underscore the significance of integrating physical activity as a fundamental element in the management strategies for individuals with prediabetes.

Abbreviations

BMI Body mass index
DBP Diastolic blood pressure

DASH dietary approaches to stop hypertension

FBG Fasting blood glucose

HDL-C high-density lipoprotein-cholesterol LDL-C low-density lipoprotein-cholesterol

SBP Systolic blood pressure
T2D Type 2 diabetes
TC Total cholesterol
TG Triglyceride

Supplementary Information

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Supplementary Material 1

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Author contributions

WY, YW, SW, and LS conceived and designed this work. WY, YW, YC, SC, and XG researched data. WY analyzed the data. WY, YW, SW, and LS interpreted the results and drafted the manuscript. SW and LS supervised the study. All authors contributed to the review and revision of the manuscript and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Data availability

All data collected in the current study are available after permission of the Kailuan Institutional Review Board. Written proposals can be addressed to the corresponding authors for appropriateness of use.

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Declarations

Ethics approval and consent to participate

The study was performed according to the guidelines of the Helsinki Declaration and was approved by the Ethics Committee of Kailuan General Hospital (Approval Number: 2006–05). All participants were agreed to take part in the study and provided informed written consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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