

Independent and joint associations of total physical activity and sedentary time on the risk of type 2 diabetes in adults

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Abstract

Background/objectives: Physical activity (PA) and sedentariness are two common lifestyle-related behaviours associated with obesity and type 2 diabetes (T2D). However, evidence regarding the association between physical activity and sedentary or sitting time (ST) in the combination and type 2 diabetes remains inconclusive. This study assessed the relationship between physical activity, sedentary in the combination and risk of T2D in Vietnamese adults.

Subjects/methods: A hospital-based case-control study was conducted in Vietnam during 2013–2015. A total of 599 newly diagnosed diabetic cases (age 40–65 years) and 599 hospital-based controls, frequency matched by age and sex, were recruited in Hanoi, capital city of Vietnam. Information on physical activity and sitting time, together with demographics, habitual diet and lifestyle characteristics, anthropometrics was obtained from direct interviews using a validated and reliable questionnaire. Unconditional logistic regression analyses were performed to examine this association. **Results:** After adjusting for confounding factors, an inverse association with T2D was found for the high tertile of moderate activity, equivalent more than 5 hours/week compared to the low tertile adjusting for age and sex: adjusted odds ratio (aOR) = 0.71 (95% CI: 0.54, 0.93; $P < 0.05$). Conversely, the high ST (>32 h/

week) was significantly associated with increased odds of T2D compared to the low tertile (<21 h/week), controlling for total PA, BMI, body fat percent and other variables (model 3): aOR = 2.31 (95% CI: 1.67, 3.21; $P < 0.001$). When using the Low PA and High/medium ST group as the reference group, “Low PA & Low ST” and “Medium/high PA & Low ST” groups appeared to be significantly associated with reduced odds of T2D in the full models. The reduced odds in both groups were similar; 42% for the “Low PA & Low ST” group and 49% for the “Medium/high PA & Low ST” group.

Conclusions: High tertile of moderate physical activity was associated with a lower T2D risk in Vietnamese adults while the high ST (>32 h/week) was significantly associated with increased risk of T2D. Active lifestyle of those who were less sedentary and more active in physical activity was found associated with lower risk of T2D.

Keywords: Case-control study; physical activity; sitting time; risk factors; type 2 diabetes;

1. Introduction

The number of people with type 2 diabetes (T2D) has increased substantially over the past decade (WHO 2011), with an estimated 415 million adults with diabetes affected worldwide in 2015. Particularly, the Western Pacific region alone accounted for about 37% (~ 154 million) (IDF 2015). The estimated annual global health spending attributable to diabetes reached to USD 1099 billion (Yisahak et al. 2014). T2D is known to impose serious morbidities and complications related to cardiovascular diseases (Lim et al. 2015, WHO 2016) and premature deaths (Saydah et al. 2002). The role of lifestyle modification in reducing T2D risk has raised in studies recently (The Diabetes Prevention Program 2002).

Physical activity (PA) and sedentariness are two common lifestyle-related behaviours associated with obesity and T2D. PA is classified as a movement, requiring at least 1.6 units of metabolic equivalent (MET) value. Sedentary behaviour, or ‘sitting’, in turn refers to the absence of movement, requiring 1.5 METs or less (Ainsworth et al. 2000), and may impact on health independently by increasing chronic inflammation (Laufs et al. 2005, Toledo and Goodpaster 2013), or simply through displacement of PA (Hammer, Stamatakis, and Steptoe 2014). A meta-analysis indicated that regular participation in moderate PA compared to sedentary can substantially reduce the risk of T2D (Jeon et al. 2007). Studies often consider PA and sedentary time (ST) individually while these behaviours are mutually linked (Hamilton et al. 2008). The combination of high PA and low ST was associated with a lower risk of developing obesity (Boone et al. 2007) and cardiovascular diseases (Chaput et al. 2013, Halloway et al. 2016), but little known for T2D.

As an economically emerging country in Southeast Asia, Vietnam has undergone an upward trend in the prevalence of T2D over the past decade (Nguyen et al. 2015). Early study indicated that the prevalence of T2D was only 1.4% in 1994 among urban residents (Quoc et al. 1994), however, it peaked at 12.4% in 2010 (Ta et

al. 2010). The upward trend may be attributed to advancing age, overweight/obesity or a sedentary lifestyle (Pham and Eggleston 2015). Occupational PA comprises a major portion of total PA in Vietnam due to the large population living in rural areas with the high physical demands of jobs. The decline in occupational PA was evident as increasing the pace of urbanisation which may impose Vietnamese adults at more sedentary (Bui et al. 2015). However, whether the change of PA is linked to T2D risk remains unknown. We thus investigate the association between PA and ST with T2D risk among adults, independently or in the combination.

2. Methods

2.1. Study design and participants

A case-control study was conducted between 2013 and 2015. Details of the study design and methodology were described elsewhere (Nguyen et al. 2016). Briefly, a total of 599 T2D cases and 599 controls were recruited. Newly diagnosed T2D patients aged 40-65 years were recruited from the Endocrinology Department of a general hospital in Hanoi, capital city of Vietnam. Hospital-based controls, being frequency-matched to cases on sex and age (± 3 years) on a 1:1 ratio, were selected from outpatient clinics of the same hospital.

2.2. Diagnoses of case and control status

Confirmed cases of T2D were determined through fasting glucose and/or 2 hour-oral glucose tolerance test. Similarly, eligible controls undertook such testing on the day of their outpatient clinic visit. Case-control status was diagnosed according to the 2006 World Health Organization's criteria.

2.3. Physical activity and sedentary assessment

PA and ST were assessed by a face-to-face interview. The PA questions were adapted from the validated International Physical Activity Questionnaire-Short Form (Tran et al. 2013) and

WHOSTEPs (WHO 2008) with nine modified items. Participants were asked to report the number of hours engaging in different levels of physical activity per week during the last year: (a) strenuous sports including jogging, bicycling on hills, tennis, racquet ball, swimming, aerobics; (b) vigorous work including moving heavy furniture, shovelling, weight lifting, loading/unloading trucks, or equivalent manual labor; (c) moderate activity including housework, brisk walking, golfing, bowling, bicycling on level ground, gardening, walking and tai chi. Total ST including sitting time at home, work, travel, watching television, eating meals, readings, listening radios, playing cards, or computer games, etc. was asked

2.4. Other variables

A trained interviewer used a unique questionnaire to interview participants which each took about 40 minutes to complete. The interview was to obtain information on socio-demographic characteristics, family history of diabetes, dietary habits and lifestyle (PA, alcohol consumption and cigarette smoking).

After interview, anthropometric characteristics and blood pressures were measured using standard instruments and protocols. Body fat percent was measured by Bioelectrical Impedance Analysis (TanitaCorp., Tokyo). Total cholesterol was extracted from patient log-books or medical records.

2.5. Statistics

Characteristics between case and control groups were compared using chi-square (χ^2), two-sample t-test or Wilcoxon rank-sum test. For each PA variable, the tertile among controls was used as the cut-off point, resulting in three increasing levels of exposure, whereas the lowest level was taken as the reference group. The association of total PA with T2D was expressed in terms of metabolic equivalent task hours per week (METs-h/week). Following the compendium of physical activities (Ainsworth et al. 2000), intensity codes 8.5, 6.0 and 4.5 MET were assigned for strenuous sports, vigorous work and moderate activity, respectively. Total PA was the sum of all types of PA then was classified into tertile for

analyses (low, <13 METs-h/week; medium, 13–24 METs-h/week; high, >24 METs-h/week). Total ST was also divided into tertile (low, <21 h/week; medium, 21–32 h/week; high, >32 h/week). PA and ST were further combined to form four groups. The “Low PA & Medium/high ST” was used as the reference group, representing the assumed lowest level of energy expenditure. Unconditional logistic regression models were used to compute odds ratios (ORs) with accompanying 95% confidence intervals (CIs) as estimates of associations of total PA and total ST, separately and in combination, with T2D risk. Tests for linear trend were conducted to examine the dose-response relationship. A two-sided p-value <0.05 was taken to indicate statistical significance. Stata 12.0 for windows (StataCorp LP., College Station, TX) was used for the statistical analysis.

3. Results

Table 1 shows characteristics of the sample by case-control status. The sample is 54% females and an average age of 58 years (SD=6.5) for all participants. Univariate analysis indicates that case patients had higher BMI, WHR, total energy intake and prevalence of hypertension, but had lower levels of total cholesterol, educa-

Combined effect of physical activity and sedentary time on diabetes risk in Vietnamese adults (Updated 30.06.2016)

Table 1: Demographics and characteristics of study subjects

	Cases	Controls	p ^a
No. of subjects	599	599	
Age, years, mean (SD)	58.6 (6.5)	58.3 (6.6)	Matched
Female, n (%)	324 (54.0)	324 (54.0)	Matched
Secondary school completion ^b , n (%)	283(47.2)	169 (28.2)	<0.001

Family history of diabetes, n (%)	158 (26.4)	56 (9.3)	<0.001
Alcohol consumption, n (%)	275 (45.9)	253 (42.2)	0.20
Smoking status, n (%)			0.051
Never	408 (68.1)	444 (74.1)	
Former	100 (16.7)	88 (14.7)	
Current	91 (15.2)	67 (11.2)	
Hypertension, n (%)	121 (20.2)	90 (15.0)	0.019
Total cholesterol, mmol/l, mean (SD)	5.4 (1.5)	5.5 (1.2)	0.017
Body mass index, kg/m ² , mean (SD)	23.5 (3.2)	22.7 (2.9)	<0.001
Body fat percent, %, mean (SD)	22.2 (8.7)	19.0 (6.7)	<0.001
Total energy, kcal, mean (SD)	1532 (565)	1330 (474)	<0.001
Strenuous activity, n (%)	58 (9.7)	46 (7.7)	0.21
Vigorous activity, n (%)	17 (2.8)	4 (0.7)	NA
Moderate activity, h/week, mean (SD)	3.6 (3.0)	4.6 (3.4)	<0.001
Total physical activity, MET-h/week, mean (SD)	17.0 (13.9)	21.4 (15.2)	<0.001
Lifelong physical activity			<0.001
Never been much involved, n (%)	276 (46.1)	189 (31.5)	
Intermittently active, n (%)	87 (14.5)	93 (15.5)	
Always been involved, n (%)	236 (39.4)	317 (53.0)	
Sedentary time, h/week, mean (SD)	38.5 (21.7)	30.2 (17.6)	<0.001

Abbreviations: MET: metabolic equivalent; SD, standard deviation.

^aBased on t-test for continuous variables and χ^2 test for categorical variables.

^bParticipants completed secondary school education (9th grade) according to the Vietnamese Education System.

tional attainment and physical activity than their control counterparts. The proportion of first-degree family history of diabetes was three-fold higher in the case group than the controls. Compared to the control group, the diabetic patients were less physically active. The average of total PA among case patients was lower but ST was higher than that of their controls.

The results of logistic regression analyses for PA and ST were presented in Table 2. After adjusting for confounding factors, an inverse association with T2D was found for the high tertile of moderate activity, equivalent more than 5 hours/week compared to the low tertile adjusting for age and sex: adjusted odds ratio (aOR) = 0.71 (95% CI: 0.54, 0.93; $P < 0.05$). This association remained significant after adjusting BMI, body fat percent, ST and other variables in model 2 and model 3. For the high tertile of total PA (>24 MET-h/week), reduced odds of T2D was evident after adjusting for age and sex, but appears to be borderline in model 2 and model 3. Conversely, the high ST (>32 h/week) was significantly associated with increased odds of T2D compared to the low tertile (<21 h/week), controlling for total PA, BMI, body fat percent and other variables (model 3): aOR = 2.31 (95% CI: 1.67, 3.21; $P < 0.001$).

The joint associations of total PA and ST on T2D risk, in comparison to the “high-risk” reference group (“Low PA & Medium/high ST”), using different logistic regression models (Table 2). We found consistent inverse associations with T2D for two groups of combined exposures: aOR = 0.58 (95% CI: 0.36, 0.92) for “Low PA & Low ST”; and aOR = 0.51 (95% CI: 0.35, 0.74) for “Medium/high PA & Low ST” group. However, a non-significant association between the “Medium/high PA & Medium/high ST” group and T2D was found with aOR = 0.74 (95% CI: 0.53, 1.01).

4. Discussion

This study retrospectively examined PA and ST associations with T2D separately and in the combination. High levels of PA including moderate and total PA were inversely associated with odds

Table 2: Independent and joint associations of habitual physical activity and sedentary time with risk of type 2 diabetes

	Cases, n (%)	Controls, n (%)	Model 1 ^a OR (95% CI)	Model 3 ^b OR (95% CI)	Model 3 ^c (95% CI)
Habitual physical activity					
Moderate activity (h/week)					
<3	254 (42.4)	216 (36.1)	1.00 (reference)	1.00 (reference)	1.00 (reference)
3-5	169 (28.2)	176 (29.4)	0.81 (0.61-1.07)	0.88 (0.64-1.20)	0.86 (0.62-1.18)
>5	176 (29.4)	207 (34.5)	0.71 (0.54-0.93)	0.72 (0.53-0.97)	0.72 (0.53-0.98)
p-trend ^d			0.14	<0.05	<0.05
Total physical activity (MET-h/week)					
<13	239 (39.9)	208 (34.7)	1.00 (reference)	1.00 (reference)	1.00 (reference)
13-24	190 (31.7)	193 (32.2)	0.85 (0.64-1.11)	0.91 (0.67-1.24)	0.87 (0.64-1.20)
>24	170 (28.4)	198 (33.1)	0.74 (0.56-0.97)	0.74 (0.54-1.01)	0.74 (0.54-1.01)
Per 5-MET-h/week			0.90 (0.86-0.93)	0.91 (0.87-0.95)	0.90 (0.86-0.94)
p-trend ^d			0.25	<0.01	<0.01
Life long physical activity					
Never been much involved	276 (46.1)	189 (31.5)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermittently active	87 (14.5)	93 (15.5)	0.63 (0.45-0.90)	0.51 (0.35-0.76)	0.47 (0.31-0.70)
Always been involved	236 (39.4)	317 (53.0)	0.49 (0.38-0.63)	0.50 (0.38-0.67)	0.51 (0.38-0.68)
p-trend ^d			<0.01	<0.01	<0.01
Total sedentary time (h/week)					
<21	159 (26.5)	218 (36.4)	1.00 (reference)	1.00 (reference)	1.00 (reference)
21-32	129 (21.5)	182 (30.4)	1.00 (0.74-1.36)	1.05 (0.74-1.48)	1.03 (0.72-1.46)
>32	311 (52.0)	199 (33.2)	2.37 (1.78-3.14)	2.57 (1.87-3.55)	2.31 (1.67-3.21)
Per 5 h/week			1.13 (1.10-1.17)	1.13 (1.09-1.18)	1.12 (1.08-1.16)

p-trend ^d									
Combined PA and ST ^e									
Low PA & Medium/high ST	184 (30.7)	141 (23.5)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	<0.01
Medium/high PA & Medium/high ST	256 (42.7)	240 (40.1)	0.80 (0.60-1.06)	0.80 (0.60-1.06)	0.76 (0.56-1.04)	0.74 (0.53-1.01)	0.74 (0.53-1.01)	0.74 (0.53-1.01)	<0.01
Low PA & Low ST	55 (9.2)	67 (11.2)	0.59 (0.39-0.91)	0.59 (0.39-0.91)	0.54 (0.34-0.86)	0.58 (0.36-0.92)	0.58 (0.36-0.92)	0.58 (0.36-0.92)	<0.01
Medium/high PA & Low ST	104 (17.4)	151 (25.2)	0.49 (0.35-0.70)	0.49 (0.35-0.70)	0.48 (0.33-0.70)	0.51 (0.35-0.74)	0.51 (0.35-0.74)	0.51 (0.35-0.74)	<0.01
p-trend ^d									

Abbreviations: CI: confidence interval; OR: odds ratio; PA: physical activity; ST: sedentary time.

^a Adjusted for age (years) and sex (female, male)

^b Adjusted for variables included in Model 1 plus education level (secondary school or lower, above secondary school), family history of diabetes in first-degree relatives (yes, no), alcohol consumption (yes, no), smoking status (never, former, current), hypertension (yes, no), total cholesterol (mmol/l), total energy intake (kcal) and mutual adjustment for physical activity (MET-h/week) and sedentary time (h/week).

^c Adjusted for variables included in Model 2 plus BMI (kg/m²) and body fat (%).

^d Based on unconditional logistic regression, treating physical activity and sedentary time as continuous variable.

^e Low PA: ≤ 13 MET-h/week (1st tertile); Medium/high PA: > 13 MET-h/week (2nd and 3rd tertiles); Low ST: ≤ 21 h/week (1st tertile); Medium/high ST: > 21 h/week (2nd and 3rd tertiles).

of T2D after adjusting for confounders. For each 5-MET-h/week increment, about 6-14% reduction of T2D risk in the full model. Sedentary or sitting time was associated with a slightly increased risk of T2D for spent 21-32 h/week (3%), but become robust as spent more than 32 h/week (131%) in sedentary. For each 5 h/week increment, about 12% of substantially increased odds of T2D was found with P for trend value <0.01 . The joint association of “low PA and low ST” and “medium/high PA and low ST” were inversely associated with T2D as compared to the reference group (“Low PA & Medium/high ST”). However, there was no significant association with T2D for the combination between Medium/high PA and Medium/high ST in models.

Our findings of independent associations of PA and ST with T2D are consistent with previous studies across different populations. A meta-analysis indicated that PA of moderate intensity was substantially associated with reduced risk of developing T2D in cohort studies. Those who regularly engaged in moderate PA had a 30% lower risk of T2D risk as compared with sedentary individuals (Jeon et al. 2007). Similarly, about 29% reduced odds of T2D was found among participants who regularly participated in moderate physical activities compared to participant spent less than three h/week for these activities. However, a cohort study conducted in multiple ethnic populations showed that moderate PA was non-significantly associated with T2D risk for participants who spent more than 4 h/week compared to those spent less than one h/week, except the Caucasian (Steinbrecher et al. 2012). The weaker association observed in Japanese American adults may be due to non-Caucasian groups was more susceptible to T2D at lower BMI. Our study finding was consistent with previous studies which supported for the hypothesis that high ST was an independent risk factor for T2D (Hamilton, Hamilton, and Zderic 2014). For individuals who spent more than 32 h/week in sedentary, the odds of T2D substantially increased 131% as compared to those spent less than 21 h/week, accounting for BMI, body fat percent, total PA, age, sex, educational levels, family history of diabetes, alcohol consumption, smoking status, hypertension and total cholesterol (model 3). For each 5

h/week increment of sitting, the odds of T2D increased about 12% with P for trend <0.01 .

The joint association of total PA and ST in our study showed that ST remains a strong risk factor for T2D as combining with total PA. When using the Low PA and High/medium ST group as the reference group, “Low PA & Low ST” and “Medium/high PA & Low ST” groups appeared to be significantly associated with reduced odds of T2D in the full models. The reduced odds in both groups were fairly similar; 42% for the “Low PA & Low ST” group and 49% for the “Medium/high PA & Low ST” group. A previous study (Bell et al. 2014) also indicated that the combined effect of high PA and low leisure time sitting after 10 years of follow-up was associated with 49% reduction of obesity risk, compared to the reference group (Low PA & high ST). Despite the different levels of PA engagement, individuals who had a low ST were beneficial in reducing the risk of T2D. In contrast, for the medium/high sedentary individuals who spent less than 21 h/week were at high risk of having T2D regardless of their engagement in medium/high PA.

The mechanisms underlying this interaction are unclear. In principle, lower levels of ST may strengthen protective effects of higher physical activity, either through independent physiological mechanisms (Hamilton, Hamilton, and Zderic 2007) or as a marker for greater engagement in low-intensity activity including standing (Katzmarzyk 2014). PA and ST combinations may also simply refer incremental increases in energy expenditure, with the lowest PA/highest ST group expending the least amount of energy overall, and the highest PA/lowest ST group expending the most. In the present study, joint associations of medium/high PA and low ST on risk of T2D were stronger compared with independent association of high moderate PA or high total PA. The strength of odds reduction in the combination may be explained by adding the medium and high PA levels instead of high PA used in independent analysis.

Several limitations should be mentioned. First, a cause-effect relationship between exposures (PA and ST) and T2D cannot be established due to the retrospective cross-sectional design. Second, there are inherent biases from this observational study. To minimise

selection bias, only incident T2D patients were chosen while non-diabetic controls were recruited from the outpatient clinics of the same hospital. These control subjects were frequency matched to the cases by age and sex but unlikely to share the same risk profiles. Third, recall bias may lead to spurious associations between exposures and the outcome of interest (Gordis 2000). In this study, the direct interview of both case and control groups by the same trained interviewer to reduce recall bias and improve the accuracy of information obtained. Finally, our findings cannot be generalised to the entire Vietnamese population despite all participants were recruited from the same catchment area within Hanoi city.

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Conflict of Interests

All authors declare that they have no conflict of interest.

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Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

All participants gave their written informed consent before participating in the study. The study complied with the Declaration of Helsinki and was approved by the Human Research Ethics Committee of Curtin University under the number: HR105/2013.

Informed consent:

Informed consent was obtained from all individual participants included in the study.

Abbreviation: - T2D: Type 2 diabetes, - EGCG: Epigallocatechin-3-gallate, - OR: Odds ratio,
-CI: Confidence interval, - BMI: Body mass index, - WHR: Waist-hip ratio

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