Association between physical activity and insulin resistance in Iranian adults: National Surveillance of Risk Factors of Non-Communicable Diseases (SuRFNCD-2007)

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Abstract

Background. Insulin resistance is an underlying mechanism of metabolic syndrome. We attempted to determine the association between physical activity and insulin resistance in Iranian adults.

Methods. The data of the third national Surveillance of Risk Factors of Non-Communicable Diseases (SuRFNCD-2007) in Iran were used. We ran the Global Physical Activity Questionnaire (GPAQ) over a nationally representative sample of 3101 adults. Total physical activity (TPA) was calculated using metabolic equivalents (MET) for intensity of physical activities. Insulin resistance was measured by the homeostasis model assessment of insulin resistance (HOMA-IR).

Results. When physical activity was classified into high, moderate, and low categories, HOMA-IR values significantly increased from the high category to the moderate and low categories (p<0.01). After adjustment for age, area of residence, smoking, and body mass index (BMI), TPA (r=−0.26, p<0.01 in males and r=−0.21, p<0.01 in females), duration of vigorous-intensity activity (r=−0.28, p<0.01 in males and r=−0.18, p=0.01 in females), duration of moderate-intensity activity (r=−0.16, p=0.01 in males and r=−0.17, p<0.01 in females), and the time spent on sedentary behaviors (r=−0.16, p<0.01 in males and r=−0.22, p<0.01 in females) were significantly correlated to HOMA-IR. The prevalence of physical inactivity increased linearly with increasing HOMA-IR quintiles.

Conclusions. Our findings indicate a significant relationship between physical inactivity and insulin resistance. For communities in a transition phase of lifestyle, encouraging physical activity may help prevent insulin resistance and its adverse consequences.

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Introduction

Insulin resistance has an important role in the pathogenesis of several conditions including obesity (Esteghamati et al., 2008a), hypertension (Esteghamati et al., 2008c), type 2 diabetes (Meigs et al., 2007), dyslipidemia (Semenkovich, 2006; Chapman & Sposito, 2008), and cardiovascular disease (Bonora et al., 2007, 2002). We and others have recently shown that the prevalence of such conditions is rather high in the Iranian population (Esteghamati et al., 2008a, 2008b; Janghorbani et al., 2007). As a result of progressive urbanization and industrialization, adults tend to experience a decline in their level of physical activity and replacement of their comparatively healthier traditional diets by calorie-dense, high-fat foods (Ghassemi et al., 2002). These changes in lifestyle seem to be making obesity an increasingly common problem in the country, and may subsequently lead to insulin resistance and its adverse metabolic consequences.

Physical activity has been suggested to improve insulin sensitivity (Bradley et al., 2008; Balkau et al., 2008; Nowak et al., 2008; Kavouras et al., 2007). However, the association between different levels of physical activity, defined by an international standard questionnaire, and insulin resistance is yet to be explored in large scale population-based studies. Furthermore, it is interesting to explore this association in different domains of physical activity (i.e., work, commuting, and leisure time) and evaluate the independent association of sedentary lifestyle behaviors with insulin resistance. It is particularly important to discover ways to improve health conditions in populations undergoing socio-cultural phase transitions. The homeostasis model assessment of insulin resistance (HOMA-IR) is a practical method for estimating insulin resistance in epidemiologic studies (Wallace et al., 2004). For the first time in Iran, we investigated in this study the association between HOMA-IR and physical activity, assessed by the Global Physical Activity Questionnaire (GPAQ) (WHO, 2008), in a large national-representative sample of Iranian adults.
Materials and methods

Participants

This study was based on the data of the third SuRFNCD in Iran carried out in 2007. Details of the survey are reported elsewhere (CDC of Iran, 2008). In brief, a cluster sampling scheme was applied to randomly select a representative sample of Iranian adults aged 25–64 years. Addresses were randomly selected from the postal codes across the country. Two males and two females were assigned to each age category (15–24, 25–34, 35–44, 45–54, and 55–64 years). The sample taken from each province was proportional in size to the total population of the province. For instance, 51 (1020 participants) and 2 (40 participants) clusters were taken from Tehran and Ilam, the largest and smallest provinces in Iran, respectively. Trained healthcare professionals conducted household interviews and physical examinations. Interviewers were instructed on details of the survey and how to conduct the interviews in a 1-day workshop in Tehran prior to the commencement of the survey. All interviews were in Persian. The data were recorded in standardized questionnaires and were rechecked based on a predetermined schedule. Blood sampling was done within a few days of the interview. The survey received ethics approval from the Center for Disease Control (CDC) of Iran and all participants gave informed consent.

Physical activity assessment

The second version of the GPAQ was employed in the survey (WHO, 2008). This questionnaire, which has been developed by WHO, is composed of 16 questions about physical activity in a typical week and assesses physical activity in three domains, namely, work, transportation, and recreational activities. The evaluation of physical activity in three domains is one of the factors that make GPAQ distinct from other questionnaires including the less sophisticated, short version of the international physical activity questionnaire IPAQ (available at: http://www.ipaq.ki.se). It also determines the intensity of activity (i.e., vigorous or moderate) in each domain as well as the time spent on sedentary behaviors such as watching TV. Sedentary behavior was defined as activities such as sitting at a desk, traveling in car/bus/train, reading, working with computer, and watching television.

In order to measure energy expenditure, the concept of metabolic equivalents (MET) was used. MET is the ratio of a person’s working metabolic rate relative to the resting metabolic rate. One MET is defined as the energy cost of sitting quietly, and is equivalent to a calorific consumption of 1 kcal/kg/h. It is estimated that a person’s calorific consumption is four times as high when being moderately active, and eight times as high when being vigorously active. Therefore, when calculating a person’s overall energy expenditure using the GPAQ data, four METs are assigned to the time spent on moderate-intensity activities, and eight METs to the time spent on vigorous activities. The total physical activity score (TPA) was calculated as the sum of all MET×minutes for moderate- or vigorous-intensity physical activity performed in work, commuting, and recreation.

Participants were classified into the following three categories, as defined by the GPAQ analysis framework:

1) High: a person reaching any of the following criteria is classified in this category:
   • Vigorous-intensity activity on at least 3 days a week achieving a minimum of at least 1500 MET-minutes per week, or
   • Seven or more days of any combination of walking and moderate- or vigorous-intensity activities achieving a minimum of at least 3000 MET-minutes per week.
2) Moderate: a person not meeting the criteria for the “high” category, but meeting any of the following criteria is classified in this category:
   • Three or more days of vigorous-intensity activity of at least 20 min per day, or
   • Five or more days of moderate-intensity activity or walking of at least 30 min per day, or
   • Five or more days of any combination of walking and moderate- or vigorous-intensity activities achieving a minimum of at least 600 MET-minutes per week.
3) Low: a person not meeting any of the above mentioned criteria falls in this category.

Physical examination and biochemical measurements

Weight and height of participants were determined in light clothing and without shoes. Portable calibrated electronic weighing scale and portable measuring inflexible bars were used. Waist circumference was measured using constant tension tape at the end of a normal expiration, with arms relaxed at the sides, at the midpoint between the lower part of the lowest rib and the highest point of the hip on the mid-axillary line. Blood pressure was measured with a calibrated Omron M7 sphygmomanometer (HEM-780-E). The average of three measurements, made at intervals of 5 min, was used for analysis. The body mass index (BMI; kg/m²) was calculated according to the Quetelet formula. Venous blood (10 ml) was taken in sitting position, collected in four tubes, centrifuged immediately, and transferred under cold chain condition to the Central Reference Laboratory of Ministry of Health of Iran (Tehran, Iran). Fasting plasma glucose (FPG) was measured by the enzymatic colorimetric method using glucose oxidize test (intra- and inter-assay coefficients of variation of 2.1% and 2.6%, respectively). One tube was treated with 2 μl sodium fluoride for glucose preservation to enhance the accuracy of glucose measurement. The two remaining tubes were transferred to the endocrine laboratory of Vahid Hospital (Tehran University of Medical Sciences, Tehran, Iran) for fasting plasma insulin (FPI) measurement. Plasma insulin was measured by the radioimmunoassay method (Immunotech, Prague, Czech Republic). Sensitivity was 0.5 mU/ml, and the upper limits of intra- and inter-assay coefficients of variation were 4.3 and 3.4, respectively.

Statistical analysis

HOMA-IR was calculated as FPG (mmol/l)/× FPI (mU/l)/22.5 (Matthews et al., 1985). Complex sample survey analysis was performed using SPSS 16 for Windows (Chicago, IL). Data were weighted for sex, age, and residential area (urban/rural) strata, according to the population of Iran (national census, 2006). The method of general linear modeling was used to adjust the variables of interest for factors such as age, sex, area of residence, BMI, and smoking, and to compare the adjusted variables across quintiles of HOMA-IR (1.237, 1.556, 1.947, and 2.822) and categories of physical activity. Multivariate regression analysis was used to find independent correlates of HOMA-IR, p<0.05 was considered statistically significant.

Results

After excluding participants with missing data in questionnaires (n=113), analyses were performed in the remaining 3101 individuals.

Table 1

<p>| Variables (except age, sex, and area of residence) are standardized for age, sex, and residential area of the 2006 population of Iran. |</p>
<table>
<thead>
<tr>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOMA-IR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.2 (0.2)</td>
<td>26.6 (0.2)</td>
<td>25.9 (0.2)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>83.8 (1.7)</td>
<td>83.3 (1.7)</td>
<td>76.2 (1.7)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>3.9 (0.5)</td>
<td>4.6 (0.7)</td>
<td>6.2 (0.8)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>123 (1.5)</td>
<td>121 (1.4)</td>
<td>176 (1.5)</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/l)</td>
<td>5.30 (0.08)</td>
<td>5.12 (0.06)</td>
<td>5.03 (0.05)</td>
</tr>
<tr>
<td>Fasting plasma insulin (mU/l)</td>
<td>9.78 (0.24)</td>
<td>9.74 (0.27)</td>
<td>9.24 (0.21)</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.71 (0.08)</td>
<td>2.32 (0.07)</td>
<td>1.99 (0.06)</td>
</tr>
</tbody>
</table>

Variables (except age, sex, and area of residence) are standardized for age, sex, and residential area of the 2006 population of Iran.

a National estimate rounded to the nearest million.
| Mean (SE). |
| % (SE). |
Table 2
Association between several features of physical activity with HOMA-IR after adjustment for potential confounders (SuRFNCD-2007, Iran).

<table>
<thead>
<tr>
<th></th>
<th>Males Standardized beta</th>
<th>Females Standardized beta</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total physical activity (TPA)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Adjusted for</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age and area of residence</td>
<td>−0.28</td>
<td>−0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age, area of residence, BMI, and smoking</td>
<td>−0.26</td>
<td>−0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age, area of residence, BMI, smoking, and duration of sedentary behaviors</td>
<td>−0.24</td>
<td>−0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Duration of vigorous activity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age and area of residence</td>
<td>−0.30</td>
<td>−0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>Age, area of residence, BMI, and smoking</td>
<td>−0.28</td>
<td>−0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>Age, area of residence, BMI, smoking, duration of moderate activity, and sedentary behaviors</td>
<td>−0.25</td>
<td>−0.01</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Duration of moderate activity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age and area of residence</td>
<td>−0.15</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>Age, area of residence, BMI, and smoking</td>
<td>−0.16</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>Age, area of residence, BMI, smoking, duration of vigorous activity, and sedentary behaviors</td>
<td>−0.13</td>
<td>0.03</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Duration of sedentary behaviors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age and area of residence</td>
<td>0.17</td>
<td>0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age, area of residence, BMI, and smoking</td>
<td>0.16</td>
<td>0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age, area of residence, BMI, smoking, and TPA</td>
<td>0.12</td>
<td>0.03</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Anthropometric characteristics of participants are presented in Table 1. The body mass index (BMI; \( p < 0.01 \)), waist circumference (\( p < 0.01 \)), systolic blood pressure (\( p = 0.02 \)), fasting plasma glucose (\( p < 0.01 \)), and HOMA-IR (\( p < 0.01 \)) significantly increased across categories of decreasing physical activity.

In both genders (and after adjustment for age, area of residence, BMI, and smoking), HOMA-IR was significantly associated with TPA, the duration of vigorous- and moderate-intensity activity, and sedentary behaviors. The association between HOMA-IR and TPA was independent of the duration of sedentary behaviors. Similarly, the association between HOMA-IR and both vigorous and moderate types of activity was independent of the duration of sedentary behaviors (Table 2).

TPA and MET-minutes of activity at work and at commuting were significantly lower at higher HOMA-IR quintiles after adjustment for age, sex, area of residence, BMI, and smoking (\( p < 0.01 \)). The same pattern was seen for the duration of vigorous- or moderate-intensity physical activity (\( p < 0.01 \)), whereas the duration of sedentary behaviors was significantly (\( p < 0.01 \)) higher at higher HOMA-IR values (Fig. 1). As shown in Fig. 2, the percentage of individuals with vigorous-intensity activity was significantly lower while that of inactive individuals was significantly higher at higher HOMA-IR quintiles (\( p < 0.01 \)). The percentage of individuals in high (low) category activity was negatively (positively) correlated with HOMA-IR quintiles (\( p < 0.01 \)).

In order to evaluate the situation in postmenopausal women, we restricted the analysis to this subset of participants (\( n = 545 \)). HOMA-IR was significantly associated with TPA (\( r = −0.17, p < 0.01 \)), duration of vigorous-intensity activity (\( r = −0.15, p = 0.02 \)), duration of moderate-intensity activity (\( r = −0.13, p = 0.01 \)), and duration of sedentary behaviors (\( r = 0.27, p < 0.01 \)). The associations remained significant after additional adjustment for BMI and smoking.

Discussion

Our study population represents the adult population of Iran. The duration and intensity (vigorous vs. moderate) of physical activity in three domains of work, commuting, and recreation were assessed using the GPAQ questionnaire. Considering that most physical activities in developing countries take place while working and commuting, separating these domains from recreational activities is a logical approach recommended by WHO in GPAQ, in order to yield a more comprehensive estimate of overall physical activity. In addition, through controlling the potential confounding effects of work and

Fig. 1. The association between HOMA-IR and TPA, activity at work, activity at commuting, and activity at recreation after adjustment for age, sex, residential area, BMI, and smoking (A). The association between HOMA-IR and the duration of sedentary behaviors, moderate activity, and vigorous activity after adjustment for age, sex, residential area, BMI, and smoking (B) (SuRFNCD-2007, Iran). *\( p < 0.05 \), **\( p < 0.01 \), ***\( p < 0.001 \). Handles represent SE.
commuting activities, this approach assesses the association between physical inactivity and metabolic abnormalities more precisely than traditional questionnaires which focus mainly on evaluating recreational activities.

To estimate physical activity energy expenditure, MET-minutes of activities in different domains were calculated and summed up to yield TPA. After adjustments for age, gender, residential area, smoking, and BMI, we demonstrated a significant association between TPA and HOMA-IR. Furthermore, both moderate- and vigorous-intensity activities were independently correlated with lower HOMA-IR values. The time spent on sedentary behaviors was also associated with HOMA-IR independent of physical activity at other domains. As shown in Fig. 1A, work-time physical activity had a higher (compared to commuting and recreation) contribution to the association between TPA and HOMA-IR.

The advantages of this study include a large sample size representative of the nation, using a standardized international questionnaire (WHO, 2008) and the concept of metabolic equivalents, exploring the association in different domains of physical activity (i.e., work, commuting, and recreation) and evaluation of the association between some of the less studied aspects of physical activity and insulin resistance. For example, the association between sedentary behavior and insulin resistance has not been evaluated in previous works. The association between insulin resistance and physical activity or exercise has been the topic of many recent studies (Balkau et al., 2008; Nowak et al., 2008; Bradley et al., 2008; Kavouras et al., 2007; Franks et al., 2007; Foy et al., 2006; Mohan et al., 2005; Brage et al., 2004; Kriska et al., 2001; Mayer-Davis et al., 1998). The results of the available reports, however, have sometimes been inconsistent, mainly due to differences in the study design, sampling protocol, age range of participants, method for assessing physical activity (e.g., different questionnaires), and insulin resistance estimation methods. Mayer-Davis et al. (1998) showed in a study on 1467 individuals aged 40–69 years that physical activity (total, vigorous-intensity, and moderate-intensity) has a direct relationship with insulin sensitivity measured by the frequently sampled intravenous glucose test (FSIGT). Using the clamp technique and accelerometer to measure insulin resistance and physical activity, respectively, Balkau et al. (2008) showed in 801 adults that the duration of physical activity and total physical activity is significantly related to insulin sensitivity in both genders. After adjusting for total activity, however, the relationship between the duration of activity and insulin sensitivity lost its significance. In another study on 1262 adults aged 20 years or older in south India, physical activity was measured in three domains: job-related activity, leisure-time activity, and exercise. Subjects were then categorized into three groups: light-, moderate-, and heavy-grade activity. HOMA-IR was significantly higher in subjects with light-grade activity compared to those with heavy-grade activity (Mohan et al., 2005).

Different mechanisms have been proposed to explain the effect of physical activity on insulin sensitivity. One theory points out that physical activity enhances glucose transport into the muscle cells, possibly by up-regulating the expression of glucose transporter 4 (Goodyear & Kahn, 1998; Perseghin et al., 1996; O’Gorman et al., 2006; Holloszy, 2005). Moreover, regular physical activity decreases the fat mass and replaces it with lean mass, such that the amount of muscle available for glucose absorption increases (Perseghin et al., 1996). Obesity stimulates the production of inflammatory cytokines which result in insulin resistance (Bradley et al., 2008). Indeed, lowering the body weight may be a mechanism through which physical activity increases insulin sensitivity (Balkau et al., 2008). Enhanced blood perfusion of muscles during physical activity is another mechanism (Baron et al., 1995).

Our study is the first attempt of its kind in Iran and one of the largest studies on the subject. A recent study on 3600 adults (age: 20–70 years) living in urban areas of northern Iran showed that job-related activity was low in 64.3% of individuals, and leisure-time activity was very low or low in 81.3% of subjects. Furthermore, 79.2% of subjects had less than 2 h of exercise per week (Hajian-Tilaki & Heidari, 2007). A study in Tehran indicated that 45% of women aged 40–60 years have low levels of physical activity, as assessed by the IPAQ questionnaire (Azadbakht & Esmailzadeh, 2008). Together with our results, one can conclude that the level of physical activity among Iranian adults is low in several dimensions.

Fig. 2. The percentage of individuals with vigorous, non-vigorous, and without activity across quintiles of HOMA-IR (A). The percentage of individuals in different categories of activity across quintiles of HOMA-IR (B). Sufficient activity is defined as high or moderate categories of physical activity (B). The number in each box refers to the percentage of individuals that correspond to the given activity category/intensity. Variables are adjusted for age, sex, and area of residence (SurFNCD-2007, Iran).
Conclusions

The findings of our study indicate a significant, inverse relationship between physical activity and insulin resistance. This relationship is manifested in terms of the intensity and level of activity as well as energy expenditure during activity. Our results have important implications for healthcare professionals and policymakers. In particular, encouraging physical activity needs to be the focus of more attention in order to help prevent insulin resistance and its adverse consequences. Community-based lifestyle intervention programs have been recently tried in our country and have been associated with promising success. For example, a recent 4-year lifestyle intervention program in two Iranian communities in central Iran led to an increase in leisure-time activity. Energy expenditure for total daily physical activities showed a decreasing trend over the study period, but the mean drop from baseline was significantly smaller in the intervention areas than in the control area (Sarrafzadegan et al., 2009).

The main limitation with our study is its cross-sectional nature which does not allow us to assess causal relationships. The other limitation concerns recall bias related to the use of questionnaires. Insulin resistance is best assessed by the hyperinsulinenemic euglycemic clamp technique (DeFronzo et al., 1979). Because of its costs and invasiveness, however, we preferred to use the HOMA-IR index to estimate insulin resistance. HOMA-IR is probably the most suitable method for measuring insulin resistance in large epidemiological studies such as the present study (Bonora et al., 2007; Wallace et al., 2004). Finally, we used a Persian translation of GPAQ. The authors are currently trying to determine the validity and reliability of this translation for future use in Iran.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Acknowledgments

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Authors’ contributions: A.E. provided clinical expertise throughout the project. O.K. performed statistical analysis and contributed to writing. A.R. edited manuscript drafts and helped with data presentation. A.M. supervised data analysis and controlled data quality. M.H. and M.M.G. participated in the design and coordinated different stages of the survey. F.A. supervised the flow of the survey. M.A. designed the manuscript structure. S.R. helped with the final draft of the manuscript. All authors read and approved the final manuscript.

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