Relationship Between Changes in Physical Activity and Plasma Insulin During a 2.5-Year Follow-up Study

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The association between changes in physical activity, body weight, and diet and fasting plasma insulin was analyzed in a 2.5-year follow-up study of 146 men aged 50 to 60 years. Physical activity was assessed by a 7-day physical activity recall interview, diet by a 4-day food record, and plasma insulin radioimmunologically. Total physical activity decreased from (mean ± SD) 45.1 ± 10.1 to 39.0 ± 6.1 metabolic equivalent (MET) hours (METh) · d^{-1} and conditioning physical activity (>5.0 METs) from 8.0 ± 11.2 to 2.7 ± 5.0 METh · d^{-1}, whereas plasma insulin increased from 8.2 ± 5.8 to 9.2 ± 6.7 mU · L^{-1} and body weight from 80.5 ± 12.0 to 81.6 ± 11.6 kg during the follow-up period ($P \leq .001$ for all). The change in conditioning physical activity correlated inversely ($r = -.34$, $P < .001$) and change in body weight positively ($r = .42$, $P < .001$) with the change in plasma insulin level. With data adjusted for the baseline insulin level, cardiovascular health status, alcohol intake, change in body weight, smoking, age, and follow-up time, the odds ratio for an increase in fasting plasma insulin was 8.9 (95% CI, 2.1 to 37.1; $P = .003$) for men with the greatest decrease in conditioning physical activity (<−7 METh) compared with men who reported an increase in conditioning physical activity. The same logistic regression model showed an odds ratio of 9.9 (95% CI, 2.1 to 45.4; $P = .003$) for the increase in plasma insulin for subjects who gained more than 3.3 kg body weight compared with subjects who lost at least 0.6 kg. Men who consumed at least 12 g · d^{-1} alcohol at both examinations had an odds ratio of 12.8 (95% CI, 1.7 to 94.5; $P = .012$) compared with nondrinkers. These data suggest that in middle-aged men, a reduction in physical activity increases the risk for increased plasma insulin independently of alcohol intake and changes in body weight.

INSULIN PLAYS A MAJOR ROLE in the regulation of carbohydrate, protein, and lipid metabolism. Insulin resistance and hyperinsulinemia usually develop as a consequence of decreased insulin sensitivity of the peripheral tissues. The decrease in insulin action may have a genetic origin, or it could be induced by environmental factors.[1] The clinical spectrum of insulin resistance is broad, varying from mild hyperinsulinemia but normoglycemia to overt diabetes mellitus. Insulin-resistant subjects usually also manifest other metabolic disorders such as hyperlipidemia, hypertension, hyperthrombogenicity, and hypofibrinolysis. All of these factors contribute to the increased risk of cardiovascular disease. However, it has been shown that hyperinsulinemia per se is an independent risk factor for ischemic heart disease.[2-5]

Lack of physical activity has been widely accepted as a major risk factor for several public health problems.[6-8] It has been estimated that about one third of the deaths due to coronary heart disease, colon cancer, and diabetes are related to sedentary living, and that by increasing physical activity levels, the death rate from these diseases would be only two thirds of the current rate.[9] Therefore, increasing the physical activity level is a major public health objective.[7] The majority of epidemiologic data on the health consequences of physical inactivity are based on observational studies with one baseline measurement of physical activity or physical fitness. Only two studies have reported the relation between the change in physical activity/fitness and the risk of subsequent health problems. The men who increased their level of physical activity[10] or fitness[11] had a markedly lower risk of coronary heart disease than those who showed a reduction in activity or fitness over the years. The purpose of our study was to analyze the relation between changes in physical activity, body weight, and diet and the change in plasma insulin level during a 2.5-year follow-up study in 146 middle-aged men.

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SUBJECTS AND METHODS

Subjects and Study Design

In 1992, a 6.2% random sample of Eastern Finnish men aged 50 to 60 years (N = 4,853) living in the city of Kuopio (82%) and a nearby suburban community (18%) were invited to participate in the study. Of 300 men initially invited, 206 agreed to participate, 47 stated an unwillingness to participate, and another 47 did not respond at all. Of those unwilling to participate, 41% reported cardiopulmonary, metabolic, or musculoskeletal problems, whereas 59% did not report any regular medication or chronic disease. The same cohort was invited to the first follow-up examination 12 months later in 1993 and to the second follow-up examination 30 months after the baseline examination in 1994/1995. Participation rates in the 12- and 30-month follow-up examinations were 90% (n = 186) and 72% (n = 150), respectively. Since plasma insulin levels were not measured in the 12-month follow-up examination, the present analyses are based only on subjects with complete physical activity, anthropometry, and plasma insulin data at the baseline and 30-month follow-up periods. Of 150 men completing the 30-month follow-up protocol, one was excluded from the analyses due to diagnosed non–insulin-dependent diabetes mellitus (NIDDM) at baseline. In addition, due to difficulties in blood sampling, baseline plasma insulin values were not available for three subjects. During the follow-up period, no attempt was made to influence the physical activity or dietary and smoking habits of the subjects.

At the baseline period, there were no differences in body weight (mean ± SD, 83.0 ± 11.5 *v* 80.5 ± 12.0 kg, $P = .169$) or body mass index ([BMI] 27.8 ± 3.8 *v* 26.7 ± 3.6 kg · m^{-2}, $P = .068$) between the study dropouts and the men who completed both examinations. However, waist circumference (97.9 ± 10.7 *v* 94.6 ± 10.1 cm, $P = .038$), waist to hip ratio (0.99 ± 0.055 *v* 0.97 ± 0.049, $P = .006$), and plasma insulin (11.0 ± 6.3 *v* 8.2 ± 5.8 mU · l^{-1}, $P = .001$) were greater in study dropouts. In addition, the dropouts reported less conditioning physical activity than those completing the follow-up period (4.7 ± 8.9 *v* 8.0 ± 11.2 metabolic equivalent [MET] hours [METh], $P = .007$). Subjects provided written informed consent, and the study protocol was approved by the Ethics Committee of Kuopio University.

Laboratory Analyses

Venous blood samples were taken without stasis after a 12-hour fast and a 30-minute rest in the supine position. The subjects were advised not to take any antiinflammatory analgesics for 1 week before blood sampling and not to engage in strenuous physical exercise the day before blood sampling. In the case of any acute respiratory infection, blood samples were taken at the earliest 1 week after the symptoms disappeared. Plasma insulin level was determined radioimmunologically (Phadeseph Insulin RIA; Kabi Pharmacia Diagnostics, Uppsala, Sweden). Blood glucose level was measured using a glucose dehydrogenase method (Merck, Darmstadt, Germany). The coefficient of variation for insulin assays was 10.0% and 3.8% at the baseline and follow-up periods, respectively.

Physical Activity

Physical activity was assessed using the Stanford Seven-Day Recall Interview[12] by adding cross-country skiing and distance skating to the activity list.[13] The men were asked to recall the time spent sleeping and in mild, moderate, and heavy physical activity during the previous 7 days. Examples of mild activity requiring an energy expenditure between 3 and 5 METs (working metabolic rate/resting metabolic rate) included brisk walking, golfing, and bicycling not strenuous enough to cause breathlessness. Examples of moderate activity (5.1 to 6.9 METs) included cross-country skiing, swimming, and dancing with sufficient intensity to cause sweating and/or breathlessness. Examples of heavy exercise (≥7.0 METs) included jogging and cross-country skiing at a sufficient intensity to cause exhaustion or profound sweating and/or breathlessness; also, recovery from heavy exercise had to require an extended period. Very mild activities (1.0 to 2.9 METs) also were calculated. MET values used for calculations were as follows: sleep, 1; very mild activity, 1.5; mild activity, 4; moderate activity, 6; and heavy activity, 10. The average daily physical activity index (METh) was then determined by multiplying MET values by the number of hours spent in each of the five categories of activity. In addition to total physical activity, the METh values of conditioning physical activity ([cMETh] moderate + heavy activity) and of individual activity categories were calculated. Physical activity interviews were conducted by the same investigator in all phases of the study.

Anthropometry

Subjects were weighed with a digital scale in light clothing without shoes. The BMI was calculated as body weight (in kilograms) divided by the height squared (in meters). Waist circumference was measured midway between the lower rib margin and the iliac crest, and hip circumference at the level of the greater trochanters. Body fatness was estimated based on the sum of four skinfold (biceps, triceps, subscapular, and suprailiac) measurements.[14] The same trained nurse performed anthropometric measurements both at baseline and at follow-up visits.

Dietary intake was measured using 4-day food records; recording days included 3 weekdays and Sunday. Portion sizes were estimated using a picture booklet[15] or household measurement units. Subjects were individually instructed on how to complete the records on the same laboratory visit as when blood samples were taken. The records were also checked 1 week later at the time of the exercise stress test. Records were analyzed using the MicroNutrica software based on a nutrient file from Finnish food analyses.[16]

Cardiorespiratory Fitness

For assessment of cardiorespiratory fitness, maximal oxygen uptake ($\dot{V}O_2max$) was determined using breath-by-breath respiratory gas analyses during an incremental (20 W · min^{-1}) bicycle ergometer exercise test until the subjective[17] or objective maximum (increase in oxygen consumption of <150 mL/min despite increased workload) was attained. Blood pressure was measured by an automatic device, and the electrocardiogram was continuously monitored and recorded every minute during exercise and up to 7 minutes postexercise. At baseline, $\dot{V}O_2$ max was assessed using the SensorMedics MMC 4400tc system, but at the 30-month follow-up evaluation, the SensorMedics (Yorba Linda, CA) 2900 Metabolic Measurement Cart was used. Although both systems use similar zirconium oxide sensors, the 2900 unit yielded systematically greater $\dot{V}O_2max$ values than the 4400tc unit.

Statistical Methods

Due to the skewed distribution of plasma insulin and measures of physical activity, relationships between plasma insulin and physical activity, body weight, and diet were analyzed with nonparametric Spearman correlation coefficients. Differences between quartiles of conditioning physical activity were analyzed with ANOVA (normally distributed variables) or Kruskal-Wallis one-way ANOVA (insulin and conditioning physical activity). Changes in plasma insulin and independent variables were analyzed using only absolute values.

Logistic regression analysis was used to calculate the odds ratio for independent variables for the increase in plasma insulin during the follow-up period. The dependent variable, ie, change in plasma insulin, was dichotomized (Δinsulin ≤ 0 mU · L^{-1} = 0; Δinsulin > 0 mU · L^{-1} = 1). Of the independent variables, the change in conditioning physical activity and change in body weight were classified in quartiles and alcohol intake in three groups, and baseline insulin level, cardiovascular health status, smoking, age, and follow-up time were dichotomized (cutoff points for each classification are listed in Table 3). For calculation of odds ratios, the subgroups of independent variables used as reference groups (ie, odds ratio set at 1.0) are also shown in Table 3. Logistic regression analyses were made in two steps. In first step, only ΔcMETh was entered into the model to derive the crude odds ratio. In the second step, the other independent variables were added into the model. The second step was repeated using a stepwise method to include the independent variables into the model, but since the results did not change, data are presented based on the simultaneous inclusion model. Statistical analyses were made with the SPSS (Chicago, IL) for Windows 6.1 software package.

RESULTS

Characteristics of the subjects at the baseline and follow-up examinations are shown in Table 1. Reported daily total physical activity decreased by 6.1 METh · d^{-1} (95% CI, −7.7 to −4.4; $P < .001$) and conditioning physical activity by 5.2 METh · d^{-1} (95% CI, −7.0 to −3.5; $P < .001$) during the follow-up period, whereas body weight, BMI, and waist circumference increased by 1.1 kg (95% CI, 0.4 to 1.7; $P = .001$), 0.4 kg · m^{-2} (95% CI, 0.2 to 0.6; $P < .001$), and 1.0 cm (95% CI, 0.4 to 1.7; $P = .004$), respectively. Moreover, fasting plasma insulin increased from 8.2 to 9.2 mU · L^{-1} and blood glucose from 5.0 to 5.3 mmol · L^{-1} ($P < .001$ for both).

Table 1. Characteristics of the 146 Men (mean ± SD)

Characteristic	Baseline	Follow-up	Change (95% CI)
Plasma insulin ($mU \cdot L^{-1}$)	8.2 ± 5.8	9.2 ± 6.7	+1.0 (0.1-1.8)
Blood glucose ($mmol \cdot L^{-1}$)	5.0 ± 1.2	5.3 ± 1.3	+0.3 (0.2-0.4)
Body weight (kg)	80.5 ± 12.0	81.6 ± 11.6	+1.1 (0.4-1.7)
BMI ($kg \cdot m^{-2}$)	26.7 ± 3.6	27.2 ± 3.4	+0.4 (0.2-0.6)
Waist to hip ratio	0.97 ± 0.05	0.98 ± 0.05	+0.01 (0.001-0.012)
Waist circumference (cm)	94.6 ± 10.1	95.6 ± 9.6	+1.0 (0.3-1.7)
Sum of skinfolds (mm)	39.4 ± 12.1	39.9 ± 10.9	+0.5 (−0.7-1.6)
Total physical activity (METh)	45.1 ± 10.1	39.0 ± 6.1	−6.1 (−7.7-−4.4)
Conditioning physical activity (METh)	8.0 ± 11.2	2.7 ± 5.0	−5.2 (−7.0-−3.5)
Energy intake (MJ)	9.6 ± 2.6	9.5 ± 2.4	−0.1 (−0.4-0.3)
Protein intake (E%)	16.9 ± 2.9	16.6 ± 2.7	−0.3 (−0.8-0.3)
Carbohydrate intake (E%)	44.8 ± 7.2	45.9 ± 6.9	+1.1 (−0.0-2.3)
Fat intake (E%)	36.0 ± 5.4	35.2 ± 5.4	−0.8 (−1.9-0.2)
Alcohol intake (g)	7.4 ± 13.4	7.2 ± 11.7	−0.2 (−2.2-1.7)

At baseline, 53 men (36.3%) were retired, 86 (57.5%) were working, and nine (6.2%) were unemployed. During the follow-up period, 20 men retired, 14 men became unemployed, and none of the men who were unemployed at baseline became employed. The men who lost their job during the follow-up period showed a greater decrease in total and conditioning physical activity (−10.9 and −11.0 $METh \cdot d^{-1}$, respectively) compared with those who retired during the follow-up period or those who were working, retired, or unemployed already at baseline. However, there were no differences in the changes of plasma insulin or anthropometric measures between these groups.

Both total and conditioning physical activity correlated inversely with plasma insulin level at the baseline and follow-up measurement periods (Table 2). In addition, anthropometric measures showed strong and consistent relations to plasma insulin at both examinations. The change in physical activity (ΔMETh) correlated inversely and the changes in body weight, BMI, waist circumference, and sum of skinfolds correlated positively with the change in plasma insulin during the follow-up period (Table 2). Of the individual physical activity intensity classes, moderate activities showed the strongest correlation with plasma insulin (baseline, $r = -.17$, $P < .05$; follow-up, $r = -.29$, $P < .001$; change, $r = -.26$, $P < .001$), whereas mild activities were not associated with insulin. The change in conditioning physical activity (sum of moderate and heavy activities) was the strongest activity index correlate of the change in plasma insulin level.

Table 2. Spearman Correlation Coefficients Between Physical Activity and Anthropometric Variables and Plasma Insulin at Baseline and Follow-up Examination, and Between Changes During the Follow-up Period, in 146 Middle-Aged Men

Parameter	Plasma Insulin		
	Baseline	Follow-up	Change
Total physical activity	−.27‡	−.22†	−.29‡
Conditioning physical activity	−.24†	−.26†	−.34‡
Body weight	.50‡	.51‡	.42‡
BMI	.59‡	.61‡	.39‡
Waist circumference	.57‡	.62‡	.22†
Waist to hip ratio	.48‡	.59‡	.01
Sum of skinfolds	.58‡	.51‡	.25†
$\dot{V}O_2max$§	−.39‡	−.47‡	−.26†

*$P < .05$.
†$P < .01$.
‡$P < .001$.
§n = 136.

Of the dietary variables, carbohydrate intake correlated inversely ($r = -.30$, $P < .001$) and fat ($r = .27$, $P < .001$) and cholesterol ($r = .23$, $P < .01$) intake correlated positively with insulin at baseline, but these associations were no longer evident at the follow-up examination. Also, changes in energy and other energy nutrient intake were not associated with insulin changes. Alcohol intake did not correlate with insulin at either the baseline follow-up period, but baseline alcohol consumption was directly related ($r = .28$, $P < .001$) to the change in insulin level during the follow-up period. Men who consumed at least 12 g alcohol (ie, ≥ one drink) per day at baseline showed a 2.5-$mU \cdot L^{-1}$ increase (from 8.8 to 11.2) in insulin level, whereas the change in nondrinkers was +0.2 $mU \cdot L^{-1}$ (from 8.4 to 8.6, $P = .004$ for trend). In addition, the increase in plasma insulin in men consuming at least 12 g alcohol per day in both examinations was 3.5 (95% CI, 1.6 to 5.4) $mU \cdot L^{-1}$, whereas in constant nondrinkers the change was +0.5 (95% CI, −0.5 to 1.4) $mU \cdot L^{-1}$ (P for trend = .010). The baseline insulin level and body weight, as well as changes in body weight, were similar across alcohol consumption groups.

When the men were divided into quartiles according to ΔcMETh (Fig 1), those reporting a decrease of at least 7 METh showed an increase of 3.3 (95% CI, 1.1 to 5.6) $mU \cdot L^{-1}$ in plasma insulin, whereas men who increased their conditioning physical activity (ΔcMETh > 0) during the follow-up period showed a decrease of −0.1 (95% CI, −1.0 to 0.8) $mU \cdot L^{-1}$ (P for trend = .001). Baseline plasma insulin levels did not differ between the quartiles. Baseline values and changes in fasting blood glucose, body weight, BMI, and waist circumference were similar across the quartiles of ΔcMETh. Also the duration of the follow-up period and the number of smokers were similar among the quartiles.

In the univariate logistic regression model, the odds ratio for an increase in fasting plasma insulin during the follow-up period was 7.3 (95% CI, 2.3 to 23.1; $P = .001$) for men in the lowest ΔcMETh quartile and 3.1 (95% CI, 1.1 to 8.5; $P = .027$) for those in the second lowest quartile compared with men who reported increases in cMETh. When the data were adjusted for the baseline insulin level, change in body weight, cardiovascular health status, alcohol intake, smoking, age, and follow-up time, the odds ratio for men in the lowest ΔcMETh quartile remained statistically significant (8.9; 95% CI, 2.1 to 37.1; $P = .003$). The same logistic regression model showed an odds ratio of 9.9 (95% CI, 2.1 to 45.4; $P = .003$) for men who gained more than 3.3 kg body weight during the follow-up period

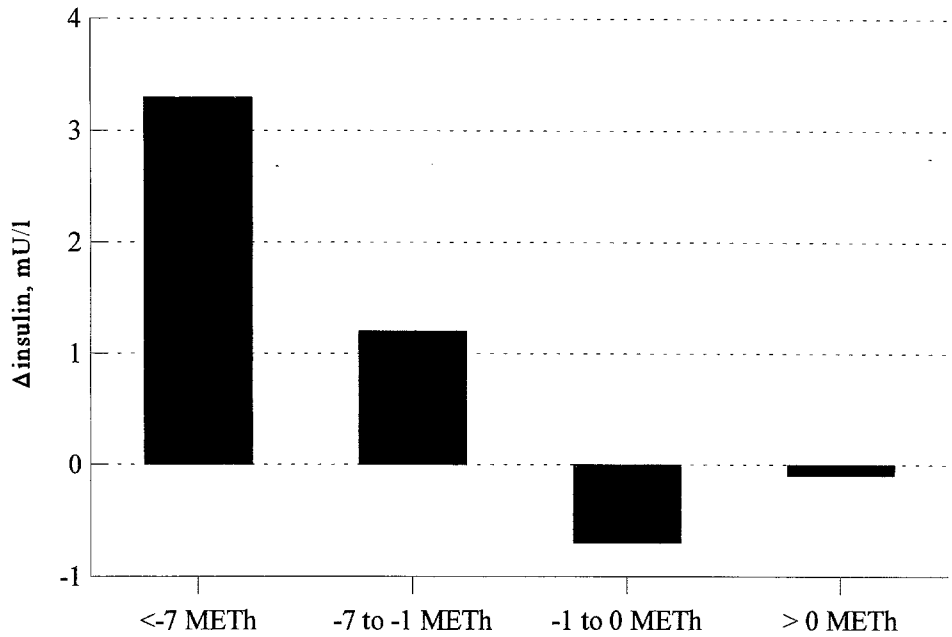

Fig 1. Change in plasma insulin level in the quartiles of ΔcMETh during a 2.5-year follow-up period in 146 middle-aged men (ANOVA, *P* for trend = .001).

compared with those who lost at least 0.6 kg. Men who consumed at least 12 g alcohol per day at both examinations had a relative risk of 12.8 (95% CI, 1.7 to 94.5; $P = .012$) compared with constant nondrinkers for an increase in plasma insulin (Table 3).

DISCUSSION

The main finding of the present study is that in the middle-aged men physical activity decreased markedly during the 2.5-year follow-up period, and that men with the greatest reduction in activity showed the greatest increase in fasting plasma insulin, suggesting increasing insulin resistance[18] and an augmented risk for NIDDM and cardiovascular disease.[2-5] Our results agree with studies showing that physically inactive people have an increased risk for insulin resistance and NIDDM.[19-22] The present study is also in line with the observation of decreased insulin sensitivity following 14 to 20 days of inactivity in young subjects.[23,24] The results are concordant with the observation that regular aerobic exercise training improves insulin sensitivity in sedentary middle-aged men,[25] subjects with impaired glucose tolerance,[26] elderly men and women,[27] and obese premenopausal women.[28]

Several possibilities have been suggested for the mechanisms by which physical activity regulates plasma insulin levels: enhanced insulin receptor and postreceptor function, increased skeletal muscle insulin-sensitive glucose transporter proteins, increased skeletal muscle capillary density, and loss of body fat. Both in sedentary healthy subjects[25,29] and in subjects with impaired glucose tolerance,[26] aerobic exercise training induced a 60% to 98% increase in skeletal muscle GLUT-4 concentration, an increase that corresponds to the difference commonly reported between exercise-trained and sedentary men.[30] In addition to increased GLUT-4 production, exercise seems to induce translocation of GLUT-4 from an intracellular domain to the cell surface, thus enhancing glucose transport.[31] Similarly,

Table 3. Odds Ratios Derived From Logistic Regression Analysis for the Increase in Plasma Insulin During a 2.5-Year Follow-up Study in 146 Middle-Aged Men

Variable	Odds Ratio (95% CI)	*P*
Change in conditioning physical activity		
>+0 METh · d^{-1}	1.0	
−1 to 0 METh · d^{-1}	0.9 (0.2-3.7)	.946
−7 to −1 METh · d^{-1}	2.6 (0.7-9.8)	.170
<−7 METh · d^{-1}	8.9 (2.1-37.1)	.003
Change in body weight		
≤−0.6 kg	1.0	
−0.6 to 1.3 kg	0.9 (0.3-3.2)	.883
1.3 to 3.3 kg	1.9 (0.6-6.3)	.315
≥3.3 kg	9.9 (2.1-45.4)	.003
Alcohol intake*		
None	1.0	
<12 g · d^{-1}	0.9 (0.3-2.8)	.909
≥12 g · d^{-1}	12.8 (1.7-94.5)	.012
Baseline insulin level		
≤7.0 mU · L^{-1}	1.0	
>7.0 mU · L^{-1}	0.1 (0.1-0.3)	<.001
Baseline CVD health status		
No	1.0	
Yes	0.6 (0.2-1.7)	.338
Smoking		
No	1.0	
Yes	0.4 (0.1-1.3)	.121
Age (baseline)		
<55 years	1.0	
≥55 years	1.4 (0.6-3.8)	.450
Follow-up time		
≤889 days	1.0	
>889 days	1.2 (0.4-3.3)	.773

*Classification is based on alcohol consumption data (4-day food records) from the baseline and follow-up examinations (none, no alcohol in either examination; ≥12 g · d^{-1}, consumption of >12 g per day in both examinations).

physical inactivity[32] and denervation models of muscle disuse[33] have been reported to decrease the number of skeletal muscle glucose transporter molecules.

Another possible link between physical activity and plasma insulin level is the exercise-induced increase in capillary density of the muscles. Capillary density is inversely related to the fasting plasma insulin level[34,35] and insulin resistance,[35] and aerobic exercise training has been shown to increase capillary density by 20% to 40%,[36] whereas the number of capillaries decreases between 14% and 25% within 3 weeks of detraining.[37] Also, the lower incidence of obesity among physically active people may partly explain the exercise-insulin relationship, since weight gain is a strong independent predictor of insulin resistance and NIDDM.[20] In the present study, an increase in body weight was associated with an increase in plasma insulin. In obese subjects, the function of insulin receptors seems to be depressed,[1] and in obese NIDDM patients, weight loss improves the kinase activity of insulin receptors.[38] However, in our study, multivariate analyses showed that both decreased conditioning physical activity and weight gain during the follow-up period were independent predictors of the increase in plasma insulin. In addition, the changes in body weight were similar in the lowest and highest ΔcMETh quartiles. This suggests that although a change in body weight may partly mediate the effects of exercise on the plasma insulin level, it is not the only mechanism involved.

In our study, more strenuous exercise (ie, >5 METs) was negatively associated with plasma insulin levels, whereas less intensive activities (3 to 5 METs) showed no correlation. It is possible that to induce physiologically significant changes in skeletal muscle glucose transport, the exercise stimulus has to exceed some intensity threshold. In studies showing improved insulin sensitivity or muscle GLUT-4 concentration after a training period, exercise intensity was 50% to 85% of maximal heart rate reserve and the improvement of $\dot{V}O_2$max reached, on average, about 20%.[26,27,39] On the other hand, the lack of correlation between insulin and mild physical activity could be simply due to the methodological difficulties associated with quantification of such activities. The mild activity category included several everyday activities such as walking at work and gardening chores, which are more difficult to recall and report accurately than specific activities like jogging, cross-country skiing, or bicycling, common examples of moderate and heavy activities.[40] Therefore, the question of both the minimal and the optimal amount of exercise required to improve insulin sensitivity remains a relevant research issue for controlled clinical trials.

Although several studies have reported increased plasma insulin as a risk factor for cardiovascular disease, the risk factor profile of insulin is not as clearly defined as that of other traditional risk factors, ie, elevated low-density lipoprotein cholesterol, hypertension, and smoking. In the Quebec Cardiovascular Study cohort,[5] the odds ratio for development of ischemic heart disease during a 5-year follow-up period was 1.7 with each increase of 1 SD (~4.7 $\mu U \cdot mL^{-1}$) in fasting plasma insulin. In our study, men with the greatest reduction in conditioning physical activity showed an increase of 3.3 $mU \cdot L^{-1}$ in insulin concentration. It is difficult to estimate to what extent this elevation in plasma insulin contributes to the risk of ischemic heart disease in these men, but if the increase continues after the follow-up period, even at the slower pace, it is reasonable to assume that it also has clinical relevance. However, interpretation of the results is further complicated due to differences in plasma insulin assay methods between the studies.[5]

Our results suggest that regular alcohol consumption increases the likelihood of an increase in plasma insulin. Ethanol acutely increases plasma insulin in a dose-dependent fashion both in healthy subjects[41,42] and in NIDDM patients.[43] The possible mechanisms by which ethanol exerts hyperinsulinemic effects include increased insulin secretion from the β cell[42] and suppressed inhibition of insulin on its own release.[44] Moreover, alcohol also suppresses insulin-stimulated glucose metabolism in muscle cells and thereby favors a state of generalized insulin resistance.[45] Despite an apparent physiologically sound background, our observation should be taken with caution. Even though food diaries usually reflect alcohol intake more accurately than questionnaires,[46] it is likely that the 4-day food record underestimated the true level of alcohol consumption. On the other hand, previous studies suggest that food records rank subjects according to alcohol consumption reliably.[15] Therefore, it is justified to assume that our subjects with an alcohol intake of at least 12 $g \cdot d^{-1}$ really drank more alcohol than those who reported no consumption. Thus, regular alcohol intake may increase plasma insulin and induce insulin resistance, but it is unclear what dose and duration of the exposure to alcohol are required to induce the effect.

In conclusion, a reduction in physical activity increases the risk for an increase in plasma insulin independently of changes in body weight and alcohol intake in middle-aged men. Together with the results of previous studies,[10,11] our results suggest that in public health, the focus should be not only on increasing the activity level of sedentary people but also on maintaining the exercise habits and physical activity level of individuals who are already active.

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