Associations of Cardiorespiratory Fitness and Obesity With Risks of Impaired Fasting Glucose and Type 2 Diabetes in Men

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OBJECTIVE — The purpose of this study was to examine the associations of cardiorespiratory fitness (hereafter fitness) and various obesity measures with risks of incident impaired fasting glucose (IFG) and type 2 diabetes.

RESEARCH DESIGN AND METHODS — This was a prospective cohort study of 14,006 men (7,795 for the analyses of IFG), who did not have an abnormal electrocardiogram or a history of heart attack, stroke, cancer, or diabetes.

RESULTS — Of the men, 3,612 (39,610 person-years) and 477 (101,419 person-years) developed IFG and type 2 diabetes, respectively. Compared with the least fit 20% in multivariate analyses, IFG and type 2 diabetes risks in the most fit 20% were 14 and 52% lower, respectively (both $P < 0.001$). Men with BMI ≥30.0 kg/m^2, waist girth >102.0 cm, or percent body fat ≥25 had 2.7-, 1.9-, and 1.3-fold higher risks for type 2 diabetes, respectively, compared with those for nonobese men (all $P < 0.01$), and the results for IFG were similar. In the combined analyses, obese unfit (least fit 20%) men had a 5.7-fold higher risk for type 2 diabetes compared with normal-weight fit (most fit 80%) men. We observed similar trends for the joint associations of BMI and fitness with IFG and those of waist girth or percent body fat and fitness with both IFG and type 2 diabetes.

CONCLUSIONS — Low fitness and obesity increased the risks of IFG and type 2 diabetes by approximately similar magnitudes. When considered simultaneously, fitness attenuated but did not eliminate the increased risks of IFG and type 2 diabetes associated with obesity, and the highest risk was found in obese and unfit men.

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Type 2 diabetes, one of the most costly chronic diseases, is a major risk factor for cardiovascular disease (CVD) mortality (1). Impaired fasting glucose (IFG), a pre-diabetic state, is a strong predictor of type 2 diabetes and CVD (2). Type 2 diabetes rates have increased substantially in recent years, and this trend is expected to continue (3). The American Diabetes Association (ADA) reported that approximately one in five health care dollars in the U.S. is spent caring for someone with diagnosed diabetes (4).

Physical inactivity and obesity are well-known independent risk factors for type 2 diabetes (5–7). However, according to objective data on physical activity in the recent National Health and Nutritional Examination Survey, adherence to the recommended amount of physical activity was <5% in U.S. adults (8), and more than one-third of adults were obese in 2005–2006 (9).

Previous studies have examined physical inactivity and obesity in relation to the risk of type 2 diabetes (5–7). However, in many studies, physical activity was measured by self-report questionnaire, which may cause an underestimation of the true associations between physical activity and health outcomes (8). Cardiorespiratory fitness (hereafter fitness) obtained from a laboratory maximal exercise test can be a marker for recent physical activity and provide objective information on the relationship between physical activity and health outcomes. Various measures of adiposity and fat distribution, such as percent body fat and waist girth, can more precisely assess the associations between obesity and type 2 diabetes.

Although several studies have reported single independent associations between fitness or obesity with type 2 diabetes (10–14), the relative contributions of physical activity or fitness and obesity to the risk of type 2 diabetes are still controversial. Some previous studies concluded that the relative contribution of obesity was more important than physical activity on the risk of type 2 diabetes in women (6,7). However, in our recent study of women using objectively measured fitness instead of self-reported physical activity, obesity and fitness made similar contributions to the risk of type 2 diabetes (15). To date, no study on this issue has been conducted in men.

Therefore, we examined the combined associations of fitness and obesity on the risk of type 2 diabetes in a large sample of men with various objective measures of obesity and fat distribution. We also examined the joint associations of these exposures with the risk of IFG, which is a strong predictor of type 2 diabetes and CVD.

RESEARCH DESIGN AND METHODS

— A total of 16,745 men aged 20–79 years received at least two medical examinations at the Cooper Clinic in Dallas, Texas, during 1974–2006. Among these participants, men with BMI <18.5 kg/m^2, abnormal resting or exercise electrocardiogram, or a history of heart attack, stroke, or cancer at baseline were excluded (n = 1,751). In addition,

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men who did not achieve at least 85% of their age-predicted maximal heart rate (220 minus age in years) on the treadmill test were excluded ($n = 229$).

For the analyses of type 2 diabetes as the outcome, men with diabetes at baseline according to a fasting plasma glucose level ≥7.0 mmol/l (126 mg/dl), a history of diabetes, or current therapy with insulin also were excluded from the analyses ($n = 759$), resulting in 14,006 men in the entire cohort. In analyses that examined IFG as the end point of interest, men who had IFG, defined as a glucose level 5.6–6.9 mmol/l (100–125 mg/dl) at baseline ($n = 6,149$), and men with normal baseline glucose who developed diabetes during follow-up ($n = 62$) were also excluded, leaving 7,795 men. Therefore, there were two groups of men in this study, the larger group for the analyses of incident diabetes ($n = 14,006$) and the smaller group for the analyses of incident IFG ($n = 7,795$). Most of them were well-educated, non-Hispanic whites from middle to upper socioeconomic strata and employed in or retired from professional positions.

All participants gave written informed consent for the baseline clinical examination and follow-up study. The study was reviewed and approved annually by the institutional review board at the Cooper Institute.

Diagnosis of IFG and type 2 diabetes

IFG and type 2 diabetes were diagnosed at a follow-up examination according to the ADA criteria, which defines IFG and type 2 diabetes as a fasting plasma glucose concentration 5.6–6.9 and ≥7.0 mmol/l, respectively (16). The follow-up time for each participant was counted from the baseline examination to the first follow-up event of IFG or type 2 diabetes or the last follow-up observation through 2006 in the men who did not develop either condition.

Clinical examination

Participants completed a medical questionnaire consisting of demographic questions, lifestyle habits, and past and present chronic disease history. In addition, they underwent a clinical evaluation that included a treadmill maximal exercise test, body composition assessment, blood chemistry analysis, blood pressure measurement, and a physical examination by a physician.

Fitness was quantified as the total duration of a treadmill test using a modified Balke and Ware protocol (17), which is highly correlated with measured maximal oxygen uptake in men ($r = 0.92$) (18). Participants were encouraged to reach their maximal effort, and the test was terminated when they requested to stop because of exhaustion or the physician stopped the test for medical reasons. Participants who did not achieve 85% of their age-predicted maximal heart rate were excluded, because they were assumed to be likely to have subclinical medical problems, and less than near-maximal effort would lead to an underestimate of fitness. Detailed information on the exercise test has been published elsewhere (19). Classification of fitness level was determined on the basis of fifths of treadmill time in each age-group (20–39, 40–49, 50–59, and ≥60 years) from the entire Aerobics Center Longitudinal Study (ACLS) cohort, as in our previous studies (19,20). The lowest 20% were classified as having fitness level 1, and in continuing increments of 20%, participants were classified as fitness levels 2 through 5, respectively. Because unhealthy individuals who had a history of diabetes, heart attack, stroke, or cancer or an abnormal electrocardiogram at baseline were excluded, the number of participants in this study classified as having fitness level 1 was <20%, compared with the entire ACLS cohort. In additional analyses, we dichotomized fitness level as either fit (the most fit 80%) or unfit (the least fit 20%) for the joint analyses of fitness and obesity on IFG and type 2 diabetes. We used this cut point because there is no consensus for the clinical definition of unfitness: this cut point has been used in previous ACLS studies, which have shown low fitness to be an independent risk factor of various morbidity and mortality outcomes (20).

BMI was calculated from measured weight and height and categorized as normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥30 kg/m^2) (21). Waist girth was taken at the level of the umbilicus with an inelastic tape and classified as ≤102.0 or >102.0 cm according to clinical guidelines (21). Percent body fat was determined by hydrodensiometry (underwater) weighing or seven-site skinfold measurements or both with standardized procedures (22) and defined as <25 or ≥25% as indicated in a previous study (20).

After at least a 12-h overnight fast, blood chemistry analysis for plasma glucose and total cholesterol was performed with automated bioassays in the Cooper Clinic laboratory in accordance with the Centers for Disease Control and Prevention Lipid Standardization Program. Resting blood pressure was measured by standard auscultatory methods after at least 5 min of seated rest and was recorded as the average of two or more readings separated by 2 min. Alcohol consumption, smoking status, and parental or personal history of diabetes, heart attack, stroke, and cancer were ascertained through a standardized medical questionnaire. Waist girth was not available for all participants.

Statistical analyses

SAS software (version 9.1; SAS Institute, Cary, NC) was used for statistical analyses. Baseline characteristics were summarized across fitness levels, and tests for linear trends were calculated using general linear models. Incidence rates of IFG and type 2 diabetes were computed per 1,000 person-years adjusted for baseline age and examination year.

We used Cox proportional hazard models to estimate the relative risks (RRs) and 95% CIs of IFG and type 2 diabetes across categories of fitness, BMI, waist girth, and percent body fat. Ordinal linear trends across five fitness levels and three BMI categories were tested using regression models.

We assessed the joint associations of fitness and each obesity measure with risks of developing IFG and type 2 diabetes. We created six categories of BMI and fitness combinations and four categories of waist girth or percent body fat and fitness combinations using nonobese and fit men as the referent. In Cox regression models, baseline age, examination year, parental diabetes, current smoking, alcohol consumption, blood pressure, total cholesterol, baseline IFG, BMI, and treadmill time were considered as potential confounders as in previous studies (11–13,15,23). The proportional hazards assumption was tested by examining the log-log survival plots grouped on exposure categories. There were no significant interactions between fitness and each obesity measure with IFG and type 2 diabetes risks, using interaction terms in the Cox regression models and comparing stratum-specific risk estimates in the stratified analyses. All P values were two-sided, and $P < 0.05$ was considered statistically significant.

RESULTS — Among 7,795 men with normal baseline glucose (mean 5.1 years

Table 1—*Baseline characteristics by cardiorespiratory fitness level: ACLS, 1974–2006*

	All	1 (low)	2	3	4	5 (high)
n	14,006	1,706	2,594	2,848	3,407	3,451
Age (years)	43.0 ± 8.8	41.9 ± 7.9	42.2 ± 8.4	43.6 ± 8.6	43.3 ± 9.0	43.3 ± 9.4
Treadmill time (min)	18.8 ± 4.7	12.0 ± 2.2	15.2 ± 1.9	17.4 ± 2.0	20.2 ± 2.1	24.6 ± 2.9
BMI (kg/m^2)	26.0 ± 3.3	28.7 ± 4.6	27.0 ± 3.3	26.2 ± 2.9	25.5 ± 2.5	24.3 ± 2.2
18.5–25.0 kg/m^2 (%)	42.2	20.3	28.6	35.1	45.7	65.6
25.0–29.9 kg/m^2 (%)	47.2	48.2	54.1	54.3	49.6	33.3
≥30.0 kg/m^2 (%)	10.6	31.5	17.2	10.6	4.7	1.1
Waist girth (cm)†	93.0 ± 9.8	102.9 ± 12.1	97.3 ± 9.6	94.7 ± 8.7	91.7 ± 7.8	87.0 ± 7.2
>102 cm (%)	17.0	50.9	30.6	19.3	9.7	2.6
% body fat	20.7 ± 6.3	25.6 ± 6.4	23.2 ± 5.7	21.8 ± 5.5	19.7 ± 5.3	16.4 ± 5.3
≥25% (%)	24.1	54.6	38.2	26.8	15.1	5.1
Fasting glucose (mmol/l)	5.5 ± 0.5	5.5 ± 0.6	5.5 ± 0.5	5.5 ± 0.5	5.4 ± 0.5	5.4 ± 0.5
≥5.6 mmol/l (%)	43.9	49.1	47.0	45.0	41.6	40.5
Systolic blood pressure (mmHg)	120.4 ± 12.7	122.7 ± 13.8	120.5 ± 11.9	120.3 ± 12.6	119.8 ± 12.6	119.8 ± 12.9
Diastolic blood pressure (mmHg)	80.4 ± 9.3	83.1 ± 10.0	81.6 ± 9.4	80.8 ± 9.4	79.8 ± 9.1	78.6 ± 8.5
Total cholesterol (mmol/l)	5.4 ± 1.1	5.6 ± 1.0	5.5 ± 1.0	5.5 ± 1.0	5.3 ± 1.0	5.2 ± 1.2
Alcohol consumption (g/week)	132.4 ± 255.2	152.0 ± 250.9	138.7 ± 250.0	136.1 ± 255.5	126.4 ± 258.1	120.7 ± 257.2
Current smoking (%)	16.4	30.8	22.9	16.9	12.6	7.7
Parental diabetes (%)	5.4	4.1	5.6	5.4	6.2	5.0
Physically inactive (%)‡	27.5	65.2	47.7	29.9	14.6	4.6

Data are means ± SD unless indicated otherwise. *All P_{trend} values across fitness level were <0.001 except for parental diabetes ($P = 0.03$). †Data from 10,326 men. ‡No leisure-time physical activity in the 3 months before the examination as reported on medical questionnaire.

[39,610 person-years] of follow-up), 3,612 developed IFG, and among 14,006 men (7.2 years, 101,419 person-years of follow-up), 477 developed type 2 diabetes. In Table 1, fit men were less obese and had lower fasting glucose, blood pressure, and total cholesterol; they also smoked and drank alcohol less than unfit men (all $P_{trend} < 0.001$).

According to Pearson correlation coefficients, treadmill time was inversely correlated with percent body fat ($r = -0.59$), waist girth ($r = -0.54$), and BMI ($r = -0.44$). Among obesity measures, BMI was positively correlated with waist girth ($r = 0.84$) and percent body fat ($r = 0.64$), and waist girth also was correlated with percent body fat ($r = 0.75$). All correlation coefficients were statistically significant ($P < 0.001$).

Table 2 shows the single independent associations of fitness and obesity measures with the outcomes of IFG or type 2 diabetes. IFG and type 2 diabetes risks in the highest fitness level were 25 and 70% lower, respectively, compared with those in the lowest fitness level in model 1. Men with BMI ≥30.0 kg/m^2, waist girth >102.0 cm, and percent body fat ≥25% had 3.9-, 2.7-, and 1.8-fold higher risks for type 2 diabetes, respectively, compared with lean reference groups. Trends across adiposity exposures for IFG were in the same direction as for type 2 diabetes but were weaker. After additional adjustment for BMI or fitness in model 2, the associations were attenuated but remained significant except for percent body fat on IFG. There were dose-response relationships across five fitness levels and three BMI categories for both risk of IFG and type 2 diabetes in all multivariate-adjusted models (all $P_{trend} < 0.001$). The trends across fitness levels remained significant even after further adjustment for waist girth and percent body fat for both IFG and type 2 diabetes (both $P_{trend} < 0.05$).

Table 3 shows the joint associations of obesity measures and fitness with the risks of IFG and type 2 diabetes. Obese unfit men had 1.5 and 5.7 times higher risk of developing IFG and type 2 diabetes, respectively, compared with the normal-weight fit referent. We also calculated the RRs of developing both outcomes within each BMI group, with the unfit men as the referent. The only significant finding was that the fit obese men had a lower risk of type 2 diabetes compared with the unfit obese men (RR 0.47 [95% CI 0.31–0.72]). Obese men had significantly higher risks of IFG and type 2 diabetes in both fit and unfit groups compared with normal-weight men ($P < 0.01$).

The highest risks of developing IFG or type 2 diabetes were found in unfit men with waist girth >102 cm or percent body fat ≥25%. We saw no differences in risk of IFG between the fit and unfit men within waist girth or percent body fat groups. Fit men with waist girth >102 cm and in both percent body fat categories had a lower risk of developing type 2 diabetes.

Because the definition of unfit may influence the findings, we conducted sensitivity analyses in which we reclassified unfit as the least fit 40, 60, and 80%. The patterns of the joint association of fitness and obesity on the risk of both IFG and type 2 diabetes across different definitions of unfit were similar (data not shown).

Men with a BMI in the overweight (25.0–29.9 kg/m^2) or obese (30.0–34.9 kg/m^2) category are considered to have even higher risk for poor health outcomes if the waist girth is also >102 cm (20). We examined the joint associations of BMI and waist girth for both outcomes after adjustment for age, examination year, parental diabetes, smoking, alcohol consumption, blood pressure, cholesterol, treadmill time, and percent body fat. Compared with overweight men with waist girth ≤102 cm, the RRs (95% CIs) for developing IFG were 1.30 (1.09–1.55) for overweight men with waist girth >102 cm, 0.95 (0.68–1.33) for obese men (BMI 30.0–34.9 kg/m^2) with waist

Table 2—*RRs of IFG and type 2 diabetes by cardiorespiratory fitness and obesity: ACLS, 1974–2006*

	No. of cases	Person-years	Rate*	Adjusted RR (95% CI) Model 1†	Adjusted RR (95% CI) Model 2‡
IFG					
Fitness level					
1 (low)	410	3,801	109.2	1.00 (referent)	1.00 (referent)
2	688	6,535	107.9	1.03 (0.91–1.17)	1.09 (0.96–1.24)
3	748	7,628	95.6	0.92 (0.81–1.04)	1.00 (0.88–1.13)
4	912	10,225	89.2	0.88 (0.78–0.99)	0.98 (0.86–1.11)
5 (high)	854	11,419	74.5	0.75 (0.66–0.85)	0.86 (0.75–0.98)
P_{trend}				<0.001	<0.001
BMI					
18.5–25.0 kg/m^2	1,633	21,058	79.2	1.00 (referent)	1.00 (referent)
25.0–29.9 kg/m^2	1,673	15,997	101.8	1.23 (1.15–1.32)	1.18 (1.10–1.27)
≥30.0 kg/m^2	306	2,555	123.1	1.41 (1.24–1.60)	1.28 (1.12–1.46)
P_{trend}				<0.001	<0.001
Waist girth§					
≤102 cm	2,175	25,072	87.2	1.00 (referent)	1.00 (referent)
>102 cm	388	2,878	130.6	1.39 (1.24–1.55)	1.27 (1.13–1.43)
% body fat					
<25%	2,850	33,007	88.2	1.00 (referent)	1.00 (referent)
≥25%	762	6,603	106.0	1.14 (1.05–1.23)	1.04 (0.95–1.13)
Type 2 diabetes					
Fitness level					
1 (low)	94	10,640	12.4	1.00 (referent)	1.00 (referent)
2	102	17,802	5.6	0.65 (0.49–0.86)	0.80 (0.60–1.08)
3	102	20,331	4.5	0.53 (0.40–0.71)	0.71 (0.52–0.96)
4	101	25,460	3.5	0.43 (0.32–0.58)	0.62 (0.45–0.85)
5 (high)	78	27,162	2.4	0.30 (0.22–0.41)	0.48 (0.34–0.68)
P_{trend}				<0.001	<0.001
BMI					
18.5–25.0 kg/m^2	146	49,226	2.9	1.00 (referent)	1.00 (referent)
25.0–29.9 kg/m^2	231	44,491	5.1	1.59 (1.29–1.97)	1.36 (1.09–1.69)
≥30.0 kg/m^2	100	7,677	14.0	3.85 (2.93–5.06)	2.66 (1.96–3.60)
P_{trend}				<0.001	<0.001
Waist girth‖					
≤102 cm	218	57,692	3.8	1.00 (referent)	1.00 (referent)
>102 cm	102	8,835	11.6	2.66 (2.08–3.41)	1.91 (1.46–2.50)
% body fat					
<25%	316	82,071	4.0	1.00 (referent)	1.00 (referent)
≥25%	161	19,328	7.9	1.79 (1.47–2.18)	1.27 (1.02–1.58)

*Per 1,000 person-years adjusted for age and examination year. †Adjusted for age, examination year, parental diabetes, current smoking, alcohol consumption, systolic and diastolic blood pressure, total cholesterol, and IFG (for type 2 diabetes). ‡Adjusted for model 1 plus BMI (for fitness) or treadmill time (for BMI, waist girth, and percent body fat). §Data from 5,836 men (2,563 IFG events). ‖Data from 10,326 men (320 type 2 diabetes events).

girth ≤102 cm, and 1.24 (1.03–1.49) for obese men with waist girth >102 cm, and those for developing diabetes were 1.22 (0.78–1.89), 0.84 (0.31–2.29), and 2.41 (1.64–3.54), respectively.

CONCLUSIONS — This study revealed significant inverse dose-response relationships of fitness and positive associations of obesity measures with the risks of IFG and type 2 diabetes after adjustment for several potential confounding factors. Men in the highest fitness level showed a 52% lower risk of type 2 diabetes, and obese men identified by BMI showed a 2.7-fold higher risk of type 2 diabetes, compared with low fitness and normal-weight men, respectively. Evidence from several previous studies also indicated that higher fitness is associated with a lower risk for type 2 diabetes of 40–70% compared with lower fitness in men (11,13). Obese men, on the other hand, showed about a two- to fivefold higher risk of developing type 2 diabetes than men of normal weight (13).

In the joint associations of obesity and fitness, obese (BMI ≥30 kg/m^2) unfit men showed 1.5 and 5.7 times higher risks of IFG and type 2 diabetes, respectively, compared with nonobese fit men after multivariate adjustment. Some joint analyses of self-reported physical activity instead of fitness and obesity provided parallel results showing that inactive obese individuals had a >10 times higher risk of type 2 diabetes than active nonobese individuals (5–7). However, our results differed in that we observed that lack of fitness and obesity each increase risk to a similar extent, whereas other studies comparing physical inactivity and obesity

Table 3—*Joint associations of cardiorespiratory fitness and obesity with IFG and type 2 diabetes: ACLS, 1974–2006*

	Fit*				Unfit*				
	No.	No. of cases	Rat†	Adjusted RR (95% CI)‡	No.	No. of cases	Rat†	Adjusted RR (95% CI)‡	*P* value§
IFG									
BMI									
18.5–24.9 kg/m^2	3,461	1,538	79.0	1.00 (referent)	202	95	85.4	1.03 (0.84–1.27)	0.88
25.0–29.9 kg/m^2	3,047	1,470	100.9	1.23 (1.14–1.32)	424	203	108.2	1.26 (1.08–1.46)	0.73
≥30 kg/m^2	430	194	116.9	1.37 (1.18–1.60)	231	112	135.0	1.48 (1.22–1.80)	0.25
Waist girth‖									
≤102 cm	4,799	2,072	87.3	1.00 (referent)	262	103	86.4	0.93 (0.76–1.14)	0.42
>102 cm	570	282	124.6	1.35 (1.19–1.53)	205	106	149.4	1.50 (1.22–1.83)	0.10
% body fat									
<25%	5,760	2,639	87.4	1.00 (referent)	435	211	100.4	1.08 (0.93–1.24)	0.33
≥25%	1,178	563	101.8	1.12 (1.02–1.23)	422	199	118.2	1.21 (1.04–1.40)	0.48
Type 2 diabetes									
BMI									
18.5–24.9 kg/m^2	5,565	134	2.8	1.00 (referent)	346	12	4.6	1.55 (0.86–2.81)	0.30
25.0–29.9 kg/m^2	5,787	199	4.8	1.58 (1.26–1.97)	823	32	6.7	2.10 (1.41–3.12)	0.17
≥30 kg/m^2	948	50	10.2	3.00 (2.13–4.23)	537	50	21.2	5.69 (4.04–8.00)	<0.001
Waist girth¶									
≤102 cm	8,115	201	3.6	1.00 (referent)	451	17	6.8	1.77 (1.07–2.93)	0.06
>102 cm	1,293	67	9.6	2.38 (1.78–3.17)	467	35	18.3	4.00 (2.76–5.80)	0.01
% body fat									
<25%	9,857	284	3.7	1.00 (referent)	774	32	6.9	1.78 (1.23–2.58)	0.01
≥25%	2,443	99	6.1	1.53 (1.21–1.94)	932	62	13.0	2.79 (2.10–3.70)	<0.001

*Fit (most fit 80%); unfit (least fit 20%). †Per 1,000 person-years adjusted for age and examination year. ‡Adjusted for age, examination year, parental diabetes, current smoking, alcohol consumption, systolic and diastolic blood pressure, total cholesterol, and baseline IFG (for type 2 diabetes). §*P* values between fit and unfit in each category of obesity measures. ‖Data from 5,836 men (2,563 IFG events). ¶Data from 10,326 men (320 type 2 diabetes events).

showed that the magnitude of risk associated with obesity was much greater than that associated with physical inactivity (5–7). Recently, our study of women also reported that lack of fitness and obesity each increased the risk of type 2 diabetes to a similar extent and that fitness did not attenuate the adverse effect of obesity (23).

We found that all three obesity measures were independent predictors of IFG and type 2 diabetes, except for percent body fat on the risk of IFG. However, in the joint analyses of BMI and waist girth, normal abdominal fat (≤102 cm) was likely to eliminate the increased risk of IFG and type 2 diabetes associated with whole-body obesity defined by BMI 30–34.9 kg/m^2. Therefore, maintenance of normal abdominal fat among obese men should be considered as an important factor for IFG and type 2 diabetes prevention as reported in an earlier study (20).

IFG is a strong predictor of type 2 diabetes and CVD (2), and our study also showed a 3.3-fold higher risk of type 2 diabetes in men with baseline IFG compared with men with normal glucose tolerance. Therefore, we examined the associations of fitness and obesity measures with type 2 diabetes separately in these two groups. However, the associations were similar in two groups, so we combined the groups in further analyses.

Biological mechanisms supporting the roles of physical activity and obesity on the development of type 2 diabetes have been well established by a large number of studies. Regular physical activity can improve insulin sensitivity, blood pressure, lipoprotein profile, inflammation, and weight reduction, but obesity is related to inflammation and fat metabolism, which lead to insulin resistance (23,24). In addition, individuals with low fitness are more likely to have insulin resistance and fewer glucose transporters, and fitness also is associated with insulin sensitivity (23,24).

Strengths of our study include the valid and various measurements of exposure and outcome variables. Fitness, BMI, waist girth, percent body fat, and identification of IFG and type 2 diabetes were all objectively measured during the process of medical examinations at baseline and follow-up. Type 2 diabetes can remain undiagnosed for many years (25). In our study, 88.5% of men with type 2 diabetes identified on the basis of fasting plasma glucose did not report diabetes on their last follow-up medical questionnaire. The objective measure of type 2 diabetes from the baseline and follow-up examinations in our study results in less misclassification on the outcome measures. However, whereas cardiorespiratory fitness is an accurate marker of habitual physical activity, it is more costly and time-consuming to assess than physical activity. Further, from a clinical perspective, one can give advice to increase physical activity, whereas advice to "increase your physical fitness" is less practical.

Limitations of the present study include the following. Because there was no information about the type of diabetes in this study, we could not differentiate precisely between type 1 (insulin-dependent) and type 2 diabetes. However, we examined men who reported insulin use on the last follow-up medical questionnaire among men diagnosed with type 2 diabetes on the basis of fasting plasma glucose. Only 2.7% of men (13 of 477) reported insulin use. Among them, none were diagnosed with

type 2 diabetes at age <30 years; thus, there were likely to be few men with type 1 diabetes in this study.

The majority of participants were well-educated white men, limiting the generalizability of the findings. However, the biological processes underlying the roles of physical inactivity and obesity in the etiology of type 2 diabetes are likely to be similar across individuals of different race/ethnic and educational groups.

Although we did not have data from an oral glucose tolerance test, a fasting plasma glucose test is an objective clinical method to diagnose type 2 diabetes as supported by the ADA and the World Health Organization and used in numerous prospective studies (5,12,13,15). In addition, participants in this study frequently revisited the clinic (every 1.5 years on average) for their medical examination; thus, fasting glucose tests during these frequent follow-up medical examinations are likely to identify most type 2 diabetes events. Because dietary data were not available in this study, we were unable to assess the effect of diet on our findings.

Because loss to follow-up may be related to the exposure or outcome variables, we compared the main clinical variables between men with follow-up versus men lost to follow-up for any reason. Age, treadmill time, BMI, fasting plasma glucose, and other clinical measures at baseline were relatively similar between two groups.

In summary, although fitness did not eliminate the harmful effect of obesity, both low fitness and obesity were each associated with increased risks of IFG and type 2 diabetes of approximately equal magnitude in men, after accounting for possible confounders. Because obese and unfit men showed the highest risks of IFG and type 2 diabetes, both fitness and weight control should be emphasized to slow down the current epidemic of IFG and type 2 diabetes, together with its commensurate economic burden. Increasing physical activity in daily life is an effective practical strategy to improve both fitness and obesity.

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