

Original Article

Obesity and changes in body weight related to 10-year diabetes incidence in women in Taiwan (1993-2003)

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This study aimed to investigate the relation of obesity and changes in body weight through adulthood with risks of type 2 diabetes. This study of 954 middle-aged women free of diabetes (mean age, 37.1±9.6 years) was conducted in a hospital. The baseline and biannual health check-ups were performed from 1993 to 2003. The cumulative incidence rate of type 2 diabetes was 3.64 per 1000 person-years during the mean follow-up period of 10 years. 73.3% of subjects who developed type 2 diabetes were overweight (16.6%) or obese (56.7%). Obese subjects (body mass index more than 25 kg/m²) had a relative risk of type 2 diabetes of 10.4 (95% confidence interval 2.95-36.9) compared with subjects with an optimal body mass index (18-22.9 kg/m²). Long-term weight gain was strongly related to the risk of type 2 diabetes. Each 1 kg of weight gain was associated with a 16% increase in risk of developing diabetes. This study indicated that obesity at young adult and weight gain appreciably increase risk for type 2 diabetes. Maintaining a lean weight throughout adulthood seems to be beneficial in the primary prevention of type 2 diabetes.

Key Words: obesity, body mass index, weight change, incidence, type 2 diabetes, Taiwan

INTRODUCTION

Obesity is an epidemic problem in the industrialized world¹⁻⁴ and is also a growing problem in Taiwan.⁵ Obesity is well recognized as a major risk factor for the development of type 2 diabetes. According to series reports of data on Caucasians, risks for diabetes are greatly increased in obese subjects.⁶⁻¹¹ The diabetes risk was four times higher in males in the Health Professionals Follow-up Study, and eight times higher in women in the Nurses' Health Study, where subjects with body mass index (BMIs) > 26 were compared to analogs with BMIs < 21.¹² Although Asian adults have a much lower prevalence of obesity in comparison with Caucasian populations by World Health Organization criteria, similar risks have been shown in Asian populations, such as Japanese and Chinese.^{13,14} The risks associated with weight gain or changes have been elucidated in Caucasian populations.¹⁵⁻²² But there was no Taiwanese data to evaluate the relations between weight changes and the risk of diabetes.

Because treating diabetes over a long period is costly, the best approach for the control of diabetes is primary prevention. Examining the modifiable risks for diabetes, including obesity and weight changes, has important public health implications. The purpose of this study was to examine cohort data of middle-aged Taiwanese women to describe the effects of weight excess and its changes on the incidence of diabetes.

MATERIALS AND METHODS

Subjects

Participants were employees of a hospital in Taipei, Taiwan. A total of 1,434 women aged 21 – 55 years received health examination in 1993. We excluded subjects who, at baseline, had pregnancy (n=11), body mass index (BMI) less than 18 (n=74) or reported diabetes (n=10) and who resigning from job (n=349), during follow-up period, or died from other diseases (n=36). Subjects who retired (n=125) were included. Data from the 954 participants (66.5% follow-up rate) were used in the analysis. There were no significant differences comparing the study subjects and loss-of-follow-up groups for age, BMI and prevalence of baseline metabolic disorders.

The baseline health examination consisted of history-taking, physical examinations, anthropometric measurements (body height and weight), and blood pressure, fasting plasma glucose, total cholesterol, and triglyceride in 1993. Venous blood was drawn for measurements after an overnight fast and analyzed at a central laboratory in hospital. Blood pressure was measured by sitting position after resting for 10 minutes. BMI was calculated by weight in

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kilograms divided by the height squared in meters. These cutoffs of BMI corresponded to the definition of overweight and obesity suggested by the 2000 World Health Organization Asian Pacific Guideline.²³ Subjects were classified into normal weight (BMI: 18-22.9 kg/m²), overweight (BMI: 23-24.9) and obese (BMI>25) at baseline. Subjects were asked to fill out a questionnaire including family history of diabetes and alcohol intake. The biannual health examination has been performed from 1993 to 2003. We recorded the further BMI of subjects who had type 2 diabetes at the first diagnosis by reviewing their medical charts, and of those who did not have diabetes at regular health checkup in 2003. Hypertension was defined as systolic blood pressure > 140 mmHg and/or diastolic blood pressure > 90 mmHg, or physician-diagnosed hypertension. Hyperlipidemia was defined as serum total cholesterol > 6.20 mmol/L and/or triglyceride > 2.25 mmol/L according to Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Full Report.

Criteria of type 2 diabetes

Diabetes was defined according to the American Diabetes Association criteria.²⁴ Medical charts were reviewed, and a diagnosis of incident diabetes was confirmed if the subject met one of the following criteria: 1) a fasting plasma glucose level of at least 7.0 mmol/L and a 2 hr postprandial plasma glucose level of at least 11.1 mmol/L; or 2) elevated fasting plasma glucose level (≥ 7.0 mmol/L) on at least two different occasions; or 3) treatment with hypoglycemic medication. We recorded the date of the first diagnosis.

Statistical analysis

Analysis of variance (F test) was performed to compare the continuous covariates among different categories of

BMI. Incidence rates were obtained by dividing the number of cases by person-years in each category of BMI. Person-years for each subject with diabetes were estimated from the date of their first checkup in 1993 to the date when diabetes was diagnosed by clinical physicians, or the last examination in 2003. Relative risk was used as the measure of association. Proportional hazards analyses (Cox regression models) were performed to compute age-adjusted and multivariate-adjusted relative risks with 95% confidence intervals. Covariates included age, alcohol intake (never, occasional and regular), family history of diabetes and baseline measurements (fasting plasma glucose, hypertension, hyperlipidemia).

Weight changes in either direction were used, with loss of weight having a negative value and gain in weight having a positive value. To obtain greater statistical power in assessing the relationship between weight change and risk of diabetes, weight changes were fitted as a continuous covariate. We divided two Cox regression models of weight loser (model I: weight change < 0) and weight gainer (model II: weight change > 0). We determined the relative risk of diabetes for weight gain or loss in 10 years, controlling for age, BMI, family history of diabetes, hypertension, hyperlipidemia, fasting plasma glucose levels and alcohol intake.

RESULTS

Table 1 shows baseline characteristics at the start of this study in 1993. In 1993, a total 954 of women were 21 – 55 years of age, with a mean age of 37.1 (standard deviation, SD 9.6) years. The prevalences of hypertension and hyperlipidemia were 14.1% and 7.6%, respectively. The mean body mass index at baseline in this cohort was 22.1 (SD 3.0) kg/m²; while most subjects (66.2%) were of an optimal BMI, 17.4% were overweight, and 16.4% were obese. Total follow-up time was 8,234.5 person-years. There were 30 incident cases of diabetes during the mean

Table 1. Baseline characteristics related to subsequent type 2 diabetes over 10 years follow up

Characteristics	Diabetes (n=30)	Non diabetes (n=924)	Total (n=954)
Age (y)	44.8 (9.7)***	36.8 (9.5)	37.1 (9.6)
Family history of diabetes (%)	63.3***	22.4	23.7
Hypertension (%)	43.3***	13.1	14.1
Hyperlipidemia (%)	13.3	7.4	7.6
Current alcohol drinker (%)	5.9	4.7	4.7
BMI† (kg/m ²)	26.1 (4.0)***	22.2 (2.7)	22.1 (3.0)
Overweight (%), BMI 23-24.9	16.7	17.4	17.4
Obesity (%), BMI ≥ 25	56.7***	15.3	16.4
Fasting plasma glucose (mmol/L)	5.7 (0.7)***	5.0 (0.7)	5.0 (0.5)
Systolic blood pressure (mmHg)	129 (18.9)***	114 (15.1)	115 (15.4)
Diastolic blood pressure (mmHg)	83.1 (11.4)**	75.9 (9.8)	76.2 (9.9)
Total cholesterol (mmol/L)	5.0 (0.9)	4.8 (0.9)	4.8 (0.9)
Triglyceride (mmol/L)	1.4 (0.7)**	1.0 (0.7)	1.0 (0.6)

Data are means (SD) and %. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, as compared to non diabetes subjects.; † Body mass index.

Table 2. Rate per 1,000 person-years and adjusted relative risk (RR) of type 2 diabetes by body mass index categories

	Body mass index categories (kg/m ²)			<i>p</i> -level
	18.0-22.9 (n=630)	23.0-24.9 (n=166)	≥25.0 (n=158)	
Age (y)	34.6 (8.3)	39.9 (9.9)	43.7 (10.2)	<0.001
Body mass index (kg/m ²)	20.6 (1.3)	23.9 (0.6)	27.2 (2.2)	<0.001
Family history of diabetes (%)	20.6	26.5	33.1	0.0030
Hypertension (%)	7.6	21.7	31.7	<0.001
Hyperlipidemia (%)	3.0	15.1	17.7	<0.001
Current alcohol drinker (%)	3.8	9.2	4.5	0.04
Fasting plasma glucose (mmol/L)	4.9 (0.5)	5.1 (0.5)	5.3 (0.6)	<0.001
Total cholesterol (mmol/L)	4.7 (0.8)	5.1 (1.1)	4.9 (0.9)	<0.001
Triglyceride (mmol/L)	0.8 (0.3)	1.1 (0.7)	1.5 (1.0)	<0.001
Systolic blood pressure (mmHg)	111 (12.9)	118 (17.1)	124 (17.7)	<0.001
Diastolic blood pressure (mmHg)	74.1 (8.9)	78.9 (9.7)	81.6 (11.1)	<0.001
Cumulative incidence (per 1,000 person-years)	1.3	4.0	18.7	<0.001
RR (adjusted for age)	1.00	1.81 (0.57-5.77)	5.93 (2.32-15.15)	
RR† (adjusted for multivariates)	1.00	1.02 (0.10-5.56)	10.4 (2.95-36.9)	

† Cox regression model: adjusted for age, alcohol intake status, family history of diabetes, and medical history of hypertension, and hyperlipidemia.

Table 3. Cox regression analysis of the effect of weight change over 10 years and baseline characteristics on risk of subsequent type 2 diabetes

variables	model I (weight gain)		model II (weight loss)	
	RR	95% CI	RR	95% CI
Weight change (kg)	1.16	1.01-1.33	0.99	0.61-1.62
Baseline BMI† (kg/m ²)	1.31	1.07-1.58	1.77	1.01-3.09
Family history of diabetes (yes/no)	6.43	1.53-20.0	8.19	1.90-72.2
Fasting plasma glucose (mmol/L)	8.65	1.70- 44.0	4.50	1.09-22.6
Age (y)	1.08	0.98-1.21	1.07	0.89-1.27
Current alcohol intake (yes/no)	3.68	0.41-33.1	-	-
Hypertension (yes/no)	3.35	0.74-15.3	2.29	0.28-18.7
Hyperlipidemia (yes/no)	1.38	0.25-7.59	5.01	0.46-54.4

† Body mass index.

follow-up period of 10 years, a rate of 3.64/1,000 person-years. The subjects who developed diabetes were older, with positive family diabetes history and higher baseline levels of fasting blood glucose, BMI, systolic blood pressure, diastolic blood pressure, and triglyceride (Table 1). 73.3% of subjects who developed diabetes were overweight (16.6%) or obese (56.7%).

The incidence of diabetes increased progressively with increasing categories of baseline BMI, and the incidence (18.7/1000 pys) was significantly increased at BMI levels more than 25.0 kg/m² (Table 2). The age-adjusted risk for type 2 diabetes was not significantly different between subjects with BMI 18-22.9 and those with BMI 23-24.9.

However, subjects with BMI more than 25 kg/m² had a 5.93-fold higher relative risk than subjects with BMI 18-22.9 kg/m². After adjustment for the possible confounding factors, the risk remained significant in obese subjects. The multivariate-adjusted RRs and 95% CIs for overweight group and obesity group were 1.02 (0.10-5.56) and 10.4 (2.95-36.9), respectively.

Baseline BMI was a significant predictor for the development of type 2 diabetes regardless of long-term weight gain or loss. Long-term weight gain was strongly related to the risk of diabetes (Table 3) after controlling for family history of diabetes, alcohol intake status, hypertension, hyperlipidemia, baseline fasting plasma glucose, and

body mass index. Each 1 kg weight gain was associated with a 16% increase in risk of developing diabetes in the subsequent 10 years. However, the effect of weight loss was not significant.

DISCUSSION

The present study, based on 10 years of follow-up, confirms that the risk of diabetes increased progressively with increasing baseline BMI and significantly increased at levels of BMI ≥ 25 kg/m². We also found positive associations between greater weight gains and risk of diabetes, independent of known risk factors.

Type 2 diabetes is strongly associated with obesity in both genders in many ethnic groups.⁶⁻¹¹ This association has been also found in populations from industrialized and non-industrialized areas. The risk of diabetes was lowest in individuals with a BMI less than 22 kg/m² in the Nurses Health Study and 24 kg/m² in the Health Professionals Follow-Up Study.^{9,10} As BMI increased, the relative risk increased, such that at a BMI of 35 kg/m², the relative risk increased 40-fold to 60-fold. Our study is consistent with previous studies, indicating a strong relation between BMI in midlife and subsequent risk for diabetes. Higher BMI was strongly related to an increased risk for subsequent diabetes, and the risk was still appreciable after we controlled for weight changes later in life. At a BMI above 25 kg/m², the multivariate-adjusted relative risk for diabetes increased 10-fold. It was still significant when BMI was treated as a continuous variable; increase in BMI of 1 kg/m² increased risk by 32 %.

In addition to BMI, weight gains appeared to precede the onset of diabetes. The finding of increased risk of diabetes among weight gainers is consistent with those of several other adult population studies.¹⁰⁻²² In the Health Professionals Follow-Up Study, relative risk of developing diabetes increased with weight gain as well as with increased baseline BMI, whereas a 3-kg weight loss was associated with a reduction in relative risk, and relative risk declined by nearly 50% with a weight loss of 5–11 kg. Weight loss seems to be a promising method for reducing incidence of diabetes among high-risk populations.²⁵⁻²⁸ However, in this study, the effect of weight loss was not significant after adjustment for covariates. The information of further body weight in incident cases of diabetes was available in their medical chart on the date of diagnosis. Body weight may loss due to disease process which could lead to an underestimation of the benefits of weight loss for diabetes incidence and, thus, bias our result toward the null. Another potential cause was that the extenuatory weight over the follow up period (mean: -2.1 kg) was trivial and insufficient to reduce the risk of diabetes. Indeed, the efficacy of weight reduction approach in the primary prevention of diabetes is not well established. Some investigators have observed an increased risk of diabetes,²⁹ and others have suggested that weight fluctuation (weight loss followed by weight gain) may be diabetogenic.³⁰

Because as many as one million Taiwanese, or one in ten adults more than 40 years old, are classified as diabetic, an effective means of preventing diabetes has great clinical and public health importance. Our data provide the evidence that long-term weight gain dramatically in-

creases the incidence of diabetes, although this study revealed no significant benefit for subsequent diabetes when subjects lost weight during 10 years. We found those subjects who developed diabetes among weight losers had higher baseline fasting plasma glucose (mean: 5.9 vs. 5.3 mmol/L), higher baseline BMI (mean: 26.3 vs. 25.8 kg/m²), and higher prevalence of family history of diabetes than those who developed diabetes among weight gainers.

The mechanisms leading to diabetes in obese persons are not completely known. It is hypothesized that increased insulin resistance and hyperinsulinemia.^{31,32} Obesity results in the increase secretion of free fatty acids from fat cells that are then stored in the liver or muscle, and reduced production of adiponectin, which induce an insulin-resistant state, hyperinsulinemia, and diabetes develops. Previous study shows that insulin resistance and hyperinsulinemia are reversible with weight loss.³³

Both obesity and type 2 diabetes are preventable.²⁷ Lifestyle choices such as increased consumption of fruit punch and sugar-sweetened soft drinks were associated with greater weight gain and incidence of diabetes.³⁴ Previous studies have demonstrated that changes in lifestyle are effective in preventing both diabetes and obesity in high-risk adults with impaired glucose tolerance.^{27,35} Increasing physical activity, improving diet, then sustaining these lifestyle changes can reduce both weight and risk of diabetes.

In conclusion, our findings indicate that excess BMI during young adulthood and sequential weight gain appreciably increase risk for developing diabetes. Thus, maintaining a lean weight throughout adulthood seems to be beneficial in the primary prevention of diabetes. Public health strategies to prevent type 2 diabetes need to focus on preventing obesity and further weight gain.

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AUTHOR DISCLOSURES

Lee-Ching Hwang, Chien-Jen Chen and Boniface J Lin, no conflicts of interest.

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Original Article

Obesity and changes in body weight related to 10-year diabetes incidence in women in Taiwan (1993-2003)Lee-Ching Hwang MD PhD^{1,2}, Chien-Jen Chen PhD³ and Boniface J Lin PhD⁴¹Department of Family Medicine, Mackay Memorial Hospital, Taipei, Taiwan²Mackay Medicine, Nursing and Management College, Taiwan³Graduate Institute of Epidemiology, College of Public Health, National Taiwan University, Taipei, Taiwan⁴Graduate Institute of Clinical Medicine, College of Medical School, National Taiwan University, Taipei, Taiwan**臺灣女性肥胖及體重增加與 10 年後糖尿病發生率的相關**

研究目的在探討成人期肥胖與體重增加是否影響第二型糖尿病的發生率，本研究對象為 954 位女性(平均年齡 37.1±9.6 歲)，自 1993 年起至 2003 年定期健康檢查，追蹤 10 年之後發現第二型糖尿病的發生率為每千人年 3.64，發生糖尿病的人之中有 16.6% 是屬於體重過重，而 56.7% 是肥胖者，身體質量指數超過 25kg/m² 的人發生第二型糖尿病的危險性是身體質量指數介於 18-22.9kg/m² 的 10.4 倍。體重增加亦是發生第二型糖尿病的高危險群，每增加一公斤體重可以增加 16% 的風險，在女性成人期若是能避免體重過重或是肥胖，並維持適當體重有利於預防第二型糖尿病。

關鍵字：肥胖、身體質量指數、體重改變、發生率、第二型糖尿病、臺灣。