Original Paper

Annals of Nutrition & Metabolism

Ann Nutr Metab 143
DOI: 10.1159/000XXXXXX

Received: July 14, 2008
Accepted after revision: January 16, 2009
Published online: ■■■

Patterns and Predictors of Long-Term Weight Change in Patients with Type 2 Diabetes Mellitus

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Key Words
Adults · Diabetes mellitus · Obesity · Overweight · Weight change

Abstract
This study describes patterns of long-term weight changes among patients with type 2 diabetes mellitus (DM) and identifies factors associated with weight changes. During the mean follow-up period of 9.1 (SD 3.6; range 1–15) years, 7,820 patients with type 2 DM have been examined to determine weight changes. Their weight at the last clinic visit was compared with that at the initial visit. The mean age of the participants was 51.3 (SD 10.5) years, with a mean DM duration of 6.1 (SD 5.6) years at initial registration. Mean weight change was –1.9% (95% confidence interval, CI –2.1 to –1.7) and varied according to the severity of baseline obesity (–4.1%; 95% CI –4.6 to –3.6) for normal weight, –8.9% (95% CI –13.0 to –4.8) for underweight, –1.7% (95% CI –2.1 to –1.3) for overweight and –0.3% (95% CI –0.03 to +0.73) for obese, and +0.2% (95% CI –1.8 to +2.1) for morbidly obese patients. Using a stepwise multiple regression model, higher body mass index, follow-up, fasting plasma glucose, systolic blood pressure, triglyceride level and treatment with insulin increased the percent weight change, and higher number of follow-up, cholesterol and smoking significantly decreased it. Although this Iranian patients with type 2 DM had negligible weight change over 9.1 years on average, several clinical and lifestyle characteristics were associated with weight change.

Introduction

At the time of diagnosis of type 2 diabetes mellitus (DM), much attention is directed toward modifying the patient's lifestyle and major DM risk factors, including obesity, blood pressure (BP) and cholesterol levels. The impact of overweight and obesity on health in type 2 DM patients is dramatic, as evidenced by the association of a high body mass index (BMI) with morbidity and mortality [1, 2]. Fortunately, weight is a potentially modifiable risk factor, and weight reduction has been associated with changes in DM complications and glycemic control [3–8]. Weight control efforts are an important component of the clinical management of DM because good glycemic control is often achieved at the cost of weight gain [9]. Although most studies have shown intentional weight reduction to be associated with a significant improvement in glycemic control [3–8, 10–12], no study evaluated long-term patterns and predictors of weight change in Iranian

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patients with type 2 DM. In light of the known benefits of weight reduction on type 2 DM management, as well as emerging therapies for weight reduction, deeper insights into patterns of long-term weight change in DM, along with patient and treatment characteristics associated with weight change, are urgently needed. By understanding patterns and predictors of long-term weight change in patients with type 2 DM, new potential interventions can be developed.

The purpose of this study was to describe patterns of long-term weight change in patients with type 2 DM and to identify factors associated with weight change.

Patients and Methods

Data Collection

The recruitment methods and examination procedures of the Isfahan Endocrine and Metabolism Research Center outpatient clinics have been described before [13]. In summary, clinical data are collected for all consecutive patients at the first attendance and at review consultations (usually annually) using standard encounter forms. These include an examination of ocular fundus, lens, limbs and BP, and construction of a problem list by the clinician, measurement of height, weight, fasting plasma glucose (FPG), glycosylated hemoglobin (HbA_{1c}), urine protein, triglyceride, cholesterol and serum creatinine levels, and reporting of smoking as part of a completed questionnaire on demography, family history and smoking by the patient. A registry clerk of the clinic enters the data from these forms into a computer file.

After the start of therapy, all patients were referred for nutritional and weight management to qualified nutritionists to evaluate the patient and – if necessary – recommend a weight management program.

Patients

Between 1992 and 2007, a total of 12,971 patients with type 1 and type 2 DM were registered in the system. However, this study uses only the data from 7,820 patients [2,990 (38.2%) men and 4,830 (61.8%) women] with type 2 DM who had at least one subsequent review since registration at baseline. Tenets of the Declaration of Helsinki were followed, institutional ethical committee approval was granted, and an informed consent was signed by each patient.

Predictors of weight change were assessed using the following data from the patient's registration consultation: gender, age, age at diagnosis, educational level, duration of DM (the time between diagnosis and the baseline examination), BMI (weight/height^2 in kg/m^2), smoking status (never/current), hemoglobin A_{1c} (HbA_{1c}) (measured by spectrophotometer as an indicator of diabetic control), FPG, proteinuria, serum creatinine, triglyceride, cholesterol and BP (systolic and diastolic) at registration. DM treatment (insulin, oral agent and diet alone) used in the analysis was that recorded at the last clinic visit.

Height and weight were measured with subjects in light clothes and without shoes using a standard apparatus. Weight was measured to the nearest 0.1 kg on a calibrated beam scale. Height was measured to the nearest 0.5 cm with a measuring tape. Height was assessed at baseline only.

Definitions

BMI is recognized as the measure of overall obesity. The criteria for underweight, normal weight, overweight and class I, II and III obesity used in the present study were based on BMI and were consistent with the definitions set forth by the World Health Organization and the National Heart, Lung and Blood Institute as follows: underweight <18.5, normal weight 18.5–24.9, overweight 25–29.9, class I obesity 30–34.9, class II obesity 35–39.9 and class III obesity ≥40 [14, 15]. Percent weight change was determined by taking the difference between the baseline and last measured weight and dividing that by the patient's baseline weight. There was no weight fluctuation during the study period. For outcome definitions, the individuals were grouped into three weight change categories: (a) weight reduction, (b) stable, serving as the reference category, and (c) weight gain. Patients were classified as having had a clinically significant weight reduction if their weight at the last follow-up visit was at least 4% lower than the baseline weight. Those who had gained or lost <4% in body weight were classified as stable. Those who had gained ≥4% in body weight were classified as weight gain [16]. Smoking was estimated from self-report and categorized in current and non-smokers. The physician defined the type of DM according to the American Diabetes Association criteria [17].

Analysis

Statistical methods used included the Student's t test, the χ^2 test and stepwise multiple linear regression, to test associations between baseline variables and percent weight change. Forward stepwise multiple regression analysis was developed to determine independent predictors of percent weight change using the SPSS for Windows computer package (SPSS, Chicago, Ill., USA), which simultaneously adjusted for other covariates. For this analysis, number of follow-up visits, age, duration of DM, FPG, HbA_{1c}, systolic BP, total cholesterol and BMI were included as continuous variables. Percent weight change was included as a continuous variable in its original form. The percentage of weight change in either direction was used, with weight reduction having a negative value and weight gain having a positive value. The purpose was to determine the significance of the change over the continuum from the maximum weight reduction to the maximum gain. Gender and cigarette smoking (non-smoker and current smoker) were entered as dichotomous variables. Therapeutic regimen (diet, oral agent and insulin) and educational level (primary or below, secondary and matriculation or above) were included as trichotomous variables. Age-adjusted means were calculated and compared using general linear models. All statistical tests were two sided, and $p < 0.05$ was considered statistically significant.

Results

Patients had a mean duration of DM of 6.1 (SE 0.06) years and a mean age of 51.3 (SE 0.12) years at baseline. The average time of follow-up was 9.1 (SE 0.04) years (range 1–15 years). The average number of follow-up vis-

Table 1. Characteristics of 7,820 patients with type 2 DM at the baseline and last follow-up visits

	Baseline	Last follow-up	Difference (95% CI)
Age, years	51.3 ± 0.12	60.4 ± 0.13	9.1 (8.7, 9.4)*
Weight, kg	69.7 ± 0.14	70.7 ± 0.14	1.0 (0.9, 1.2)*
Height, cm	159.1 ± 0.10	–	–
BMI	27.7 ± 0.05	28.0 ± 0.05	0.3 (0.2, 0.4)*
Weight change, kg	–	1.0 ± 0.07	–
Systolic BP, mm Hg	122.1 ± 0.21	133.8 ± 0.25	11.7 (11.2, 12.1)*
Diastolic BP, mm Hg	74.8 ± 0.13	83.6 ± 13.0	8.8 (8.5, 9.1)*
FPG, mg/dl	203.9 ± 1.40	166.6 ± 0.79	–37.3 (–36.4, –32.3)*
HbA_{1c}, %	9.1 ± 0.04	7.7 ± 0.04	–1.4 (–1.5, –1.3)*
Creatinine, μM	0.9 ± 0.01	1.0 ± 0.01	0.1 (0.03, 0.12)*
Triglyceride, mg/dl	228.7 ± 1.82	202.4 ± 1.53	–26.3 (–29.5, –22.6)*
Cholesterol, mg/dl	222.9 ± 0.60	208.2 ± 0.60	–14.7 (–15.9, –13.3)*
Gender			
Men	38.2%	–	–
Women	61.8%	–	–
Therapeutic regimen			
Diet	5.0%	5.0%	0.0 (–0.7, 0.7)
Oral agent	79.6%	64.2%	–15.4 (–16.8, –14.0)*
Insulin	15.3%	30.7%	15.4 (14.1, 16.7)*
Weight change			
Loss (≥4%)	–	28.5%	–
Stable	–	52.0%	–
Gain (≥4%)	–	19.5%	–
Weight category			
Normal weight (BMI 18.5–24.9)	28.0%	26.0%	2.0 (0.4, 3.3)*
Underweight (BMI <18.5)	1.0%	0.8%	0.2 (–0.1, 5.0)
Overweight (BMI 25–29.9)	43.1%	43.6%	–0.5 (–2.1, 1.0)
Class I obesity (BMI 30–34.9)	21.8%	22.4%	–0.6 (–1.9, 0.7)
Class II obesity (BMI 35–39.9)	4.9%	5.6%	–0.7 (–1.5, –0.03)*
Class III obesity (BMI ≥40)	1.3%	1.5%	–0.2 (–0.5, 0.2)
Obesity (BMI ≥30)	28.4%	29.9%	–1.5 (–3.0, –0.05)*
Overweight and obesity (BMI ≥25)	71.9%	73.8%	–1.9 (–3.4, –0.5)*

Data are means ± SE unless indicated otherwise.
* $p < 0.001$.

its was 13.1 (SE 0.15; range 2–96 visits); 28.5% of men and 3.1% of women were smoking at the baseline evaluation. The age-adjusted mean BMI was 26.2 (SE 0.07) kg/m^2 in men and 28.6 (SE 0.07) in women.

At baseline, 38.3% (95% confidence interval, CI, 36.5–40.1) of the men and 21.4% (95% CI 20.2–22.6) of the women had normal weights. Nearly two thirds of patients were overweight or obese (BMI ≥25; 71.9%; 95% CI 70.9–72.9). Overall, 61.2% men and 78.5% women were overweight or obese, and 15.5% men and 36.3% women were obese (BMI ≥30); 1.4% of men and 0.7% of women were underweight (BMI <18.5) and 0.4% of men and 1.9% of women were morbidly obese (BMI ≥40). The prevalence of class I, II and III obesity was greater in women than in men, among insulin-treated patients compared with patients on diet or oral agents, among patients with creatinine ≤1.2 compared with creatinine >1.2 and increased with systolic and diastolic BP, and decreased with duration of DM (data not shown).

Patient characteristics at baseline and the last follow-up visit are presented in table 1. At the last clinic visit, patients had higher weight, BMI, creatinine and systolic/diastolic BP, and lower FPG, HbA_{1c}, triglyceride and cholesterol levels than at baseline ($p < 0.001$). The frequency of insulin use was higher at the last clinic visit. Of all patients, 64.2% were using hypoglycemic medication by the last visit.

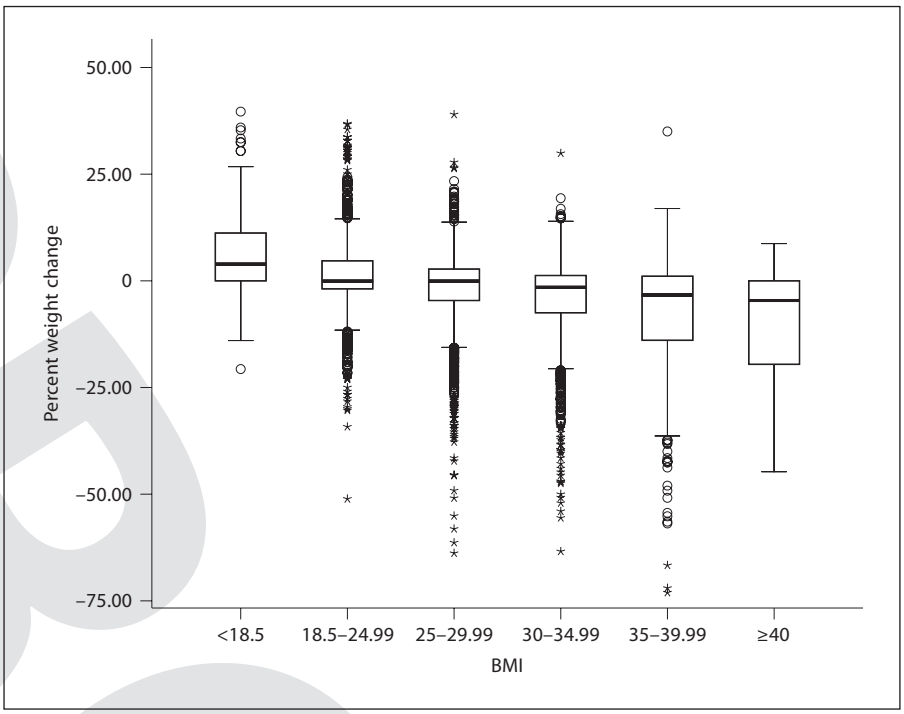

Fig. 1. Weight change after the 9.1-year follow-up by obesity categories.

Weight change was, on average, minimal. Between the baseline and last clinic visits, a mean of 1.0 (SE 0.07) kg was lost or gained. Large weight changes were infrequent; the percentage of patients that lost or gained ≥15 kg during follow-up was <7%. The percentage that lost at least 5 kg was 19.0%; 7% gained ≥5 kg. Most patients (52.0%) were stable in weight, 28.5% had lost ≥4% of their baseline weight, and 19.5% had weight gain. Only one fourth (22.7%) of the patients who lost weight were obese (BMI ≥30) at baseline, and at the last clinic visit 39.9% remained obese. The proportion of patients who lost ≥4% of their baseline weight decreased with the BMI category from 35.2 to 1.1% among patients with normal weight to morbidly obese. Initial weight was within the normal range in those who lost more weight and highest in those who had gained weight.

As a percentage of total body weight, the average weight gain during the 9.1 years was 1.9% (SE 0.12) for the entire population, representing approximately 1.0 kg. The age-adjusted mean weight change varied by level of obesity (fig. 1): 4.1% (SE 0.2; ~2.2 kg) weight reduction for normal weight patients; 1.4% (SE 0.2; ~0.8 kg) weight reduction for overweight patients; 0.3% (SE 0.2; ~0.002 kg) weight reduction for obese patients, and 0.2% (SE 1.2; ~0.7 kg) weight gain for morbidly obese patients. With increasing BMI categories at baseline, patients were less likely to lose weight than those with less severe obesity.

Table 2 describes the age-adjusted associations of patient characteristics with percent weight change. Characteristics associated with a greater weight reduction include female sex, lower education and longer duration of DM, never smokers, insulin treatment regimen and higher HbA_{1c} at baseline. Characteristics associated with greater weight gain included the cases of class II and III obesity at baseline. When the patients were classified according to different therapeutic regimens, a difference in weight change was observed. A higher proportion of those who used insulin lost weight. A small increase in weight occurred when patients were treated with oral agents or diet.

Percent weight change was slightly positively correlated with BMI ($r = 0.16$, $p < 0.001$), systolic BP ($r = 0.04$, $p < 0.001$), diastolic BP ($r = 0.04$, $p < 0.01$) and age at diagnosis of DM ($r = 0.04$, $p < 0.001$), and negatively correlated with duration of DM ($r = -0.09$, $p < 0.001$), FPG ($r = -0.14$, $p < 0.001$), HbA_{1c} ($r = -0.16$, $p < 0.001$), follow-up duration ($r = -0.06$, $p < 0.001$), number of follow-up visits ($r = -0.24$, $p < 0.001$) and cholesterol ($r = -0.03$, $p < 0.05$) at baseline.

The percent weight change category was also analyzed with multivariate regression analysis. Higher BMI (β =

Table 2. Age-adjusted associations of patient characteristics at baseline with percent weight change after an average follow-up of 9.1 years in Isfahan, Iran (means ± SE)

Variables	Age-adjusted weight change, %					
	entire group	normal weight	overweight	class I obesity	class II obesity	class III obesity
Gender						
Men	–1.3 ± 0.2***	–3.1 ± 0.3***	–5.4 ± 0.2***	+0.3 ± 0.5*	+2.7 ± 1.2	+0.4 ± 2.7
Women	–2.2 ± 0.1	–5.1 ± 0.4	–1.9 ± 0.2	–0.9 ± 0.2	+0.4 ± 0.5	+0.09 ± 1.1
Age at registration						
<40 years	–1.8 ± 0.3*	–4.0 ± 0.7*	–1.5 ± 0.4	+0.3 ± 0.6	+1.4 ± 1.2	+3.1 ± 3.0
40–49 years	–1.6 ± 0.2	–4.0 ± 0.5	–1.4 ± 0.3	–0.4 ± 0.4	+0.6 ± 0.8	+0.5 ± 1.5
50–59 years	–2.4 ± 0.2	–5.1 ± 0.4	–1.6 ± 0.3	–1.0 ± 0.4	+0.2 ± 0.8	–1.6 ± 1.7
60–69 years	–1.8 ± 0.3	–3.3 ± 0.5	–1.1 ± 0.3	–1.2 ± 0.5	+1.5 ± 1.4	+0.1 ± 3.3
≥70 years	–1.3 ± 0.5	–2.3 ± 0.9	–0.9 ± 0.7	+0.4 ± 1.3	+2.3 ± 4.1	+9.4 ± 10.0
Age at diagnosis						
<30 years	–2.1 ± 0.5*	–4.9 ± 1.1	–0.9 ± 0.7*	–0.4 ± 0.9	+0.1 ± 2.3	+7.9 ± 7.1
30–59 years	–2.0 ± 0.1	–4.2 ± 0.3	–1.5 ± 0.2	–0.8 ± 0.2	+0.6 ± 0.5	–0.07 ± 1.0
≥60 years	–1.0 ± 0.3	–2.9 ± 0.7	–0.1 ± 0.5	+0.5 ± 0.8	+3.7 ± 2.1	+0.6 ± 4.5
Duration of diabetes						
<5 years	–1.1 ± 0.2***	–3.3 ± 0.4*	–0.9 ± 0.3***	–0.006 ± 0.3**	+1.5 ± 0.6*	+1.2 ± 1.1
5–9 years	–1.9 ± 0.2	–4.1 ± 0.5	–1.1 ± 0.3	–1.0 ± 0.4	–0.1 ± 1.0	–1.8 ± 2.7
≥10 years	–3.5 ± 0.2	–5.0 ± 0.4	–2.8 ± 0.3	–2.2 ± 0.5	–2.1 ± 1.3	–5.7 ± 3.2
FPG						
<100 mg/dl	–2.3 ± 0.6***	–4.6 ± 1.4***	–2.0 ± 0.8***	–0.02 ± 1.2***	+0.2 ± 2.7	+2.2 ± 5.2
100–124 mg/dl	–0.6 ± 0.3	–2.0 ± 0.9	–0.6 ± 0.5	+0.1 ± 0.6	+2.0 ± 1.4	+4.1 ± 4.5
125–139 mg/dl	–0.6 ± 0.4	–3.0 ± 1.0	–0.6 ± 0.5	+1.4 ± 0.7	+1.6 ± 1.5	–7.5 ± 3.8
140–199 mg/dl	–0.8 ± 0.2	–2.2 ± 0.5	–0.6 ± 0.2	–0.03 ± 0.4	+1.0 ± 0.8	+0.01 ± 1.7
≥200 mg/dl	–3.2 ± 0.2	–5.6 ± 0.3	–2.3 ± 0.2	–1.8 ± 0.4	–0.3 ± 0.8	+0.6 ± 1.5
Hb_{A1}						
≤7%	–0.8 ± 0.4***	–3.1 ± 1.0*	–0.7 ± 0.5***	+1.0 ± 0.7***	+0.07 ± 1.6	–7.7 ± 4.6
7.1–9.0%	–1.6 ± 0.3	–5.3 ± 0.8	–1.5 ± 0.4	–0.1 ± 0.5	+1.7 ± 1.1	+2.2 ± 3.5
9.1–11.0%	–2.9 ± 0.3	–5.8 ± 0.8	–2.8 ± 0.5	–1.0 ± 0.6	+0.2 ± 1.7	–0.2 ± 3.2
11.1–13.0%	–3.5 ± 0.5	–5.9 ± 1.0	–3.3 ± 0.7	–0.4 ± 0.9	+1.7 ± 2.0	–3.1 ± 4.3
>13%	–7.4 ± 0.7	–8.9 ± 1.4	–6.3 ± 1.0	–8.1 ± 1.4	+1.1 ± 2.9	–2.7 ± 13.1
Systolic BP						
<140 mm Hg	–2.0 ± 0.1	–4.2 ± 0.3	–1.3 ± 0.2	–0.5 ± 0.2	+0.4 ± 0.6	–0.4 ± 1.2
140–159 mm Hg	–1.7 ± 0.3	–3.7 ± 0.7	–2.0 ± 0.4	–0.8 ± 0.5	+2.1 ± 1.2	+2.8 ± 2.7
≥160 mm Hg	–1.3 ± 0.4	–2.9 ± 1.1	–1.0 ± 0.6	–1.0 ± 0.9	+0.6 ± 1.6	+0.1 ± 3.2
Diastolic BP						
<70 mm Hg	–2.3 ± 0.2*	–4.2 ± 0.5	–1.3 ± 0.3	+0.6 ± 0.5*	–0.05 ± 1.3	–8.1 ± 3.1*
70–90 mm Hg	–2.0 ± 0.1	–4.2 ± 0.3	–1.4 ± 0.2	–1.0 ± 0.3	+0.5 ± 0.6	+1.5 ± 1.2
≥90 mm Hg	–1.3 ± 0.3	–3.4 ± 0.7	–1.3 ± 0.4	–0.6 ± 0.5	+1.7 ± 1.0	+0.2 ± 1.9
Therapeutic regimen						
Diet alone	+0.7 ± 0.5***	+0.2 ± 1.2***	+0.2 ± 0.6***	+0.9 ± 0.8***	+2.6 ± 1.6***	+5.2 ± 4.5
Oral agent	+0.1 ± 0.1	–1.0 ± 0.3	+0.3 ± 0.2	+0.7 ± 0.3	+1.6 ± 0.6	–0.2 ± 1.2
Insulin	–6.6 ± 0.2	–8.9 ± 0.4	–5.7 ± 0.3	–4.6 ± 0.4	–3.1 ± 1.0	+0.1 ± 2.2
Education						
Primary or below	–2.3 ± 0.1***	–5.1 ± 0.3***	–1.8 ± 0.2***	–0.8 ± 0.3	+0.5 ± 0.5	–0.1 ± 1.1
Secondary	–1.1 ± 0.2	–2.8 ± 0.5	–0.6 ± 0.3	+0.2 ± 0.5	+2.0 ± 1.2	+1.5 ± 3.1
Matriculation or above	–0.8 ± 0.4	–1.5 ± 0.7	–0.2 ± 0.5	–0.09 ± 1.0	+0.09 ± 3.1	–0.2 ± 5.8
Smoking						
Non-smoker	–2.1 ± 0.1**	–4.5 ± 0.3**	–1.6 ± 0.2***	–8.4 ± 0.2	+0.5 ± 0.5	+1.8 ± 0.7
Current smoker	–1.0 ± 0.3	–2.6 ± 0.6	+0.09 ± 0.4	+0.6 ± 0.8	+1.8 ± 2.6	+0.3 ± 3.0

Age-adjusted means were calculated using general linear models. Category definitions are based on the cutoffs of the World Health Organization and the National Heart, Lung and Blood Institute [14, 15]. Normal weight = 18.5–24.9, overweight = BMI 25–29.9, class I obesity = BMI 30–34.9, class II obesity = BMI 35–39.9 and class III obesity = BMI ≥40. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

0.133, $p < 0.001$), follow-up ($\beta = 0.042$, $p < 0.01$), FPG ($\beta = 0.133$, $p < 0.001$), systolic BP ($\beta = 0.034$, $p < 0.01$), triglyceride level ($\beta = 0.064$, $p < 0.001$) and treatment with insulin ($\beta = 0.260$, $p < 0.001$) increased, and higher number of follow-up visits ($\beta = -0.184$, $p < 0.001$), cholesterol ($\beta = -0.044$, $p < 0.01$) and smoking ($\beta = -0.044$, $p < 0.01$) significantly decreased the percent weight change. The overall contribution (R^2) of these factors was <18%, therefore the predictors for a percent weight change during the mean 9.1-year follow-up are yet unresolved.

Discussion

Despite the well-recognized effect of weight reduction on glycemic control in patients with DM, this is the first study to describe patterns and predictors associated with long-term weight change in Iranian patients with type 2 DM. As expected, our study of patients with type 2 DM found a higher prevalence of overweight and obesity than in the general population [18]. Only 28.4% of our patients with type 2 DM lost a clinically significant amount of weight during an average of 9.1 years. In addition, in the cohort of patients with type 2 DM, all of whom are in need of long-term weight management to reduce the cardiovascular risk by improving insulin sensitivity and control of DM, dyslipidemia and hypertension, there was only a slight decrease in weight after a mean follow-up of 9.1 years, with the most significant weight reduction observed in normal weight patients and the least weight reduction in severely obese patients at baseline. In addition, we found that long-term weight change was associated with a number of factors, including the number of follow-up visits, cholesterol, FPG, systolic BP, triglyceride and cholesterol levels, treatment regimen, smoking status and BMI. These factors remained significant even after adjusting for a wide range of patient characteristics. These data may help to alert physicians regarding the minimal weight reduction accomplished in most patients with type 2 DM and to design interventions to support weight reduction after DM diagnosis.

Although interventional studies have shown that weight reduction produces short-term improvement in glycemic control in patients with type 2 DM, few published data describe the natural history of weight changes after the diagnosis of type 2 DM in patients receiving standard care [19, 20]. Chaudhry et al. [19] reported that over the course of at least 5 years, modest weight gain is the norm in men with type 2 DM. In contrast, Looker et al. [20] reported that the general pattern of weight change after diagnosis of type 2 DM in Pima Indians of Arizona, USA, was weight loss, with the mean change in BMI ranging between –0.61 and +0.22 kg/m^2 per year. The most extensive clinical trial to study weight changes was the UK Prospective Diabetes Study (UKPDS). They examined weight changes for various intention-to-treat groups. Over a 3-year follow-up, people in all treatment groups generally gained weight. Weight gain was most pronounced in those on intensive therapy with sulfonylureas or insulin [21]. However, their study populations are very different from that of the present study with regard to age, gender, methodology and genetic background. Therefore, it is difficult to compare our results with those of their study. Nevertheless, in agreement with the abovementioned studies [19–21], in our patients long-term weight change was, on average, minimal. However, the pattern of weight change in type 2 DM is not well recognized and may be quite variable according to patients' characteristics.

Increasing duration of DM was associated with progressively lower BMI and increasing weight change. Since type 2 DM often has an insidious onset, it is difficult to establish weight change patterns with respect to duration of DM. However, we were not able to determine whether weight loss was voluntary, for example in response to medically prescribed dietary therapy, or involuntary, perhaps due to catabolic effects of severe hyperglycemia.

Another interesting observation in the present study is that the most obese patients gained the highest weight. It is not possible from this observational study to define what mediates the observed associations with weight change. However, previous studies suggest that some of our observed associations are complex, whereas others may be more straightforward. For example, patients who were more obese were less likely to lose weight than less obese patients, despite greater social pressures to lose weight. Another complex finding is the effect of gender on weight reduction, with women having a greater percentage of weight reduction than men. Body composition differs considerably by gender, with women having less fat-free mass. This might be responsible for the gender differences in weight changes. This gender difference should be addressed in future studies.

Patterns of weight changes between the initial and last clinic visits were not known in our population. Controversy exists regarding the impact of weight cycling on chronic diseases [22, 23], and its effect on glycemic control has not been demonstrated [24]. Changes in medication use, such as type and dosage, may override any effect of a previous weight change.

Our study has several strengths and limitations. The strengths of this study include the prospective design; large sample size; long-term follow-up, weight determination with a well-functioning, validly calibrated scale, and detailed information on potential confounding factors, such as smoking, body size, DM duration, FPG, HbA_{1c}, systolic and diastolic BP and total cholesterol levels. Selection and information bias were unlikely because of the prospective design and high rate of follow-up. Several limitations of this study should be considered when interpreting our results. First, we used patient weights only at the baseline and last follow-up visits. An additional limitation stems from our use of BMI to categorize obesity levels. Some may argue that the use of BMI is not as accurate as the waist-hip ratio for assessing adiposity and cardiovascular risks [25]. However, weight is an easily measurable and commonly understood risk factor, and our use of clinically accepted categories for BMI is likely to be more directly relevant to patients and physicians in routine clinical care. Individuals in the different categories of weight changes are also likely to differ in several other aspects, such as certain lifestyle and dietary factors. We could not rule out the possibility of residual confounding because of unmeasured or inaccurately measured covariates. For example, information on family history of DM was not collected in the study. People with a family history of DM are likely to pursue a healthy lifestyle. In addition, a large weight reduction, particularly among underweight subjects, may result from the presence of serious comorbidities. Nevertheless, this study provides new data from Iran, a developing country, which has been underrepresented in past studies.

In conclusion, this study highlights the difficult challenges physicians face when treating their patients with type 2 DM, such as the low frequency of achieving a clinically significant amount of weight reduction over a mean follow-up of 9.1 years. Given the importance of weight management in reducing cardiovascular risks by improving insulin sensitivity and control of DM, dyslipidemia and hypertension [26], identifying potentially modifiable factors can serve as an important stimulus for designing new interventions to support weight loss in vulnerable patients with type 2 DM.

Acknowledgments

The authors are grateful to Mr. Majid Abyar for computer technical assistance. This study was supported partially by a grant from the Research Bureau of the Isfahan University of Medical Sciences, Iran.

References

1 Flegal KM, Graubard BI, Williamson DF, Gail MH: Excess deaths associated with underweight, overweight, and obesity. JAMA 2005;293:1861–1867.
2 National Task Force on the Prevention and Treatment of Obesity: Overweight, obesity and health risk. Arch Intern Med 2000;160: 898–904.
3 Watts NB, Spanheimer RG, DiGirolamo M, Gebhart SS, Musey VC, Siddiq YK, Phillips LS: Prediction of glucose response to weight loss in patients with non-insulin-dependent diabetes mellitus. Arch Intern Med 1990; 150:803–806.
4 Wing RR, Koeske R, Epstein LH, Nowalk MP, Gooding W, Becker D: Long-term effects of modest weight loss in type II diabetic patients. Arch Intern Med 1987;147:1749–1753.
5 Hughes TA, Gwynne JT, Switzer BR, Herbst C, White G: Effects of caloric restriction and weight loss on glycemic control, insulin release and resistance, and atherosclerotic risk in obese patients with type II diabetes mellitus. Am J Med 1984;77:7–17.
6 Kelley DE, Wing R, Buonocore C, Stuns J, Polonsky K, Fitzsimmons M: Relative effects of caloric restriction and weight loss on non-insulin-dependent diabetes mellitus. J Clin Endocrinol Metab 1993;77:1287–1293.
7 Henry RR, Wallace P, Olefsky JM: Effects of weight loss on mechanisms of hypoglycemia in obese non-insulin-dependent diabetes mellitus. Diabetes 1986;35:990–998.
8 Wolffenbuttel BHR, Weber RFA, VanKoetsveld PM, Verschoor L: Limitations of diet therapy in patients with non-insulin-dependent diabetes mellitus. Int J Obes 1989;13: 173–182.
9 UK Prospective Diabetes Study (UKPDS) Group: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837–853.
10 Martin DB, Quint AR: Therapy for diabetes; in National Diabetes Data Group (ed): Diabetes in America. Bethesda, US Department of Health and Human Services, 1985, NIH Publ No 85-1468, XXIV I–XXIV30.
11 National Institutes of Health: Consensus development conference on diet and exercise in non-insulin-dependent diabetes mellitus. Diabetes Care 1987;10:639–644.
12 Davidson JK, Panayioto R: Diet therapy for non-insulin-dependent diabetes mellitus; in Davidson JK (ed). Clinical Diabetes Mellitus: A Problem-Oriented Approach. New York, ■■■, 1991, pp 186–209.
13 Janghorbani M, Amini M, Ghanbari H, Safaiee H: Incidence of and risk factors for diabetic retinopathy in Isfahan, Iran. Ophthalmic Epidemiol 2003;10:81–95.
14 WHO Consultation on Obesity: Preventing and Managing the Global Epidemic. Geneva, World Health Organization, 2000, WHO Technical Report Series 894.
15 NHLBI Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. Obes Rev 1998;6(suppl 2):51S–209S.

16 Wannamethee SG, Shaper AG: Weight change and duration of overweight and obesity in the incidence of type 2 diabetes. Diabetes Care 1999;22:1266–1272.
17 American Diabetes Association: Diagnosis and classification of diabetes mellitus. Diabetes Care 2008;(suppl 1):S55–S60.
18 Janghorbani M, Amini M, Willett WC, Gouya MM, Delavari AR, Alikhani S, Mahdavi AR: First national survey of prevalence of overweight, underweight, and abdominal obesity in Iranian adults. Obesity 2007;15:2797–2808.
19 Chaudhry ZW, Gannon M, Nutall FQ: Stability of body weight in type 2 diabetes. Diabetes Care 2006;29:493–497.
20 Looker HC, Knowler WC, Hanson RL: Changes in BMI and weight before and after the development of type 2 diabetes. Diabetes Care 2001;24:1917–1922.
21 United Kingdom Prospective Diabetes Study (UKPDS). 13: Relative efficacy of randomly allocated diet, sulphonylurea, insulin, or metformin in patients with newly diagnosed non-insulin dependent diabetes followed for three years. BMJ 1995;310:83–88.
22 Lissner L, Odell PM, D'Agostino RB, Stokes J 3rd, Kreger BE, Belanger AJ, Brownell KD: Variability of body weight and health outcomes in the Framingham population. N Engl J Med 1991;324:1839–1844.
23 National Task Force on the Prevention and Treatment of Obesity: Weight cycling. JAMA 1994;272:1196–1202.
24 Schotte DE, Cohen E, Singh SP: Effects of weight cycling on metabolic control in male outpatients with non-insulin-dependent diabetes mellitus. Health Psychol 1990;9:599–605.
25 Sowers JR: Obesity as a cardiovascular risk factor. Am J Med 2003;115(suppl 8A):37S–41S.
26 Williamson DE: Descriptive epidemiology of body weight and weight change in US adults. Ann Intern Med 1993;119:646–649.