Anna V. Ciardullo[1], Maria M. Daghio[1], Massimo Brunetti[1], Massimo Bevini[2], Ghassan Daya[2], Gaetano Feltri[2], Doriano Novi[2], Carlo A. Goldoni[3], Nicola Magrini[1]

[1] *Centre for the Evaluation of the Effectiveness of Health Care (CEVEAS), Modena*

[2] *General Practitioners, Modena*

[3] *Department of Public Health, Territorial Health Authority, Modena*

Characteristics of an Italian diabetic population and long-term changes in glycaemic control at varying body weight categories

Summary

Objectives: To describe the characteristics of a diabetic population in a primary care setting, and to evaluate changes in glycaemic control at varying body weight categories.

Methods: We collected 4610 valid baseline and three years follow-up paired data sheets sent from 77 % of the general practitioners adhering to our shared-care program (257 GPs out of 521) for people with type 2 diabetes. Three conventional body weight categories were defined: "normal" (BMI, ≤25 kg/m²), "overweight" (BMI 25.0–29.9), "obesity" (BMI ≥30). According to weight status we calculated descriptive statistics and follow-up paired changes.

Results: A fifth of the diabetic patients had a "normal" BMI, about 45 % was "overweight" and 34 % was "obese". At follow-up, the glycaemic control significantly improved both in "normal" and "overweight" people, while it significantly worsened in "obese" ones.

Conclusions: Our data confirm the crucial role played by body weight and its changes in diabetic patients.

Keywords: Diabetes – Shared-care – Overweight – Health services research – Diabetic complications.

The number of people worldwide with diabetes is increasing and expected to double by 2025 (Amos et al. 1997). The relationship between obesity and type 2 diabetes is well established, and studies have shown that overweight and obesity significantly increase the risk of developing type 2 diabetes (Albu & Pi-Sunyer 1999; Colditz et al. 1995; Knowler et al. 1997; WHO 1998). Recently, European and U.S. studies examined the effect of weight reduction in people with impaired glucose tolerance (I.G.T.). Both the Finnish Diabetes Prevention Study (Uusitupa et al. 2000; Tuomilehto et al. 2001) and the Diabetes Prevention Program (Knowler et al. 1997) showed that a small weight reduction (about 5% and 4%, respectively) reduced the risk of diabetes by 58 % in both studies. In type 2 diabetic patients, it has been demonstrated that an average intentional weight loss of 11% from initial body weight is associated with a 25% reduction in total mortality and a 28% reduction in cardiovascular and diabetes mortality (Williamson et al. 2000). In patients with type 2 diabetes, weight loss has independent effects on improvements in glycaemic control and insulin sensitivity (Wing et al. 1994); the benefits of weight loss include both improved overall glycaemic control and cardiovascular disease risk profile (Markovic et al. 1998; Heilbronn et al. 1999).

In 1998 our territorial health authority adopted a shared-care program for people with type 2 diabetes mellitus in order to address the care of well-controlled type 2 diabetic patients to general practitioners (GPs). The project evaluating centre collected annual data from GPs in order to monitor the safety and the effectiveness of the project. These data included individual cross-sectional and longitudinal anthropometric parameters and glycohaemoglobin (HbA1c).

The aims of the present work were to describe the characteristics of a type 2 diabetic population cared in general practice and to evaluate long-term changes in glycaemic control according to body weight categories defined at baseline.

Methods

Subjects and materials

257 GPs (out of 521) voluntarily adhered to the local shared-care program for well-controlled type 2 diabetic patients; 172 of them (77%) sent 4610 match-paired data sheets. The

Soz.- Präventivmed. 48 (2003) 186–190
0303-8408/03/030186–05
DOI 10.1007/s00038-003-2047-1

use of match-paired data sheets by itself guarantees not to have lost at follow up. In our territory about 16 000 inhabitants have diabetes (2.5 % prevalence). The 4610 study patients did not represent the entire type 2 diabetic population but only those who voluntarily entered in the cohort of the local shared-care program, and of whom (77 %) their GPs have sent us the data. The patients gave their written consent to participate in the project.

The local shared-care program adopted two sheets for data collection, i.e., baseline (starting year 1998) and yearly follow-up data sheets recording individual patient data on age, gender, type of diabetes, disease duration, weight, height, HbA1c (up to four measurements per year), diabetes therapy, presence of diabetic complications both micro- (nephropathy, retinopathy, peripheral neuropathy, and diabetic foot) and macro-vascular (angina pectoris, myocardial infarction [MI], transient ischaemic attack [TIA]/stroke, chronic heart failure, and claudicatio intermittens). No blood samples have been collected for HbA1c determination. HbA1c measurement had been performed in our territorial public labs by means of HPLC method, and the HbA1c values had been reported by GPs on project data sheets.

Study design and data analysis

Three conventional (NIH & NHLBI 1998) body weight categories were defined at baseline as "normal" if having a body mass index (BMI) of 25.0 kg/m^2 or lower, "overweight" a BMI ranging from 25.0 to 29.9, "obesity" a BMI of 30.0 or higher.

According to BMI categories, a cross-sectional study design was used. Descriptive statistics according to weight status were calculated to describe baseline patients' characteristics and diabetic complications' distribution.

Secondarily, a *after-minus-before* evaluation of the longitudinal match-paired changes in glycaemic control occurred in the cohort was performed; the observation period lasting from 1998 (*before*) until 2001 (*after*). *After-minus-before* match-paired changes were calculated by means of Student's paired t-test only for continuos quantitative variables – weight, BMI and HbA1c – adjusted for the mean study-period values in order to account for the baseline values founded to be strong confounders at the sensitivity analysis of the statistical model; in fact, the best model fitting with weight, BMI and HbA1c changes was obtained by adjusting for the average of the two individual values (before and after). The HbA1c value considered was the average of all the measurements per year (up to four) in order to account for the "regression towards the mean" phenomenon that only a randomised study design allows to avoid.

A multivariate regression had been used to evaluate intra-categories age- and gender-adjusted comparisons with the normal BMI category as the reference one; we did not adjust for the other baseline between groups differences, since the higher goodness-of-fit for the model was obtained by adjusting for these two parameters. Levels of significance had been expressed by means of 95 % confidence intervals (CI) or as $p < 0.05$. STATA for Windows release 7.0 statistical software package had been used.

Results

Overall 99.1 % of the cohort's patients had type 2 diabetes, mean age 67.3 ± 11.2 years ranging from 23 to 99 years, males 49.8 %, disease duration 10.9 ± 7.4 years. About a fifth of the diabetic patients had a normal BMI, about 45 % overweight and 34 % obese (Tab. 1). When compared both to overweight and obese patients, the normal ones were significantly older, they presented a fewer male representative, and a greater diabetes duration; their mean baseline HbA1c was significantly lower than obese's one (Tab. 1).

Baseline therapy profile significantly differed only between the normal and the obese patients. In fact, the obese patients were significantly less on mono-therapy with sulphonylureas (−6.2 %, 95 % CI: −9.9, −2.4), whereas they were significantly more on mono-therapy with metformin (+4.3 %, 95 % CI: +2.4, +6.1), and on therapy with an association of sulphonylureas plus biguanides (+5.8 %, 95 % CI: +2.3, +9.2); among them none was on insulin-therapy ($p < 0.01$ vs reference) (Tab. 1).

Table 1 Baseline patients characteristics according to body weight status (n = 4610)

Variables	Baseline normal BMI category (no. 974)	Baseline overweight category (no. 2060)	Baseline obese BMI category (no. 1576)
Age (years)	70.1 ± 11.4	68.3 ± 10.3 [a]	64.3 ± 11.3 [a]
Gender (% male)	42.6	55.4 [a]	47.4 [a]
Diabetes duration (years)	12.2 ± 7.9	10.9 ± 7.4 [b]	10.2 ± 6.9 [b]
Weight (kg)	62.4 ± 8.5	74.9 ± 8.9 [b]	90.9 ± 12.9 [b]
BMI (kg/m^2)	23.1 ± 1.6	27.4 ± 1.4 [b]	34.0 ± 3.8 [b]
HbA1c (%)	7.4 ± 1.7	7.5 ± 1.4	7.7 ± 1.5 [b]
Diabetes therapy:			
Diet alone (%)	29.3	33.4	29.7
Sulphonylurea alone (%)	36.0	35.5	27.5 [b]
Biguanide alone (%)	3.5	4.1	8.0 [b]
Sulphonylurea + Biguanide (%)	22.3	20.8	27.9 [b]
New oral hypoglycaemic drugs (%)	3.8	3.5	3.5
Insulin (%)	0.7	0.3	0.0
Other drugs combination (%)	4.4	2.4	3.4

[a] $p < 0.01$ vs reference (normal BMI category).
[b] $p < 0.01$ vs reference (normal BMI category) age- and gender-adjusted comparison.

Table 2 Prevalence of major cardiovascular risk factors according to weight status

Variables	Baseline normal BMI category (no. 974)	Baseline overweight BMI category (no. 2060)	Baseline obese BMI category (no. 1576)
Smoking % (no.)	17.3 (169)	14.1 (290)[a]	15.6 (245)[a]
Hypertension % (no.)	52.3 (509)	58.9 (1 214)[a]	65.7 (1 036)[a]
High blood cholesterol % (no.)	27.1 (264)	31.2 (659)[a]	35.7 (562)[a]
High blood tryglyceride % (no.)	18.1 (176)	27.9 (575)[a]	35.1 (553)[a]

[a] $p < 0.01$ vs reference (normal BMI category) age- and gender-adjusted comparison.

Table 3 Prevalence of diabetic micro-vascular complications according to weight status

Variables	Baseline normal BMI category (no. 974)	Baseline overweight BMI category (no. 2060)	Baseline obese BMI category (no. 1576)
Nephropathy % (no.)	10.1 (98)	8.6 (178)	9.8 (155)
Retinopathy % (no.)	12.8 (125)	12.1 (249)	13.4 (212)
Neuropathy % (no.)	6.7 (65)	7.4 (153)	7.2 (114)
Diabetic Foot % (no.)	1.8 (17)	2.0 (39)	1.3 (19)

The prevalence of the other major cardiovascular risk factors in the three groups is shown in Table 2. When compared both to overweight and obese, the normal diabetic patients had a significant ($p < 0.01$) higher prevalence of smoking, and a lower prevalence of hypertension and high blood cholesterol and tryglyceride (Tab. 2).

The three groups did not significantly differ in the prevalence of diabetic micro-vascular complications, i.e., nephropathy, retinopathy, peripheral neuropathy, and diabetic foot (Tab. 3).

The prevalence of diabetic macro-vascular complications – angina pectoris, myocardial infarction, TIA/stroke, heart failure, and claudicatio intermittens – is shown in Table 4. When compared both to overweight and obese, the normal diabetic patients showed only a significant ($p < 0.01$) higher prevalence of claudicatio intermittens (Tab. 4).

Weight, BMI and HbA1c *after-minus-before* matched-paired changes for each BMI category, and intra-categories comparisons, are shown in Table 5; both the crude and the differences adjusted for the average of the two individual (before and after) study-period values have been reported. Such a statistical adjustment was performed since the starting values were found to be strong confounders at the sensitivity analysis of the statistical model; in other words, it

Table 4 Prevalence of diabetic macro-vascular complications according to weight status

Variables	Baseline normal BMI category (no. 974)	Baseline overweight BMI category (no. 2060)	Baseline obese BMI category (no. 1576)
Angina pectoris % (no.)	8.3 (81)	9.8 (201)	7.1 (112)
Myocardial infarction % (no.)	5.2 (51)	7.5 (154)	5.5 (87)
Stroke/TIA % (no.)	8.0 (78)	8.3 (172)	4.9 (78)
Heart failure % (no.)	5.4 (53)	4.2 (87)	3.4 (53)
Claudicatio intermittens % (no.)	7.9 (77)	4.7 (96)[a]	4.6 (72)[a]

[a] $p < 0.01$ vs reference (normal BMI category) age- and gender-adjusted comparison.

accounted for individual metabolically adverse conditions at the beginning of the study period.

At the end of the study period, significant weight loss and BMI decrease were found in each of the three groups, whereas a significant HbA1c decrease was found both in the normal and overweight categories, but a significant HbA1c increase was detected in the obese one.

The intra-categories comparison showed that the normal diabetic patients had a significantly greater weight loss and BMI decrease when compared with obese ones, and they also had a greater weight loss than the overweight ones ($p < 0.01$); whereas no significant differences in HbA1c changes were found between the three categories (Tab. 5).

Discussion

Weight loss has been shown to play a vital role in the prevention and management of diabetes mellitus (Albu & Pi-Sunyer 1999; Colditz et al. 1995; Knowler et al. 1997; WHO 1998). Recent studies suggested that clinicians should use weight management to intervene early on the cascade of events leading up to type 2 diabetes and its complications (Uusitupa et al. 2000; Tuomilehto et al. 2001; Knowler et al. 1997). In fact, a relatively modest weight loss can have a very big impact on reducing the risk of type 2 diabetes complications (Williamson et al. 2000).

We are aware that our findings might be affected by a selection bias since *by indication* we did not use a random sample of diabetic patients, but a cohort of patients who voluntarily adhered to the local shared-care program for type 2 diabetes. We could only speculate that the "active refusals", i.e., the patients refusing to participate in the project, should have been less confident in their GPs than those who adhered, at least at the beginning of the project when follow-up data were still lacking. Similarly, the follow-up data are limited to body

Table 5 Weight, BMI and HbA1c after-minus-before matched-paired changes according to body weight status (n = 4610)

Baseline BMI category	*After-before* weight change kg (95 % CI)		*After-before* BMI change kg/m² (95 % CI)		*After-before* HbA1c change % (95 % CI)	
	crude	adjusted[a]	crude	adjusted[a]	crude	adjusted[a]
Normal (no. 974)	+0.6 (+0.3, +0.9)	–2.5 (–4.7, –0.3)	+0.3 (+0.2, +0.4)	–8.9 (–10.5, –7.3)	+0.01 (–0.2, +0.3)	–6.4 (–7.3, –5.5)
Overweight (no. 2060)	–0.5 (–0.7, –0.3)	–6.2 (–7.7, –4.6[b]	–0.3 (–0.4, –0.2)	–14.1 (–15.4, –12.9)	–0.1 (–0.1, +0.1)	–5.0 (–5.5, –4.5)
Obese (no. 1576)	–1.6 (–1.9, –1.3)	+0.1 (–2.1, +2.4[b]	–0.9 (–1.1, –0.8)	–4.2 –5.5, –3.0)[b]	–0.1 (–0.1, +0.03)	+1.5 (+1.0, +2.1)

[a] *After-minus-before* match-paired change adjusted for the average of the two individual (before and after) study-period values (since the starting values were found to be strong confounders at the sensitivity analysis of the statistical model).
[b] p < 0.01 vs reference (normal BMI category) age- and gender-adjusted comparison.

weight and glycohaemoglobin changes, whereas no information was given about diabetic complications because of unreliable data. Nevertheless, our study could provide some interesting information since in Italy monitoring data on type 2 diabetic patients cared by GPs are still lacking. Secondarily, it could get some light on long-term effective weight changes obtained by GPs in a common life setting.

The baseline characteristics of our cohort showed that only a fifth of the diabetic patients had a normal BMI, and that about 45 % was overweight and 34 % obese; in other words, this means that four patients out of five should need a weight reduction long-term intervention (Tab. 1). In spite of the high prevalence of the cardiovascular risk factors (Tab. 2) in the study population – two thirds of people were hypertensive and more than half of them had high blood lipids – both micro- and macro-vascular diabetic complications were fairly low, still more if advanced mean age is considered (Tab. 3, 4). The three groups did not significantly differ in the prevalence of diabetic micro-vascular (Tab. 3) nor in macro-vascular complications (Tab. 4), with the exception of a higher prevalence of claudicatio intermittens in the normal diabetic patients, when compared both to overweight and obese ones, which was consistent with the higher prevalence of smoking among them (Tab. 2).

At follow-up, the glycaemic control significantly improved both in normal and overweight people, while it significantly worsened in obese ones (Tab. 5). Our findings also showed that the long-term (3-years) glycaemic control improvement was accompanied by a significant BMI decrease (–9 % and –14 %) observed in normal and overweight groups; whereas in the obese group the glycaemic control did not improve though a significant BMI decrease (–4 %) occurred. The body weight and BMI decreases observed in the obese group were significantly lower than the normal's ones in spite of the normal patients' greater age and longer diabetes duration; the same was for overweight group's body weight changes (Tab. 5). The opposite HbA1c changes found in the normal and overweight groups (–6.4 % and –5.0 %, respectively) versus the obese one (+1.5 %) should be somehow confounded by the baseline normal and the overweight lower HbA1c mean values (Tab. 1). On the other hand, we did not collect information about parameters associated to body weight changes, such as blood lipids, glucose, and insulin; therefore we lacked information to understand whether the obese people's HbA1c levels worsening was due to unsuccessful weight losing or, conversely, because losing weight was unproductive regarding HbA1c improvement. Furthermore, even if the follow-up HbA1c value represented the average value of all the measurements per year (up to four/year), a "regression towards the mean" phenomenon should also have influenced the results since only a randomised study design could fully avoid it.

In conclusion, our findings were preliminary observations obtained by GPs in Italy in their integrated diabetes care; nevertheless, they suggested the crucial role played by body weight and its changes in diabetic patients. Secondarily, our data pointed out that significant long-term improvements in body weight and glycaemic control can be achieved also in general practice.

These results should be somehow encouraging both for clinicians and patients intended to adopt small-scale and achievable lifestyle modifications in order to obtain a long-term body weight reduction and related health advantages.

Acknowledgments

We are very grateful to all the diabetic patients and to the GPs adhering to Modena shared-care project. The present work has been supported by public health authorities. We thank Mrs. Chiara Bassi for her precious assistance in literary search, and Mr. Marco Zardi for friendly translating the summary in German and French languages.

Zusammenfassung

Merkmale einer italienischen Diabetespopulation und langfristige Änderungen der Blutzuckerkontrolle in Körpergewichtsuntergruppen

Zielsetzung: Charakterisierung einer in der medizinischen Grundversorgung befindlichen Diabetes-Population und Beurteilung langfristiger Änderungen der Blutzuckerkontrolle in verschiedenen Körpergewichtsgruppen.

Methoden: 257 der 521 Allgemeinärzte (77 %), die an unserem „shared-care"-Programm teilnehmen, übermittelten Basis- und drei Jahre Follow-up-Daten von 4 610 Typ-2-Diabetes-Patienten. Die drei üblichen Körpergewichtskategorien wurden definiert: „normal" (BMI ≤25 kg/m^2), „übergewichtig" (BMI = 25,0–29,9) und „adipös" (BMI ≥ 30). Die deskriptive Statistik und Untersuchung der zeitlichen Veränderungen wurde nach Gewichtskategorien durchgeführt.

Ergebnisse: Ein Fünftel der Diabetiker wiesen einen normalen BMI auf, etwa 45 % waren übergewichtig und 34 % adipös. Die Folgeuntersuchungen ergaben eine signifikant verbesserte Blutzuckerkontrolle bei normal- und übergewichtigen Patienten, bei den adipösen Patienten wurde eine deutliche Verschlechterung verzeichnet.

Schlussfolgerungen: Unsere Daten bestätigen die wichtige Rolle, die dem Körpergewicht und seiner Veränderung/Kontrolle beim Diabetespatienten zukommt.

Résumé

Caractéristiques d'une population diabétique italienne et variations à long terme du contrôle glycémique selon différentes catégories de poids corporel

Objectifs: Décrire les caractéristiques d'une population diabétique dans un cadre de soins de santé primaire et évaluer la variabilité des contrôles glycémiques selon des catégories de poids corporel.

Méthodes: Nous avons récolté 4 610 dossiers contenant les données de base et le suivi sur trois ans de patients diabétiques de type 2 envoyés par 77 % des généralistes participant à un programme de prise en charge intégré (257/521). Les trois catégories conventionnelles d'indice de masse corporelle (IMC) ont été définies comme: „normal" (IMC ≤ 25 kg/m^2), „surpoids" (IMC 25.0–29.9), „obésité" (IMC ≥30). Les statistiques descriptives et les changements au cours du suivi ont été calculés selon les catégories de poids corporel.

Résultats: Un cinquième des patients diabétiques avaient un IMC normal, environ 45 % avaient du surpoids et 34 % étaient obèses. Au cours du suivi, le contrôle glycémique s'améliora chez les patients normaux et ceux ayant du surpoids, alors qu'il a significativement empiré chez les patients obèses.

Conclusions: Nos données confirment le rôle crucial que jouent le poids corporel et ses changements chez les patients diabétiques.

References

Albu J, Pi-Sunyer F (1999). Obesity and diabetes. In: Bray G, Bouchard C, James W, eds. Handbook of obesity. New York: M. Dekker.

Amos AF, McCarty DJ, Zimmet P (1997). The rising global burden of diabetes and its complications: estimates and projections to the year 2010. Diabet Med *14*: S1–S85.

Colditz GA, Willett WC, Rotnitzky A, Manson JE (1995). Weight gain as a risk factor for clinical diabetes mellitus in women. Ann Intern Med *122*: 481–6.

Heilbronn LK, Noakes M, Clifton PM (1999). Effect of energy restriction, weight loss, and diet composition on plasma lipids and glucose in patients with type 2 diabetes. Diabetes Care *22*: 889–95.

Knowler WC, Barrett-Connor E, Ford ES, Williamson DF, Liu S (1997). Weight change and diabetes incidence: findings from a national cohort of US adults. Am J Epidemiol *146*: 214–22.

Knowler WC, Bassett-Connor E, Fowler SE, et al. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med *346*: 393–403.

Markovic TP, Campbell LV, Balasubramanian S, et al. (1998). Beneficial effect on average lipid levels from energy restriction and fat loss in obese individuals with or without type 2 diabetes. Diabetes Care *21*: 695–700.

National Institutes of Health, National Heart Lung and Blood Institute (1998). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. National Institute of Health. Obes Res *6*: 51S–209S.

Tuomilehto J, Lindstrom J, Eriksson JG, et al. (2001) Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med *344*: 1343–50.

Uusitupa M, Louheranta A, Lindstrom J, et al. (2000). The Finnish Diabetes Prevention Study. Br J Nutr *83*:S137–S142.

Williamson DF, Thompson TJ, Thun M, Flanders D, Pamuk E, Byers T (2000). Intentional weight loss and mortality among overweight individuals with diabetes. Diabetes Care *23*: 1499–504.

Wing R, Blair E, Bononi P, Marcus M, Watanabe R, Bergman R (1994). Caloric restriction per se is a significant factor in improvements in glycaemic control and insulin sensitivity during weight loss in obese NIDDM patients. Diabetes Care *17*: 30–6.

World Health Organization (1998). Obesity: preventing and managing the global epidemic. Report of a WHO Consultation on obesity, Geneva, 3–5 June, 1997. Geneva: WHO.

Address for correspondence

Anna V. Ciardullo, MD, MSc
CeVEAS – Centro per la Valutazione della Efficacia della Assistenza Sanitaria
Viale Muratori, 201
I-41100 Modena
Tel.: +39+059435200
Fax: +39+059435222
e-mail: a.ciardullo@ausl.mo.it