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Original

One-year effectiveness of two hypocaloric diets with different protein/carbohydrate ratios in weight loss and insulin resistance

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Abstract

Background: **The maintenance of weight loss may be influenced by the distribution of macronutrients in the diet and insulin sensitivity.**

Objective: **The objective of the study was to evaluate the long-term effect of two hypocaloric diets with different protein/carbohydrate ratios in overweight and obese individuals either with insulin resistance (IR) or without insulin resistance (IS).**

Design: **Prospective, randomized, clinical intervention study. Forty patients were classified as IR/IS after a 75 g oral glucose tolerance test and then randomized to a diet with either 40% carbohydrate/30% protein/30% fat (diet A) or 55% carbohydrate/15% protein/30% fat (diet B).**

Results: **After one year of follow-up there was no difference in weight loss between diets A and B in each group, but the IS group maintained weight loss better than the IR group [-5.7 (3.9) *vs.* -0.6 (4.1); P = 0.04]. No differences were found in either Homeostasis Model Assessment (HOMA) or other metabolic glucose parameters except lower insulin at 120 minutes with diet A [21.40 (8.30) *vs.* 71.40 (17.11); P = 0.02].**

Conclusions: **The hypocaloric diets with different protein/carbohydrate ratios produced similar changes in weight. Insulin resistance may play a negative role in maintaining weight loss.**

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Key words: *Insulin resistance. Carbohydrates. Proteins. Diet.*

EFECTIVIDAD A UN AÑO DE DOS DIETAS HIPOCALÓRICAS CON DIFERENTE PROPORCIÓN DE PROTEÍNAS Y CARBOHIDRATOS EN LA PÉRDIDA DE PESO Y EN LA RESISTENCIA A LA INSULINA

Resumen

Introducción: **El mantenimiento de la pérdida de peso puede estar influido por la distribución de macronutrientes en la dieta y la sensibilidad a la insulina.**

Objetivo: **El objetivo del estudio fue evaluar el efecto a largo plazo de dos dietas hipocalóricas con diferente distribución de proteínas y carbohidratos (HCO) en individuos con sobrepeso y obesos ya fuese con resistencia a la insulina (IR) o sin resistencia a la insulina (IS).**

Metodología: **Estudio prospectivo, aleatorizado, de intervención clínica. Cuarenta pacientes fueron clasificados como IR / IS después de una prueba de tolerancia oral de 75 g de glucosa y luego asignados al azar a una dieta con 40% de HCO/ 30% proteína /30% grasa (dieta A) o el 55% HCO /15% proteína /30% grasa (dieta B).**

Resultados: **Tras un año de seguimiento, no se observaron diferencias en la pérdida de peso entre las dietas A y B en cada grupo, pero el grupo IS mantuvo la pérdida de peso mejor que el grupo IR [-5,7 (3,9) *vs* -0,6 (4,1), p = 0,04]. No se encontraron diferencias en ninguno en el Homeostasis Model Assessment (HOMA) u otros parámetros metabólicos de glucosa excepto en una insulina inferior a los 120 minutos con la dieta A [21,40 (8,30) *vs* 71,40 (17,11), p = 0,02].**

Conclusiones: **Las dietas hipocalóricas con diferentes proporciones de proteínas y carbohidratos produjeron cambios similares en el peso. La resistencia a la insulina puede jugar un papel negativo en el mantenimiento de la pérdida de peso.**

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Palabras clave: *Resistencia a la insulina. Hidratos de carbono. Proteínas. Dieta.*

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Introduction

During the last few decades the prevalence of obesity has surged in an epidemic-like manner in both developed and developing countries.[1] Several metabolic disturbances such as dyslipidemia, diabetes, and hypertension, which are associated with increased visceral fat mass and insulin resistance, have increased in parallel. Lifestyle changes are the cornerstone of therapy for obesity, and research has been focused on which macronutrient distribution could be more beneficial for weight loss and help improve these metabolic conditions.

Nowadays there is revived interest in high-protein diets for weight loss. The protein content in these diets can vary from 25% to 45%.[2,3] Many studies in the literature indicate that high-protein diets achieve better weight loss results than high-carbohydrate diets in periods of less than 6 months.[3,4] Increasing the dietary protein content is usually accompanied by a reduction in carbohydrates. In fact, the terms high-protein and low-carbohydrate are often used indistinctly.

A recent trial comparing several hypocaloric diets with different ratios of fat, protein, and carbohydrates (20/15/65, 40/15/45, 20/25/55, 40/25/35) did not find significant differences between them in weight loss, hunger sensations or compliance;[5] a previous meta-analysis had shown that low-carbohydrate diets were not associated with a greater weight loss after 6 months of follow up.[6] Nevertheless, some authors have hypothesized that insulin resistance could influence weight loss associated with a hypocaloric diet: the trial by Cornier et al. described greater weight loss with a low-carbohydrate diet in insulin-resistant women and a high-carbohydrate diet in insulin-sensitive women.[7] A new randomized trial was conducted to test this hypothesis in which patients with and without insulin resistance received diets with different carbohydrate/ protein/fat ratios (40/30/30 or 55/15/30) for 16 weeks, and similar results regarding weight, body composition, and metabolic parameters were found.[8] Thus, we tried to evaluate the long-term effects on weight loss and insulin resistance of two hypocaloric diets with different protein/carbohydrate ratios in obese people either with insulin resistance (IR) or without insulin resistance (IS). After previously publishing the results of the first 16 weeks of this trial, we now report the results after 1 year of follow-up.

Methods

A prospective, randomized, clinical intervention study was designed to evaluate the effectiveness of different energy-restricted diets with different macronutrient compositions over a period of 1 year.

Subjects

A total of 40 obese or overweight patients (body mass index (BMI) between 28 to 35 kg/m^2; aged between 18 to 70 years old) were enrolled in the trial at the Complejo Asistencial Universitario de León, Spain. The study protocol was approved by the Ethics and Clinical Investigation Committee of the hospital (November 2005), and each participant gave informed consent. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The exclusion criteria were participation in a weight loss treatment in the 6 months prior to the trial, any severe psychiatric illness, pregnancy, diabetes (fasting plasma glucose > 126 mg/dL or > 200 mg/dL at 120 min after an oral 75 g glucose tolerance test (OGTT), previous bariatric surgery, and eating disorders.

Procedure

The patients were placed in either the insulin resistance (IR) or the insulin sensitive (IS) group after a 75-g OGTT and Homeostasis Model Assessment (HOMA) index. The latter was calculated as the product of the fasting plasma glucose level (mmol/L) and the fasting plasma insulin level (mU/mL) divided by 22.5. We established a diagnosis of IR when the HOMA index was ≥ 3.8 or the fasting plasma insulin value was ≥ 15 mU/l.[9]

Daily energy requirements were estimated using the resting metabolic rate calculated by the Harris-Benedict equation,[10] and an activity factor of 1.5 was added in order to estimate the total caloric requirement.[11] The daily caloric intake for weight loss was calculated as the total caloric requirement minus 1,000 kcal. The subjects were free living and were asked to maintain their usual patterns of activity.

The patients were randomized to follow either a 40% carbohydrate/30% protein/30% fat diet (diet A) or a 55% carbohydrate/15% protein/30% fat diet (diet B). Random allocation to each dietary group was performed by the main investigator (MDBP) by using the Web site Randomization.com (http://www.randomization.com) upon the request of the study dietitian (ACF) after the eligibility of a participant was confirmed and assignment to either of the insulin resistance or insulin sensitivity groups had been performed. The dietitian was responsible for providing individual counseling and written material to the participants on the initial visit, and then the patients were instructed to record their food intake in a daily food diary and to discuss it with the dietitian on each visit at every 2 weeks for 16 weeks at the beginning of the trial and on each 3 monthly visit for 1 year. The medical assessments were blinded to the type of diet being followed.

At baseline, a physical examination including anthropometric measurements (weight, height, BMI, waist and hip circumference) and blood pressure was performed, and a 72-h dietary recall was performed. Body weight was measured to the nearest 0.5 kg and then taken using calibrated digital scales at the same

time of day on each subsequent visit. The subjects wore street clothing, removed their shoes, and voided their bladder before being weighed. On each visit, waist and hip circumferences were measured to the nearest 0.5 cm using a spring-loaded tape measure. Waist circumference was measured at the level of the umbilicus and hip circumference at the level of the greater trochanters.[12] Body composition was evaluated by means of a tetrapolar, single-frequency bioelectrical impedance analyzer (BIA) (Holtain BC Analyzer, UK) and a segmental hand-to-hand BIA unit (Omron BF 300, Tanita Corp., Kyoto, Japan). The patients were evaluated every 2 weeks for 16 weeks during the first follow-up period and every 3 months for 1 year during the second follow-up period. The examinations included anthropometric measurements, body composition and dietary recalls and were performed by the same dietitian. Baseline and final assessments in the first and second period also included a 75-g OGTT and blood samples for total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol triglycerides, liver and kidney function tests, TSH, iron, ferritin, and C-reactive protein. The blood samples were collected via venipuncture by a nurse after an overnight fast. The analyses were performed by the Clinical Biochemistry Department at the Complejo Asistencial Universitario de León.

Dietary intake

The patients provieded prospective serial assessment of nutritional intake over 3 days, including a weekend day, written food records at the baseline visit, and 24-h dietary recall the rest of the visits. The subjects were instructed by a dietitian to provide as much information on the food and drinks consumed (e.g., volume, ingredients, type of oil, brand name, etc.) as possible. The records were reviewed by the dietitian and analyzed using a computer-based data evaluation system with Dietsource 2.0 software (Novartis Consumer Health-Cath Soft, 1997-2003).

Statistical analyses

Ene 2.0 software (http://www.e-biometria.com/ene-ctm/index.htm) was used to calculate the sample size required to detect a difference of 3-4 kg with a power of β 0.80 and a significance of α 0.05, following the methods of McLaughlin[11] and Cornier.[7]

Changes in body weight, the primary outcome analyzed, were calculated as the body weight after the first and the second periods of being on the hypocaloric diet minus the weight at the baseline visit and expressed as absolute change in kilograms or as a percentage change from baseline. The descriptive data are presented as the mean ± SD. The analysis was performed on an intention-to-treat basis, with the last observation carried forward in case of withdrawal. The significance tests are two-sided, with the significance set at $P < 0.05$. A Shapiro-Wilks' test was performed to check whether or not the quantitative data were normally distributed. Pearson's chi-square and independent-sample T-tests (or the Mann-Whitney test if normality could not be assumed) were used to compare

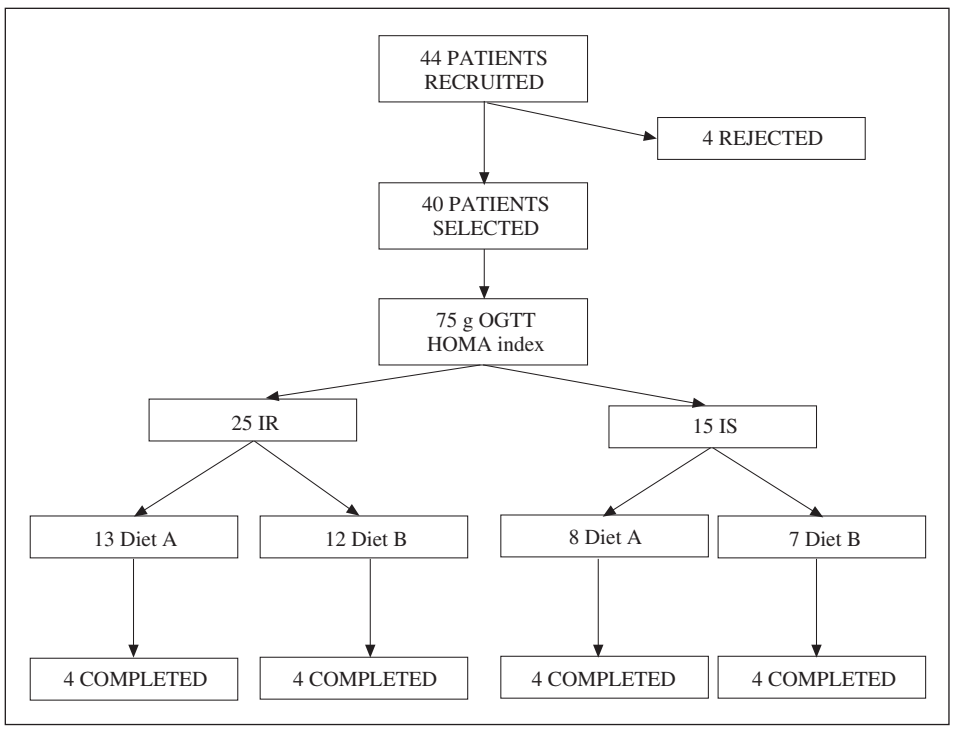

Fig. 1.—Flow chart of the study.

Table I
Baseline characteristics of the sample

	IR		*IS*	
	A *Mean (SD)*	*B* *Mean (SD)*	*A* *Mean (SD)*	*B* *Mean (SD)*
Age (years)	35.85 (12.42)	42.17 (15.08)	47.25 (11.76)	40.57 (14.55)
Sex (female/male)	7/6	9/3	7/1	4/3
Weight (kg)	90.78 (15.72)	88.09 (11.46)	85.38 (8.44)	85.56 (8.80)
BMI (kg/m^2)	31.18 (2.71)	32.02 (2.01)	32.99 (2.45)	31.44 (2.21)
Waist circumference (cm)	102.58 (7.82)	106.25 (8.87)	105.75 (6.27)*	98,50 (4.91)*
Waist-hip circumference (cm)	0.94 (0.06)	0.92 (0.05)	114.00 (4.44)	110.14 (4.45)
Fat mass (%)	31.39 (7.72)	35.91 (7.32)	31.86 (2.28)	26.91 (3.18)
Systolic blood pressure (mmHg)	123.78 (16.98)	120.00 (16.43)	126.67 (20.82)	132.50 (16.66)
Diastolic blood pressure (mmHg)	77,33 (14.67)	74.17 (9.17)	83.33 (10.41)	82.50 (15.41)
Glucose (mg/dL)	86.77 (10.46)	80.25 (26.46)	84.63 (11.40)	80.71 (6.90)
Insulin (μU/mL)	20.41 (5.45)	36.72 (49.64)	9.51 (2.26)	9.19 (3.26)
HOMA index	4.39 (0.99)	4.90 (3.06)	2.01 (0.52)	1.78 (0.50)
AST (U/L)	25.15 (10.20)	23.25 (13.35)	22.63 (11.04)	20.86 (11.73)
ALT (U/L)	39.77 (30.34)	35.50 (31.84)	30.25 (26.50)	22.14 (14.24)
Total cholesterol (mg/dL)	190.00 (36.83)	198.00 (30.73)	224.38 (38.98)	210.29 (35.30)
HDL-cholesterol (mg/dL)	47.38 (14.52)	50.58 (11.56)	59.88 (21.26)	57.14 (19.28)
LDL-cholesterol (mg/dL)	113.28 (28.81)	115.65 (28.56)	125.86 (22.77)	125.23 (28.67)
Triglycerides (mg/dL)	150.85 (91.71)	150.50 (62.46)	161.88 (122.41)	139.57 (59.26)
C-protein reactive (mg/dL)	3.47 (5.32)	4.14 (2.84)	4.00 (1.32)	2.03 (0.76)

*P = 0.026; **P = 0.004.

baseline characteristics and weight loss between the groups (IR *vs.* IS, diet A *vs.* B). Repeated measures ANOVA was performed to detect changes in HOMA, glucose, insulin and lipid profiles and also to detect any differences in dietary composition.

Results

The trial included 40 patients: 25 were insulin resistant (IR) and 15 were insulin sensitive (IS). Diet A was randomly assigned to 21 patients (13 IR, 8 IS) and diet B to 19 patients (12 IR, 7 IS). The allocation of patients is shown in figure 1. Their general characteristics are summarized in table I.

Weight loss and body composition

No differences were found between the groups in weight loss during the first 16 weeks, as described previously.[8] When compared to the first visit, no significant differences in the weight loss percentage were found between IR and IS at 6 months [-5.6% (8.7) *vs.* -5.5% (5.1); P = 0.964], but after 12 months of follow-up IS maintained weight loss better than IR [-5.7 (3.9) *vs.* -0.6 (4.1); P= 0.04]. No differences were found between diets A and B at 6 months [-4.3% (85.4) *vs.* -7.1% (9.3); P = 0.368] or 12 months [-2.2% (5.6) *vs.* -3.5% (3.4); P = 0.630] in the overall group. The change in weight did not differ according to diet in either of the IR or IS groups at any visit (table III).

No significant differences in BMI, fat mass, waist circumference, or waist-to-hip ratio were found on any visit according to insulin resistance/sensitivity or diet in the overall group or in each of the four groups.

Diet

The usual dietary intake of the four groups is reported in table II; there were no significant differences between the groups. When both diets were compared, the patients on diet A ate a lower percentage of carbohydrates at 3 [40.1 (12.6)% *vs.* 53.4 (7.4)%; P = 0.04] and 12 months [39.5 (9.0)% *vs.* 51.0 (9.9)%; P = 0.04], a higher proportion of saturated fat at 3 months [11.6 (4.0)% *vs.* 6.0 (2.8)%; P = 0.04], and a higher proportion of monounsaturated fat at 3 [18.0 (7.0)% *vs.* 13.5 (3.2)%; P = 0.046] and 12 months [16.7 (4.2)% *vs.* 9.8 (6.0)%; P = 0.03]. The differences between IR and IS according to the type of diet are reported in table IV.

Table II
Baseline nutrient intake

	Insulin resistant				*Insulin sensitive*			
	A		*B*		*A*		*B*	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Kcal	1,912	682.52	2,250	1,165.69	1,688	657.94	1,615	566.69
Carbohydrate (%)	42.85	9.15	45.90	10.06	42.25	9.39	40.43	14.32
Protein (%)	22.15	3.98	18.36	4.01	21.50	2.56	20.14	1.86
Total fat (%)	34.92	9.84	34.79	9.54	36.38	8.47	39.43	12.92
Saturated fat (%)	9.65	4.73	9.43	4.40	10.83	3.44	9.37	5.00
Monounsaturated fat (%)	16.27	4.55	15.45	3.92	14.80	4.50	18.60	6.08
Polyunsaturated fat (%)	2.98	1.29	3.30	1	3.44	0.96	4.35	2.09
Cholesterol (mg)	413.58	219.15	428.58	346	373.65	118.48	469.76	354.08
Fiber (g)	17.49	8.04	19.07	6.38	16.03	7.31	16.93	7.01

$P > 0.05$.

Table III
Weight loss and anthropometric changes

	IR		*IS*	
	A *Mean (SD)*	*B* *Mean (SD)*	*A* *Mean (SD)*	*B* *Mean (SD)*
Weight loss (%)				
3 months	-7.76 (5.87)	-10.37 (7.55)	-11.12 (3.07)	-9.19 (1.53)
6 months	-10.25 (4.88)	-10.53 (10.67)	-12.14 (3.29)	-9.63 (2.51)
9 months	-7.82 (7.44)	-10.81 (11.48)	-12.38 (4.90)	-7.53 (2.71)
12 months	-6.87 (3.29)	-7.38 (1.96)	10.57 (5.51)	-8.55 (0.83)
BMI (kg/m²)				
3 months	30 (2.78)	29.77 (3.18)	30.12 (2.58)	28.80 (2.05)
6 months	28.93 (2.19)	29.77 (3.93)	29.55 (0.90)	28.52 (2.68)
9 months	29.82 (3.06)	28.82 (3.60)	29.95 (3.27)	29.22 (2.71)
12 months	29.26 (2.63)	29.84 (2.18)	30.52 (2.90)	29.98 (2.63)
WHR				
3 months	0.92 (0.06)	0.95 (0.08)	0.91 (0.04)*	0.88 (0.01)*
6 months	0.92 (0.05)	0.92 (0.08)	0.91 (0.05)	0.95 (0.08)
9 months	0.95 (0.06)	0.95 (0.09)	0.90 (0.05)	0.91 (0.04)
12 months	0.93 (0.05)	0.94 (0.11)	0.92 (0.09)	0.93 (0.04)
Fat mass (%)				
3 months	29.40 (9.46)	37.32 (8.01)	38.18 (3.28)	33.53 (7.51)
6 months	27.61 (8.77)	37.19 (8.17)	37.22 (4.22)	33.03 (9.14)
9 months	27.44 (10.16)	34.80 (8.32)	38.33 (3.26)	34.20 (8.76)
12 months	31.18 (10.67)	39.08 (5.57)	39.38 (4.46)**	30.95 (14.21)**

* $P = 0.046$; ** $P = 0.033$.

Glucose metabolism

In the IR group, no differences were found between the levels of fasting plasma glucose, fasting insulin or the HOMA index either before the diet or at any point during follow-up; after 12 months, insulin at 120 minutes after the OGTT was lower with diet A [21.40 (8.30) *vs.* 71.40 (17.11); $P = 0.02$].

Table IV
Changes in dietary intake

	IR		*IS*	
	A Mean (SD)	*B* Mean (SD)	*A* Mean (SD)	*B* Mean (SD)
Energy (kcal)				
3 months	2,176.79 (766.73)	1,665.99 (345.62)	1,668.86 (587.99)	1,813.93 (409.68)
6 months	2,006.51 (777.74)*	1,562.67 (328.86)*	1,389.12 (376.62)	2,315.75 (889.22)
9 months	2,350.53 (547.55)	1,637.52 (398.67)	1,561.03 (177.14)	1,761.70 (677.04)
12 months	1,911.18 (409.35)	1,161.95 (302.49)	1,486.83 (301.58)	1,592.85 (408.50)
CHO (%)				
3 months	40.89 (12.77)	51.38 (8.05)	38.60 (13.58)	57.50 (3.79)
6 months	47.88 (8.92)	50.86 (11.36)	44.80 (15.14)	47 (10.74)
9 months	42.29 (7.95)	52.20 (12.03)	47.75 (6.18)	45.75 (2.06)
12 months	41.75 (11.18)	50.50 (12.66)	37.25 (7.23)	52.00 (2.83)
Protein (%)				
3 months	19.89 (6.79)*	18 (2.51)*	19.20 (3.11)	18.75 (1.71)
6 months	19.25 (5.20)	19.14 (5.79)	20 (6.04)	17 (2.94)
9 months	20.71 (2.56)	16.00 (1.58)	18.25 (4.79)	19.75 (3.20)
12 months	22.25 (2.63)	23.00 (6.78)	22.25 (2.99)	16 (0.00)
Fat (%)				
3 months	39.22 (12.74)*	30.63 (7.48)*	41.80 (13.66)*	24.25 (3.77)*
6 months	32.88 (13.13)	30 (11.25)	35.40 (13.67)	35.75 (10.14)
9 months	37 (9.76)	31.80 (12.83)	34 (8.29)*	34.50 (4.20)*
12 months	36 (13.49)	26.05 (14.82)	40.50 (8.50)	31.50 (2.12)
SFA (%)				
3 months	11.10 (5.24)	7.83 (3.48)	12.43 (8.98)	5.80 (2.40)
6 months	8.28 (5.60)	9.59 (4.43)	8.72 (3.43)	9.32 (4.27)
9 months	9.89 (4.60)	7.25 (3.75)	8.58 (3.92)	9.95 (3.59)
12 months	7.80 (4.52)	5.31 (3.28)	9.69 (3.82)	7.45 (0.07)
MUFA (%)				
3 months	18.17 (6.19)	14.35 (3.65)	17.62 (19.19)	11.75 (1.19)
6 months	14.07 (5.25)	13.15 (3.64)	14.40 (4.33)	14.43 (2.43)
9 months	16.09 (3.94)	14.08 (5.38)	16.68 (3.30)**	16.03 (0.39)**
12 months	15.25 (4.05)	6.87 (4.90)	18.20 (4.36)	15.80 (0.99)
PUFA (%)				
3 months	3.49 (1.04)	2.44 (0.73)	3.61 (1.76)	2.09 (0.48)
6 months	3.77 (2.46)	2.32 (0.68)	3.11 (0.98)	3.49 (1.23)
9 months	3.69 (1.11)	2.40 (1.17)	3.43 (0.62)	3.15 (1.34)
12 months	3.55 (1.44)	3.24 (2.86)	4.31 (0.24)**	3,75 (1.23)**
Cholesterol (mg)				
3 months	413.58 (219.15)	428.58 (346.00)	460.76 (270.53)*	342.18 (88.18)*
6 months	449.98 (247.72)	284.59 (166.80)	265.4 (218.62)	395.50 (160.17)
9 months	383.69 (204.14)	258.19 (153.51)	365.03 (238.24)*	325.80 (104.27)*
12 months	361.05 (150.69)	100.75 (143.01)	400.75 (115.17)*	437.10 (469.66)*
Fibre (g)				
3 months	16.74 (7.30)	18.20 (3.78)	11.70 (6.15)	22.60 (6.22)
6 months	20.14 (11.26)	14.66 (6.39)	11.52 (7.97)	25.38 (5.86)
9 months	22.89 (6.79)	17.76 (6.42)	20.65 (9.33)	23.40 (12.56)
12 months	15.65 (6.50)	19 (6.82)	15.53 (8.69)	19.85 (5.30)

* $p < 0.05$; ** $p < 0.005$.

Table V
Laboratory parameters at the end of the study

	Diet		*Glucose sensitivity*	
	A *Mean (SD)*	*B* *Mean (SD)*	*A* *Mean (SD)*	*B* *Mean (SD)*
Glucose (mg/dL)	81.00 (7.32)	91.00 (16.52)	86.50 (11.67)	80.00 (11.14)
Insulin (μU/mL)	6.10 (4.27)	14.32 (4.03)	11.79 (4.20)	2.95 (2.64)
HOMA index	1.24 (0.85)	3.33 (1.58)	2.59 (1.33)	0.63 (0.61)
AST (U/L)	19.50 (5.47)	18.33 (8.50)	17.83 (6.24)	21.67 (6.02)
ALT (U/L)	16.33 (5.85)*	27.33 (22.23)*	23.00 (15.70)	14.00 (2.00)
C-protein reactive (mg/dL)	2.07 (0.88)	2.70 (0.71)	2.52 (0.88)	1.73 (0.60)
Total cholesterol (mg/dL)	206.67 (54.84)	216.67 (25.01)	197.83 (31.13)	234.33 (67.01)
HDL-cholesterol (mg/dL)	54.67 (12.71)	48.67 (16.17)	48.83 (14.86)**	60.33 (4.04)**
LDL-cholesterol (mg/dL)	134.17 (46.94)	140.47 (39.08)	127.03 (29.93)	154.73 (63.80)
Triglycerides (mg/dL)	89.17 (41.22)	137.67 (8.74)	109.83 (42.29)	96.33 (44.97)

*P = 0.009; ** P = 0.030.

Other laboratory parameters

In the IR group, no differences were found in the lipid profiles between the diets. Among the patients with IR, similar levels were found in the liver function test, BUN, creatinine, and inflammatory parameters (ferritin, CRP). The differences at the end between the IR and IS groups and between the two types of diet are reported in table V.

Discussion

Weight loss is dependent on the existence of an energy deficit between intake and expenditure, which can be achieved by increasing energy expenditure through physical activity or reducing caloric intake. Both cases are conditioned by environmental, social, and genetic factors that could influence their efficacy. Over the past few decades various diets have been designed to reduce weight in an easy way. The present study describes the long-term results of following two hypocaloric diets with different protein/carbohydrate ratios and supports the theory that the macronutrient composition of a diet does not influence weight loss, body composition or improvements in insulin resistance. Nevertheless, IR was associated with poor weight loss after a period of 1 year, and the carbohydrate-rich (55% of the total calories) diet showed higher insulin levels after the OGTT.

Some data in the literature suggest that higher protein contents in the diet can contribute to weight loss. First, high-protein diets may be related to higher levels of thermogenesis, which can increase energy efficiency during weight loss and help to avoid weight regain.[12] Second, the replacement of some dietary carbohydrates by protein (up to 25% of calorie intake *vs.* 12% in controls) in an *ad libitum* fat-reduced diet has been associated with a lower energy intake and thus with greater weight loss.[13] A study by Dumesnil et al. also reported favorable changes in hunger/satiety with a high-protein diet (30%) compared to a balanced diet (16%, according to the American Heart Association), but no significant differences were found in the loss of body weight.[14] Third, dietary protein can enhance body composition by reducing fat mass and increasing lean body mass. Laymen et al. found that a higher protein/carbohydrate ratio produced a better ratio of fat-to-lean mass loss. Weight loss was similar for both diets as they were both isocaloric.[15] In studies that compared a low-carbohydrate diet with *ad libitum* energy intake or a low-fat diet, the decrease in fat mass was also significantly greater in the high-protein group.[6,16]

Despite the theoretical advantages of increasing the protein content of a diet, the results of several trials are consistent with our results regarding the lack of efficacy of increasing the composition of this macronutrient over the long term, although some studies showed better weight loss after 6 months of follow-up.[4,18] Delbridge et al., using the same protein/carbohydrate ratio as in our study, did not find any differences in weight-loss maintenance. Both groups of diet, kept the weight off over 12 months, but the authors did not study the influence of IR on weight loss.[17] This trial did not find any differences in fat loss between the diets after 1 year of dietary counseling, and neither did we. The differences between studies have several possible explanations. The amount of protein given varies between the studies and is difficult to standardize what a high-protein diet actually is, especially when the usual recommended quantity of protein (0.8 g/kg) is far from the actual intake in developed countries. Important differences were also found in the diets used as the control (e.g. balanced or low fat). One of the advan-

tages of our study was the free-living setting, where no food was provided to the patients; they had to buy and process it according to recommendations by themselves. This could also have been a disadvantage since it is very difficult to quantify compliance with the diet. However, the clinical setting varies between studies, with some of them being performed in a controlled environment. Over the ensuing months the patients changed the scheduled diet and both groups eventually consumed a diet containing a similar macronutrient composition. This result, which is consistent with that observed by Dansinger et al.,[18] shows that it is difficult to maintain dietary changes over the long time in free-living situations, which could definitively influence the outcome.

One of the most relevant results of this study was the fact that patients in the IS group maintained their weight loss better than patients in the IR group, independently of the diet. IR is related to disturbances in lipid oxidation and to other metabolic abnormalities that could make weight loss difficult. Nevertheless, some studies have shown that glycemic status does not play a role in weight loss,[19] and others showed that insulin sensitivity did not affect weight loss in obese or overweight patients treated with hypocaloric diets,[11,20,21] as noted in our initial study.[8] Our results might have been influenced by the loss of patients during follow-up, which was largest in the IR group. The insulin peak after OGTT was higher among patients who received the carbohydrate-rich diet, but this macronutrient distribution was not associated with adverse outcomes related to glucose (either glucose levels or HOMA) or lipid metabolism. Several studies have shown evidence of the cardiovascular benefits of energy-restricted high-protein diets through reducing the amount of triglycerides and increasing HDL-cholesterol.[4] In McLaughlin's study,[22] several cardiovascular disease risk factors (day-long insulin concentrations, lipid and lipoprotein concentrations and cellular adhesion molecules) significantly improved in the subjects who followed the 40% carbohydrate diet, without showing any difference in weight loss. In our study, when comparing the IS group with the IR group, a significant increase was found in triglycerides in the IS group but there were no significant changes in total cholesterol, LDL-cholesterol, or HDL-cholesterol, as found when diets A and B were compared.

Our study has several limitations that should be discussed before any conclusion is reached. The sample size required in order to find significant differences in weight was calculated following the methods of previous studies,[7,9] but the number of subjects per group was small and we could not reach statistical significance in the secondary end-points. Furthermore, only a few patients in each group attended each visit, probably those who were more motivated to lose weight. Attrition rates were high, although similar to other studies on this topic, reflecting the difficulty of maintaining long-term diets.[18,23] Also, the study was only carried out in one center, so these results cannot be generalized. Dietary intake was assessed using a 24-h dietary recall method, which probably only gave limited or biased information about the real intake. Another limitation of the trial was that energy expenditure was not measured, therefore the influence of macronutrients on this parameter or on food thermogenesis could not be quantified.

In conclusion, after 1 year of follow-up, the hypocaloric diets with different protein/carbohydrate ratios resulted in similar changes to body weight and metabolic parameters, and insulin resistance was associated with a lower weight loss independently of macronutrient distribution. Dietary changes are difficult to maintain in free-living conditions over the long term, and this imposes limits on sustained weight control.

References

1. World Health Organization, Obesity: Preventing and Managing the Global Epidemic WHO Obesity Technical Report Series 894. Geneva, Switzerland: World Health Organization; 2000.
2. McMillian-Price J, Petocz P, Atlomspm F et al. Comparison of 4 diets of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: a randomized controlled trial. *Arc Inter Med* 2006; 166: 1466-75.
3. Baba NH, Sawaya S, Torbay N et al. High protein vs high carbohydrate hypoenergetic diet for the treatment of obese hyperinsulinemic subjects. *Int J Obes Relat Metab Disord* 1999; 23: 1202-6.
4. Foster GD, Wyatt HR, Hill Jo et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* 2003; 23: 528-36.
5. Sacks FM, Bray GA, Carey VJ et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med* 2009; 360: 859-73.
6. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS Jr, Brehm BJ, Bucher HC. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. *Arch Intern Med* 2006; 166: 285-93.
7. Cornier MA, Donahoo WT, Pereira R, Gurevich I, Westergren R, Enerback S et al. Insulin sensitivity determines the effectivenesss of dietary macronutrient composition on weight loss in obese women. *Obesity Research* 2005; 13: 703-9.
8. Ballesteros-Pomar MD, Calleja-Fernández AR, Vidal-Casariego A, Urioste-Fondo AM, Cano-Rodríguez I. Effectiveness of energy-restricted diets with different protein:carbohydrate ratios: the relationship to insulin sensitivity. *Public Health Nutr* 2009; 5: 1-8.
9. Ascaso JF, Romero P, Real JT, Priego A, Valdecabres C, Carmena R. Insulin resistance quantification by fasting insulin plasma values and HOMA index in a non-diabetic population. *Med Clin (Barc)* 2001; 117 (14): 530-3.
10. Harris JA, Benedict FG. A biometric study of basal metabolism in man. Washington, DC: Carnegie Institute of Washington, 1919 (publication 279).
11. McLaughlin T, Abbasi F, Carantoni M, Schaaf P, Reaven G. Differences in insulin resistance do not predict weight loss in response to Hypocaloric Diets in Healthy Obese Women. *J Clin Endocrinol Metab* 1999; 84: 578-81.
12. Westerterp-Plantenga MS.The significance of protein in food intake and body weight regulation. *Current Opinion in Clinical Nutrition and Metabolic Care* 2003; 6: 635-8.
13. Skov AR, Toubro S, Ronn B, et al. Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *Int J Obes Relat Metab Disord* 1999; 23: 528-36.

14. Dumesnil JG, Turgeon J, Tremblay A, Poirier P, Gilbert M, Gagnon L et al. Effect of a low-glycemic index–low-fat–high protein diet on the atherogenic metabolic risk profile of abdominally obese men. *Br J Nutr* 2001; 86: 557-68.
15. Laymen DK, Boileau RA, Erickson DJ et al. A reduced ratio of dietary carbohydrate to protein improves body-composition and blood lipid profiles during weight loss in adult women. *J Nutr* 2003; 133: 411-17.
16. Brehm BJ, Seeley RJ, Daniels SR, D'Alessio DA. A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. *J Clin Endocrinol Metab* 2003; 88: 1617-23.
17. Delbridge EA, Prendergast LA, Pritchard JE, Proietto J. One-year weight maintenance after significant weight loss in healthy overweight and obese subjects: does diet composition matter? *Am J Clin Nutr* 2009; 90: 1203-14.
18. Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone Diets for Weight Loss and Heart Disease Risk Reduction. *JAMA* 2005; 293 (1): 43-53.
19. De Luis DA, Aller R, Izaola O, Gonzalez Sagrado M, Conde R. Differences in glycaemic status do not predict weight loss in response to hypocaloric diets in obese patients. *Clin Nutr* 2006; 25: 117-22.
20. Kleiner RE, Hutchins AM, Johnston CS, Swan PD. Effects of an 8-Week High-Protein or High-Carbohydrate Diet in Adults With Hyperinsulinemia. *Med Gen Med* 2006; 8 (4): 39. http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=17415320. Published online November 22, 2006. Accessed October 16, 2011.
21. Luscombe ND, Clifton PM, Noakes M, Farnsworth E, Wittert G. Effect of a high-protein, energy-restricted diet on weight loss and energy expenditure after weight stabilization in hyperinsulinemic subjects. *Int J Obes* 2003; 27: 582-90.
22. McLaughlin T, Carter S, Lamendola Abbas Fi, Yee G, Schaaf P, Basina M, Reaven G. Effects of moderate variations in macronutrient composition on weight loss and reduction in cardiovascular disease risk in obese, insulin-resistant adult. *Am J Clin Nutr* 2006; 84: 813-21.
23. Tsai AG, Wadden TA. Systematic review: an evaluation of major commercial weight loss programs in the United States. *Ann Intern Med* 2005; 142 (1): 56-66.