

Original

# Effect of protein restriction diet on renal function and metabolic control in patients with type 2 diabetes: a randomized clinical trial

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Abstract

**Objective:** To assess the effect of a low protein diet (LPD) on renal function and metabolic control in three sub-groups of patients with type 2 diabetes those with or without nephropathy.

**Research design and methods:** A randomized clinical trial was conducted on 60 patients with type 2 diabetes in primary care —19 with normoalbuminuria, 22 with microalbuminuria, and 19 with macroalbuminuria—. All patients experienced a *screening* phase during the 3 months, and were designated according to percentages of daily caloric intake (e.g., carbohydrates 50%, fat 30%, and 20% of protein). After this period, they were randomly assigned to receive either LPD (0.6-0.8 g/kg per day) or normal protein diet (NPD) (1.0-1.2 g/kg per day) for a period of 4 months. Twenty nine patients received LPD and 31 received NPD. Primary endpoints included measures of renal function (UAER, serum creatinine and GFR) and glycemic control (fasting glucose and glycosylated hemoglobin A1c).

**Results:** Renal function improved among patients with macroalbuminuria who received LPD: UAER decreased ( $1,280.7 \pm 1,139.7$  to  $444.4 \pm 329.8$  mg/24 h;  $p < 0.05$ ) and GFR increased ( $56.3 \pm 29.0$ - $74.2 \pm 40.4$  ml/min;  $p < 0.05$ ). In normoalbuminuric and microalbuminuric patients, there were no significant changes in UAER or GFR after either diet. HbA<sub>1c</sub> decreased significantly among microalbuminuric patients on both diets (LPD,  $8.2 \pm 1.6$ - $7.2 \pm 1.8\%$ ;  $p < 0.05$ ; NPD,  $8.8 \pm 1.9$ - $7.1 \pm 0.8\%$ ;  $p < 0.05$ ) and among macroalbuminuric patients who received NPD ( $8.1 \pm 1.8$ - $6.9 \pm 1.6\%$ ;  $p < 0.05$ ).

**Conclusions:** A moderated protein restriction diet improved the renal function in patients with type diabetes 2 and macroalbuminuria

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Key words: Protein restriction. Nephropathy. Kidney function. Type 2 diabetes.

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## EFFECTO DE LA DIETA CON RESTRICCIÓN PROTEICA EN LA FUNCIÓN RENAL Y EL CONTROL METABÓLICO DE PACIENTES CON DIABETES TIPO 2: ENSAYO CLÍNICO DE DISTRIBUCIÓN ALEATORIA

Resumen

**Objetivo:** Valorar el efecto de una dieta baja en proteínas (DBP) sobre la función renal y el control metabólico en tres subgrupos de pacientes con diabetes tipo 2 con y sin nefropatía.

**Diseño del estudio y métodos:** Ensayo clínico de distribución aleatoria en 60 pacientes con diabetes tipo 2, en atención primaria- 19 con normoalbuminuria, 22 con microalbuminuria y 19 con macroalbuminuria. Todos los pacientes pasaron una fase de pre-intervención durante 3 meses y se anotó los porcentajes de ingesta calórica diaria (p.ej., carbohidratos 50%, grasas 30%, proteínas 20%). Después de este periodo de lavado, fueron distribuidos de forma aleatoria, para recibir o bien una DBP (0,6-0,8 g/kg, al día) o una dieta normoproteica (DNP) (1,0-1,2 g/kg al día), durante un periodo de 4 meses. Veintinueve pacientes recibieron DBP y 31 DNP. Las principales variables de desenlace fueron las medidas de función renal (EAU, creatinina sérica y TFG) y el control glucémico (glucemia en ayunas y hemoglobina A<sub>1c</sub> glucosilada).

**Resultados:** La función renal mejoró en los pacientes con macroalbuminuria que realizaron la DBP: la EAU disminuyó (de  $1,280,7 \pm 1,139,7$  a  $444,4 \pm 329,8$  mg/24 h;  $p < 0,05$ ) la TFG aumentó ( $56,3 \pm 29,0 - 74,2 \pm 40,4$  ml/min;  $p < 0,05$ ). En los pacientes con normo y microalbuminuria, no hubo cambios significativos en la EAU o TFG tras cualquiera de las dietas. La HbA<sub>1c</sub> disminuyó significativamente en los pacientes con microalbuminuria, con ambas dietas (DBP,  $8,2 \pm 1,6$ - $7,2 \pm 1,8\%$ ;  $p < 0,05$ ; DNP,  $8,8 \pm 1,9$ - $7,1 \pm 0,8\%$ ;  $p < 0,05$ ) y en los pacientes con macroalbuminuria que siguieron la DNP ( $8,1 \pm 1,8$ - $6,9 \pm 1,6\%$ ;  $p < 0,05$ ).

**Conclusiones:** Una dieta con restricción proteica moderada mejora la función renal en pacientes con diabetes tipo 2 y macroalbuminuria.

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Palabras clave: Restricción proteica. Nefropatía. Función renal. Diabetes tipo 2.

## Introduction

Diabetic nephropathy in type 2 diabetes is the leading cause of kidney disease in patients with end-stage renal disease.<sup>1,2</sup> Hyperglycemia, hypertension, dyslipidemia, smoking habits, and genetic predisposition are the main risk factors for development of diabetic nephropathy.<sup>3</sup> The clinical course of this condition is a step-wise progression from sub-clinical disease through incipient nephropathy and macroscopic albuminuria. Once albuminuria develops, there is a considerable increase in the risk of cardiovascular morbidity and mortality, and many patients progress to end-stage renal disease over a period of several years. Current evidence supports that intensive optimization of glycemic control with either oral hypoglycemic agents or insulin use, and control of blood pressure with angiotension-converting enzyme (ACE) inhibitors, are essential strategies for slowing the advance of diabetic nephropathy in patients with type 2 diabetes.<sup>4,5</sup> Several studies have shown that dietary protein restriction may delay progression of glomerular injury and end-stage renal disease.<sup>6,7</sup> Two meta-analysis clinical trials conducted in patients with declining renal function with protein-restricted diets reported significantly slowed increase in urinary-albumin excretion rate or decline in glomerular-filtration rate.<sup>8,9</sup> In patients with type 2 diabetes and nephropathy, moderate protein restriction or modification in the origin of protein meat was associated with a reduction of urinary-albumin excretion rate.<sup>10,11</sup> On the other hand, animal dietary protein replacement by vegetarian protein, reduce glomerular filtration rate in normoalbuminuric patients with type 1 diabetes.<sup>12</sup>

Although nearly all results have shown that dietary-protein restriction slows the progression of diabetic nephropathy, at least there is one study in which protein restriction in longer-term prevention is neither feasible nor efficacious.<sup>13</sup> Indeed, certain studies have found limited benefits in these patients with regard to kidney-function markers.<sup>14-17</sup> In addition, in patients with overt diabetic nephropathy, severe dietary-protein restriction does not appear to delay renal-disease progression, whereas it may induce malnutrition.<sup>18</sup> A consensus of experts suggests a protein intake of 0.8 g/kg body weight/day when diabetic nephropathy has been identified.<sup>19</sup> Nonetheless, it is controversial the type and amount of protein in a diet for patients with type 2 diabetes with incipient and evident nephropathy. Therefore, this study was conducted to analyze the effect of low-protein diet in patients with type 2 diabetes with microalbuminuria and macroalbuminuria.

## Methods

**Patients selection.** A prospective, randomized, controlled clinical trial was performed in the Mexican Institute of Social Security (IMSS) at Regional Hospital in Mexico City. The patients were selected from a previous cross-sectional study, conducted to know diabetic nephropathy presence in primary-care units attended by the hospital.<sup>20</sup>

The protocol was approved by the Hospital Investigation Research Board, and all participants signed informed consent before study initiation.

Patients were selected if they had previously diagnosed type 2 diabetes with fasting blood glucose level > 126 mg/dL or use of antidiabetic medications and were aged 40-80 years. Urinary-albumin excretion rate was measured and patients were classified as normoalbuminuria (UAER < 30 mg/24 h), microalbuminuria (UAER 30-299 mg/24 h), or macroalbuminuria (UAER > 300 mg/24 h). Patients were also classified as normotensive or controlled hypertensive with the use of any antihypertensive drug, including (ACE) inhibitors. Patients were excluded if they had malignant hypertension, a previous history of congestive heart failure or myocardial infarction, hepatic cirrhosis, cancer, severe obesity (body mass index [BMI]  $\geq 35$  kg/m<sup>2</sup>), recurrent urinary infections, and end-stage renal disease (glomerular filtration rate < 15 mL/min). Treatment with antihypertensive and oral antidiabetic agents for diabetes was maintained during the study, and no patient used hypolipidemic agents.

The study was performed after a 3 month pre-intervention period, outcome measures included customary diet and economical food resources were identified by the dietitian and a food frequency questionnaire was applied and 24-h dietary recalls were conducted to adjust nutritional therapy. During this period, all patients were oriented toward achieving best possible metabolic control through dietary adjustment and use of oral antidiabetic agents or insulin. The prescribed diets were designed according to BMI and gender of patients. The macronutrients were designated according to percentages of daily caloric intake (e.g., carbohydrates 50%, fat 30%, and 20% of protein). Nutritional consultations had a duration of approximately 30-45 min. Dietary estimations were performed according to recommendations of the American Diabetes Association (ADA) as closely as possible.<sup>19</sup>

**Study design and diet composition.** Subjects were randomly allocated in parallel single-blinded trial, then assigned to a low-protein diet (LPD) group or to a normal protein diet (NPD) group. The patients were randomized independently of age, duration of diabetes, weight, and other clinical variables, only the LPD group was instructed to decrease protein intake to 0.6-0.8 g/kg weight per day; the NPD group followed the diet prescribed during pre-intervention period. All patients received diet and as a basis for variation, individually designed daily menus based on their usual diet. This was supported by variation lists that indicated foods containing equivalent amounts of protein, and a food composition table and recipes. For each study group, separate plenary education meetings were held separately with the dietitian and researchers each month. Both groups received the same quality of care. All patients attended dietary appointments every 2

**Table I**  
Baseline features in both groups of patients with type 2 diabetes mellitus and diabetic nephropathy

	Low protein Diet n = 29 n (%)	Normal protein Diet n = 31 n (%)
<b>Sex</b>		
Female	22 (76)	14 (45)
Male	7 (24)	17 (55)
<b>Age (years)</b>	68.0 ± 9.3	66.3 ± 10.1
<b>Known duration of diabetes</b>	18.7 ± 8.8	15.0 ± 9.0
<b>Treatment for DM2</b>		
Oral hypoglycemic	16 (55)	18 (58)
Insulin and Oral hypoglycemic	10 (34)	8 (26)
Insulin	3 (11)	5 (16)
<b>Hypertension</b>	25 (86)	14 (45)*
<b>Anti Hypertensive drugs</b>		
ACE Inhibitors	9 (36)	5 (16)
ACE Inhibitors and beta blockers	5 (20)	7 (22)
Sartanes	2 (8)	-
Beta blockers	4 (16)	2 (6)
Calcium Antagonist	3 (12)	-
Diuretics	2 (8)	-
<b>Current smoking</b>	2 (8)	11 (35)
Normoalbuminuria (< 30 mg/24-h)	9 (30)	10 (32)
Microalbuminuria (30-299 mg/24-h)	10 (35)	12 (39)
Macroalbuminuria (> 300 mg/24-h)	10 (35)	9 (29)

Data are n (%), means, ± SD. The characteristics of patients between Low Protein Diet (LPD) and Normal Protein Diet (NPD) were analyzed with X<sup>2</sup> test.

\*P < 0.05, Differences between LPD and NPD.

weeks with the research dietician to ensure compliance, and were given detailed instructions on how to manipulate the diet in keeping with appropriate protein contents. Compliance was assessed through the food frequency questionnaire before and after measurement of urea in 24-h urine samples at the end of the study. Estimation of protein intake was based on 24-h nitrogen output (standardized formula).<sup>21</sup> Dietary macronutrients and micronutrients were analyzed using Nutritional manager software released by the National Institute of Public Health in Mexico.<sup>22</sup>

**Clinical and laboratory measurements.** After the pre-intervention period and at the end of the study, clinical evaluations were performed. Body weight was measured in light-weight clothing on standard calibrated scales, and stadiometers were used to determine height. Body mass index (BMI) was calculated by dividing weight in kg by squared height in meters (kg/m<sup>2</sup>). Waist circumference was measured midway between the lower rib margin and the iliac crest. Systolic (SBP, first phase) and diastolic (DBP, fifth phase) blood pressure were measured three times with a mercury sphygmomanometer after the patient had remained seated for at least 5 min; averages of the second and third determinations were used for analysis.

Fasting venous-blood samples were obtained after a 12-h fast, at baseline, and at 4 months. Serum total glucose and lipid profile were analyzed with an automated instrument (Roche/Hitachi 917; CAN 690, USA). Low-density lipoprotein (LDL) cholesterol level was calculated by the Friedewald equation.<sup>23</sup> Hemoglobin (HbA1c) was determined by an ion-exchange high-performance liquid chromatography procedure (Merck Hitachi L-9100 glycosylated hemoglobin analyzer, reference range 2.7-4.3% (Merck, Darmstadt, Germany). Urinary-albumin excretion (UAER) was measured in 24-h timed sterile-urine samples and analyzed by nephelometry (Beckman Instrument, GmbH, Munich, Germany, order no. 441450). Protein intake was estimated from 24-h urinary-urea excretion by means of the Jaffé method (BM/Hitachi 747/737, Boeringer-Mannheim, Germany).

Urinary nitrogen was calculated by the following formula: nitrogen intake = urinary urea nitrogen (urea/2) non-urinary nitrogen (0.031 g/kg). GFR was assessed using creatinine-clearance estimation by the Cockcroft and Gault formula ( $[(140 - \text{age in years} \times \text{kg}) / (\text{serum creatinine} \times 72)] \times \text{constant of } 0.85$ ).<sup>24</sup>

**Statistical analysis.** Data are expressed as means ± standard deviation (SD). Nominal variables were analyzed with chi square (X<sup>2</sup>) test to assess differences in prevalence among group. Intergroup comparisons of UAER, GFR, variables of metabolic control, and lipid profile in the LPD and NPD groups were analyzed by unpaired *t* test, while intragroup comparisons were performed by paired *t* test. Differences were considered statistically significant when *p* < 0.05. Statistical analysis was performed using SPSS version 11.0 (Chicago, IL, USA).

## Results

### Patient Characteristics

Sixty nine patients were eligible for the study; nine patients withdrew prior to or during pre-intervention period due to non-compliance of prescribed diet, diabetes-unrelated illness, or time constraints. Sixty patients were included in the study: 29 were randomly allocated to LPD, and 31 to NPD. Those in LPD were older (68.0 ± 9.3 years vs 60.3 ± 10.1 years). LPD group had a higher proportion of women and longer diabetes-evolution time, these differences not statistically significant. Usual treatment for diabetes in both groups was sulfonylureas with metformin as well as insulin combined with oral agents. The proportion of patients with hypertension was significantly higher in the LPD group; the more frequent treatment for hypertension was ACE inhibitors and beta blockers in both groups (table I).

### Diet Characteristics

Daily protein intake, estimated through urinary-nitrogen excretion, was significantly lower in the LPD

group ( $0.82 \pm 0.36$  g/per kg weight vs  $1.2 \pm 0.48$  g/per kg weight;  $p < 0.05$ ) and protein intake was lower as assessed by 24-hour dietary recalls ( $56.0 \pm 0.12$  vs  $80.7 \pm 15$ ;  $p < 0.05$ ). There were no significant differences between diets with respect to calories, total fat and dietary fiber (table II).

#### Diet effect on metabolic control

Metabolic-control parameters before and after intervention are shown in table III. In LPD-group normoalbuminuric patients, fasting blood glucose was significantly reduced after 4 months ( $156.3 \pm 51.7$ - $95.3 \pm 35.8$  mg/dL;  $p < 0.05$ ). Subjects with microalbuminuria had significant decrease in HbA<sub>1c</sub> after the intervention period in both groups (LPD:  $8.2 \pm 1.6$ - $7.2 \pm 1.8\%$ ;  $p < 0.05$ , and NPD,  $8.8 \pm 1.9$ - $7.1 \pm 0.8\%$ ,  $p < 0.05$ ). In macroalbuminuric patients and only in the NPD group, the mean of HbA<sub>1c</sub> had a significant decrease ( $8.1 \pm 1.8$ - $6.9 \pm 1.6\%$ ,  $p < 0.05$ ). Total cholesterol, triglycerides, and C-LDL and C-HDL levels were not statistically different after use of either diet.

#### Diet effect on renal function

Renal-function parameters are shown in table IV. In LPD group, UAER levels in macroalbuminuric patients were significantly reduced ( $1,280.7 \pm 1,139.7$ - $444.4 \pm 329.8$  mg/24-h;  $p < 0.05$ ). GFR values increased in macroalbuminuric patients in the LPD group ( $56.3 \pm 29.0$ - $74.2 \pm 40.4$  mL/min;  $p < 0.05$ ). Patients with macroalbuminuria in the NPD group experienced a significant reduction in GFR ( $74.4 \pm 31.4$ - $65.1 \pm 25.5$  mL/min;  $p < 0.05$ ). In normoalbuminuric and microalbuminuric patients, no differences were observed in UAER and GFR; however, microalbuminuric patients in the LPD group had a moderate increase of GFR. Contrariwise, in NPD-group patients GFR decreased at the end of the study (table IV). Hyperfiltration (GFR  $> 115$  mL/min) was found in LPD-group eight patients and in seven patients of the NPD group. In patients with hyperfiltration, GFR baseline was significantly higher in LPD compared with NPD group ( $149.3 \pm 3.8$  vs  $123.8 \pm 6.6$ ;  $p < 0.05$ ), although at the end of the study no difference was observed between both groups in GRF values ( $132.9 \pm 13$  vs  $113.09 \pm 23.2$ ;  $p > 0.05$ ) (data not shown).

#### Discussion

We observed a sustained decrease in UAER in macroalbuminuric patients after LPD ( $0.8$  g/kg weight per day). These results support the hypothesis that protein-intake restriction, especially of animal-protein origin, can beneficially influence the course of overt diabetic nephropathy. At the same time, an important increase in GFR was observed in patients with macro-

**Table II**  
Dietary intake of the protein and normal protein diet, at the end of the study

	Low protein Diet n = 29	Normal protein Diet n = 31	p value*
Energy (kcal/day)	1.745.0 ± 218	2.016.2 ± 362	0.63
Protein (g/day)	56.0 ± 20	70.7 ± 15	0.01
Carbohydrate (g/day)	234.4 ± 43	254.2 ± 60	0.43
Fat total (g/day)	65.5 ± 9	80.8 ± 18	0.35
Cholesterol (mg/day)	205.5 ± 72	318.7 ± 65	0.04
Dietary fiber (g/day)	17.8 ± 7	19.5 ± 5	0.22

Data are expressed as means ± SD. \*Proteins Intake was assessed through the nitrogen ureic. Comparisons made by Student *t* test. Significance difference  $P < 0.05$ .

albuminuria with LPD, this result with LPD showed significantly slower down the GFR declining for the macroalbuminuric patients. The contrary in macroalbuminuric patients with NPD experienced a progressive decline in GFR levels and a non-significant decrease of UAER; our results, unlike to the MDRD (Modification of Diet in Renal Disease) study, the low-protein diet did not slow the GFR declining in 17 patients with type 2 diabetes.<sup>25</sup> Previous studies in patients with type 1 diabetes and with less evidence in patients with type 2 diabetes have shown a decrease in UAER with protein restriction or modification of origin the protein in the diet.<sup>10,26-29</sup> In this study, we did not observe a significantly UAER decrease after LPD in patients with normoalbuminuria and microalbuminuria as it has been previously suggested.<sup>11,16</sup> On the other hand, the multivariate analysis adjusted according to the type of diet, BMI, HbA<sub>1c</sub>, hypertension and fasting plasma glucose, did not show significant change in the decrease of UAER and increase in GFR in macroalbuminuric patients with LPD. We consider that the significant UAER decreases in patients with macroalbuminuria, as well as GFR increase, and it probably represent changes in hemodynamic levels of plasma renal flow with restriction of dietary-protein intake.

It has been suggested that in patients with severe nephrotic syndrome, the severe protein restriction leads to patient malnutrition.<sup>18</sup> The results of this study show that a moderate reduction in dietary protein can beneficially influence the course the overt diabetic nephropathy without affecting nutrition.

In microalbuminuric patients with LPD did not show UAER increase during the study; however, we consider that this is clinically important although it delay the progression of diabetic renal disease. In microalbuminuric patients with NPD, UAER increased despite significant reduction of HbA<sub>1c</sub>. Our results suggest that patients with type 2 diabetes and microalbuminuria not only require metabolic control, but also probably a moderate protein restriction to delay renal-disease progression. In patients with normoalbuminuria, the absence of effects of the

**Table III**  
Effect of low protein diet in patients with type 2 diabetes on metabolic control

	Low protein diet n = 29		Normal protein diet n = 31	
	Basal	4 months	Basal	4 months
<b>BMI (kg/m<sup>2</sup>)</b>				
Normoalbuminuric	24.6 ± 3.3	24.4 ± 3.6	27.3 ± 4.2	27.3 ± 4.3
Microalbuminuric	28.5 ± 8.2	28.4 ± 8.2	26.9 ± 3.2	27.0 ± 3.27
Macroalbuminuric	29.3 ± 6.7	29.0 ± 6.6	29.8 ± 4.8	28.9 ± 4.9 <sup>1</sup>
<b>Waist circumference (cm)</b>				
Normoalbuminuric	90.8 ± 8.3	88.1 ± 6.4	91.8 ± 10.8	94.3 ± 11.8
Microalbuminuric	90.9 ± 14.8	92.2 ± 12.5	94.7 ± 7.4	97.1 ± 8.4
Macroalbuminuric	97.6 ± 12.5	95.1 ± 12.3	99.4 ± 10.8	99.1 ± 9.2
<b>Systolic blood pressure (mmHg)</b>				
Normoalbuminuric	133.3 ± 17	138.8 ± 13.6	130 ± 23.2	125.5 ± 12.6
Microalbuminuric	132.2 ± 19.1	129.5 ± 19.5	127.0 ± 12.3	129.5 ± 18.1
Macroalbuminuric	139.4 ± 20.9	136.6 ± 12.2	137.7 ± 17.1	135.0 ± 13.7
<b>Diastolic blood pressure (mmHg)</b>				
Normoalbuminuric	75.5 ± 5.2	72.2 ± 6.7	74.5 ± 7.6	74.0 ± 6.9
Microalbuminuric	77 ± 6.7	76.5 ± 4.7	75.40 ± 7.3	77.2 ± 7.8
Macroalbuminuric	76.1 ± 11.1	73.8 ± 4.8	79.4 ± 11.8	78.8 ± 12.6
<b>HbA<sub>1c</sub> (%)</b>				
Normoalbuminuric	7.5 ± 1.5	6.8 ± 0.8	8.8 ± 2.2	7.9 ± 1.3
Microalbuminuric	8.2 ± 1.6	7.2 ± 1.8 <sup>2</sup>	8.8 ± 1.9	7.1 ± 0.8 <sup>3</sup>
Macroalbuminuric	8.4 ± 2.1	7.6 ± 1.0	8.1 ± 1.8	6.9 ± 1.6 <sup>4</sup>
<b>FBG (mg/dL)</b>				
Normoalbuminuric	156.3 ± 51.7	95.3 ± 35.8 <sup>5</sup>	188.4 ± 61.2	123.1 ± 51.5
Microalbuminuric	139.8 ± 45.9	123.0 ± 75.4	133.4 ± 18.3	110.1 ± 34.8
Macroalbuminuric	190.6 ± 59.2	114.5 ± 57.7	131.2 ± 75.9	86.7 ± 24.3

Data are expressed as means ± SD. BMI = body mass index, HbA<sub>1c</sub> = glycosylated hemoglobin, FBG = fasting blood glucose. Comparisons made by paired Student *t* test. Comparisons made by paired Student *t* test. Significantly different from onset: <sup>1</sup> P = 0.04, <sup>2</sup> P = 0.001, <sup>3</sup> P = 0.002, <sup>4</sup> P = 0.001.

UAER decrease could be explained by the low levels of this renal indicator. Furthermore, in the analysis performed within both groups in patients with normoalbuminuria and hyperfiltration no significant differences were found in GFR decrease. Hence, we could not confirm an association between LPD and GFR reduction in patients with hyperfiltration, as suggested by other authors.<sup>16,30,31</sup> However, previous results probably could be related with the low number of patients with hyperfiltration included in this study.

Current evidence supports an intensive optimization of glycemic control with either oral hypoglycemic agents or insulin use and blood-pressure control using ACE inhibitors as two essential strategies for preservation of renal function in patients with diabetes type 2.<sup>4,5</sup> In this study, patients with normoalbuminuria and microalbuminuria had stable blood pressure (130 mmHg) in both groups; adversely, in patients with macroalbuminuria in both groups they had higher blood-pressure levels during the study (> 135 mmHg). In this study, even when patients with hypertension were treated mainly with ACE Inhibitors and beta blockers only patients with LPD achieved

significant improvements in renal function, independently of blood-pressure levels. Only the patients with microalbuminuria and macroalbuminuria with NPD showed important reduction in HbA<sub>1c</sub>. These results confirm LPD's beneficial effect in patients with microalbuminuria, even without a significant improvement in metabolic control.

Quality control to assess dietary compliance was measured by 24-h recalls of meals every 15 days during the 4 months of the study, in addition to ureic-nitrogen measurements. These variables showed that patients complied with the amount of protein intake as prescribed by the researchers. Our results suggest that moderate protein restriction provides renal benefit in patient with type 2 diabetes with macroalbuminuria and microalbuminuria; however, we consider that the nutritional therapy in patients with type 2 diabetes and nephropathy should be individualized, and for achieving better metabolic control and normalization of body-weight, lipid-profile, and blood-pressure levels.

Other authors have suggested a limited efficacy in the long term with the protein-restriction diet on renal indica-

**Table IV**  
Effect the diets in patients with type 2 diabetes in lipid profile and renal indicators

	Low protein diet n = 29		Normal protein diet n = 31	
	Basal	4 months	Basal	4 months
<i>TC (mg/dL)</i>				
Normoalbuminuric	193.2 ± 63.9	178.5 ± 52.3	201.0 ± 50.2	209.4 ± 37.8
Microalbuminuric	207.5 ± 40.0	209.4 ± 67.3	211.3 ± 42.9	209.4 ± 40.2
Macroalbuminuric	224.6 ± 57.1	213.8 ± 30.4	243.6 ± 44.4	226.2 ± 34.7
<i>TG (mg/dL)</i>				
Normoalbuminuric	186.8 ± 100.5	180.6 ± 93.0	161.5 ± 89.6	183.1 ± 131.1
Microalbuminuric	203.0 ± 137.0	163.4 ± 45.1	161.4 ± 65.0	169.0 ± 82.2
Macroalbuminuric	204.0 ± 80.2	158.4 ± 44.3	180.6 ± 68.1	193.6 ± 112.3
<i>C-LDL (mg/dL)</i>				
Normoalbuminuric	122.5 ± 53.5	108.0 ± 43.7	125.5 ± 41.2	128.9 ± 29.9
Microalbuminuric	135.5 ± 35.7	132.3 ± 34.2	130.6 ± 35.1	133.2 ± 30.8
Macroalbuminuric	131.6 ± 22.4	132.7 ± 41.5	155.5 ± 31.6	148.2 ± 27.2
<i>C-HDL (mg/dL)</i>				
Normoalbuminuric	46.6 ± 12.0	49.8 ± 8.2	55.4 ± 10.4	56.0 ± 12.2
Microalbuminuric	53.4 ± 17.4	62.0 ± 24.7	44.9 ± 13.8	46.9 ± 10.6
Macroalbuminuric	53.8 ± 14.0	61.3 ± 21.2	57.7 ± 26.5	58.0 ± 14.1
<i>UAER (mg/24 hours)</i>				
Normoalbuminuria	11.5 ± 9.5	15.0 ± 7.3	11.5 ± 4.0	8.0 ± 4.4
Microalbuminuria	104.6 ± 70.2	106.0 ± 62.2	106.0 ± 56.9	140.12 ± 83.7
Macroalbuminuria	1,280.7 ± 1,139.7	744.4 ± 329.8 <sup>1</sup>	1,519.6 ± 1,355.0	1,286.6 ± 645.2
<i>GFR (mL/min)</i>				
Normoalbuminuric	87.5 ± 15.2	86.2 ± 18.2	81.51 ± 21.7	78.6 ± 19.7
Microalbuminuric	69.7 ± 36.9	76.2 ± 35.6	89.2 ± 32.1	81.9 ± 34.6
Macroalbuminuric	56.3 ± 29.0	74.2 ± 40.4 <sup>2</sup>	74.4 ± 31.4	65.1 ± 25.5 <sup>3</sup>

Data are expressed as means ± SD. BMI = body mass index, HbA<sub>1c</sub> = glycosylated hemoglobin, FBG = fasting blood glucose. Comparisons made by paired Student t test. Comparisons made by paired Student t test. Significantly different from onset: <sup>1</sup>P = 0.004, <sup>2</sup>P = 0.003, <sup>3</sup>P = 0.006.

tors.<sup>13</sup> One possible explanation of the outcomes is that nutritional therapy did not include comorbidity in evaluated patients; in our study, nutritional therapy in all patients included the individual's usual food and eating habits and the metabolic profile, including glucose, HbA<sub>1c</sub>, lipids, blood pressure, and body weight. In this study only patients with microalbuminuria with NPD decreased BMI with statistical significance; this might be explained by the low intake of carbohydrates in this group, as it has been reported with a low-carbohydrate diet in patients with obesity.<sup>32</sup> A significant effect on lipid reduction with pharmaceutical treatment, especially LDL-cholesterol and triglycerides, has been well documented to decrease renal-disease progression.<sup>33</sup> Patients in this study were not medically treated for low lipids; however, LPD reduced serum cholesterol and triglycerides in patients with microalbuminuria and macroalbuminuria as well as HDL-cholesterol increase was observed. This lipid-profile reduction probably was related with lower dietary-content fat and cholesterol. Contrariwise, in patients with NPD there were no significant changes compared with initial values in lipid profile. Previous results supports that insistent integral nutritional therapy

is a positive influence for hypertension and dyslipidemia, medical conditions which usually coexist in patients with diabetic nephropathy.<sup>34</sup>

Even when patients were randomized and allocated in both groups, possible limitations include the following: in the LPD group: 1) patients were older and 2) there were a higher proportion of hypertensive patients; nonetheless, statistical analyses adjusted to the previous mentioned variables were not statistically significant when comparing both groups.

We conclude that moderate protein restriction in patients with type 2 diabetes and macroalbuminuria can delay the progression of diabetic renal disease. We consider that in patients with normoalbuminuria and microalbuminuria, the effect of the protein-restriction in the diet should be confirmed in along-term study.

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