Effect of a Chicken-Based Diet on Renal Function and Lipid Profile in Patients With Type 2 Diabetes

A randomized crossover trial

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OBJECTIVE — To assess the effect of replacing red meat with chicken in the usual diet and the effect of a low-protein diet on glomerular filtration rate (GFR), urinary albumin excretion rate (UAER), and lipid levels in patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS — A randomized, crossover, controlled trial was conducted with 28 patients with type 2 diabetes (seven women; mean age 58.1 years): 15 patients were normoalbuminuric (UAER <20 µg/min), and 13 patients were microalbuminuric (UAER 20–200 µg/min). A chicken-based diet (red meat replaced with chicken) and a low-protein diet were compared with the patients' usual diet. Patients followed each diet for 4 weeks with a 4-week washout period between. GFR (^{51}Cr-EDTA single-injection technique), 24-h UAER (immunoturbidimetry), apolipoprotein B, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides were measured after each diet.

RESULTS — Normoalbuminuric and microalbuminuric patients with diabetes were analyzed separately. In normoalbuminuric patients, GFR after the chicken (101.3 ± 22.9 ml · min^{-1} · 1.73 m^{-2}) and low-protein diets (93.8 ± 20.5 ml · min^{-1} · m^{-2}) was lower than after the usual diet (113.4 ± 31.4 ml · min^{-1} · 1.73 m^{-2}; $P < 0.05$). In microalbuminuric patients, apolipoprotein B levels were lower after the chicken (113.5 ± 36.0 mg/dl) and low-protein diets (103.5 ± 40.1 mg/dl) than after the usual diet (134.3 ± 30.7 mg/dl; $P < 0.05$). Only the chicken diet reduced UAER (median 34.3 µg/min) compared with the low-protein (median 52.3 µg/min) and usual (median 63.8 µg/min) diets ($P < 0.05$). Glycemic control and blood pressure did not change after the diets.

CONCLUSIONS — A normoproteic diet with chicken as the only source of meat may represent an alternative strategy for treatment of patients with type 2 diabetes and microalbuminuria.

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Microalbuminuria affects 20% of patients with type 2 diabetes (1). It is a predictor of end-stage renal failure and an independent risk factor for coronary artery disease (2), which is the main cause of death in patients with type 2 diabetes (3). The treatment of microalbuminuric patients with diabetes includes achievement of optimal metabolic and blood pressure control and use of ACE inhibitors (4). Although high levels of serum cholesterol have been considered a risk factor for development of diabetic nephropathy in patients with type 2 diabetes (5), the effect of reducing cholesterol levels on urinary albumin excretion rate (UAER) is still controversial (6,7). ACE inhibitors have a renoprotective effect on microalbuminuric patients with type 2 diabetes because they stabilize plasma creatinine and albuminuria (8). Although ACE inhibitors are associated with few adverse effects, in some cases, cough, hypersensitivity reaction, decrease of renal function, and severe hypoglycemic episodes requiring hospitalization may limit their use (9). Furthermore, the cost of these drugs may prevent their use in a significant proportion of patients, especially in countries in which the health care system does not cover drug expenses. Therefore, in some situations, it is necessary to use additional measures to halt the progression of microalbuminuria. A low-protein diet can reduce microalbuminuria (10,11) and slow the decline of renal function in proteinuric patients with diabetes (12). However, the long-term safety of this diet is not firmly established.

We have previously described that replacement of red meat with chicken and fish in normoalbuminuric patients with type 1 diabetes reduces hyperfiltration (13), a possible risk factor for diabetic nephropathy (14). Therefore, this study was conducted to analyze the impact of replacing the red meat in the usual diet with chicken and the impact of a low-protein diet on renal function in normoalbumin-
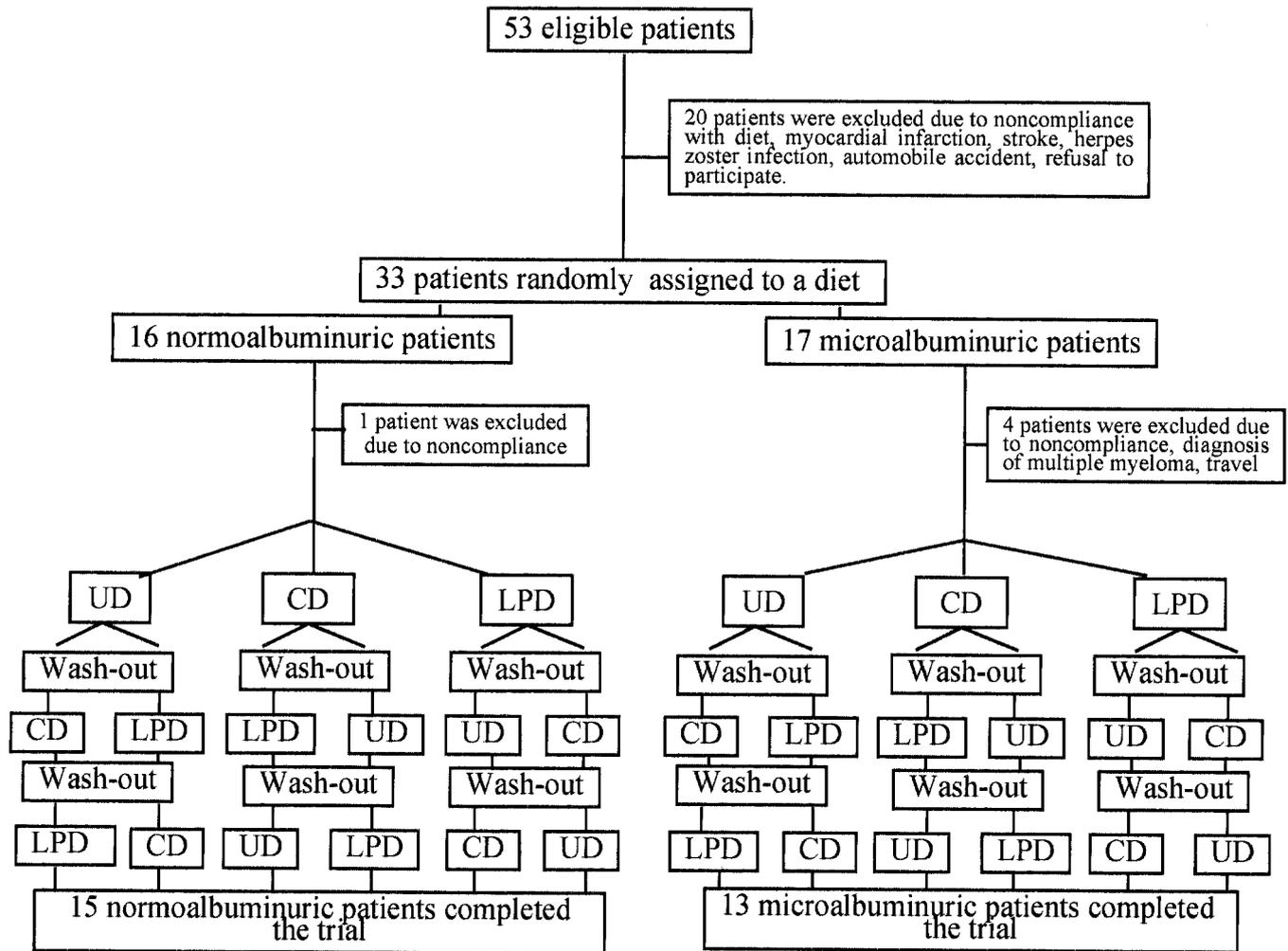
Figure 1—*Flow of patients.*

uric and microalbuminuric patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS

Patients

Patients with type 2 diabetes (according to the World Health Organization criteria) attending the Endocrine Division's outpatient clinic (Hospital de Clínicas de Porto Alegre, Brazil) were selected on the basis of the following criteria: age <75 years, BMI <32 kg/m^2, good compliance with diabetes treatment, triglyceride levels <4.52 mmol/l, UAER <200 μg/min, normal liver and thyroid function, and absence of urinary tract infection, other renal disease, and cardiac failure. Treatment with antihypertensive and oral antidiabetic agents was maintained during the study. To avoid potential confound-

ing factors on the effect of diets on renal function and lipid profile, none of the patients were using either ACE inhibitors or hypolipidemic agents. Eligible patients entered a run-in period of ~2 months in which they were oriented to achieve the best possible metabolic control through dietary adjustments and use of oral antidiabetic agents or insulin. The dietary adjustments were designed to meet the recommendations of the American Diabetes Association as closely as possible (15). However, usual protein intake (1.2–1.5 g/kg body wt) was maintained. At the end of the run-in period, a baseline evaluation was performed. BMI was calculated and sitting blood pressure was measured twice to the nearest 2 mmHg, after a 10-min rest, using a standard mercury sphygmomanometer (phases I and V of Korotkoff sounds). Hypertension was defined as blood pressure ≥140/90 mmHg

or when a patient was taking antihypertensive drugs.

Study design, diet composition, and prescription

This study followed a randomized, crossover, controlled clinical trial design. The protocol was approved by the Ethics Committee of the Hospital. All patients gave written informed consent. Three types of diets were assessed: the patient's usual diet (UD), a low-protein diet (LPD), and a chicken diet (CD). The protein content of the LPD was 0.5–0.8 g/kg per day (vegetable and milk protein only). In the CD, the red meat of the UD was replaced with chicken meat (skinless leg quarter). Patient were assigned to follow the three diets in random order for a period of 4 weeks each. Randomization was stratified according to UAER in normoalbuminuric and microalbuminuric patients separately

Table 1—*Baseline characteristics of normoalbuminuric and microalbuminuric patients with type 2 diabetes*

	Normoalbuminuric	Microalbuminuric
Sex (F/M)	4/11	3/10
Age (years)	56.8 ± 11.3	57.8 ± 6.5
Known duration of diabetes (years)	7.8 ± 6.3	13.5 ± 7.3
BMI (kg/m^2)	24.8 ± 2.6	27.9 ± 2.5
Mean blood pressure (mmHg)	94.0 ± 8.3	98.0 ± 6.8
Hypertension	7 (47)	7 (54)
Antihypertensive drugs		
β-blockers only	1 (7)	1 (8)
Calcium channel blockers only	5 (33)	5 (38.5)
Diuretics and calcium channel blockers	1 (7)	1 (8)
Current smoking	1 (7)	3 (23)
Type of treatment (D/OA/I /I + OA)	3/11/0/1	2/4/4/3
Fasting plasma glucose (mmol/l)	6.7 ± 1.3	7.1 ± 1.9
HbA$_{1c}$ (%)	5.3 ± 0.9	5.8 ± 1.0
Fructosamine (mmol/l)	3.00 ± 0.44	3.41 ± 0.42
Creatinine (mmol/l)	82.2 ± 17.7	88.3 ± 17.7

Data are means ± SD or number of patients with the analyzed characteristic (%). D/OA/I/I+OA, diet only/oral antidiabetic agent/insulin/insulin associated with oral antidiabetic agent.

after the run-in period, as shown in Fig. 1, by one of the authors (T.Z.). The executors (C.M., V.D.M.) were blinded to the randomization process. Consecutive eligible patients were assigned to a sequence of diets as follows: *1*) UD, LPD, CD; *2*) UD, CD, LPD; *3*) LPD, UD, CD; *4*) LPD, CD, UD; *5*) CD, LPD, UD; and *6*) CD, UD, LPD. After each diet, the patients underwent a 4-week washout period during which they maintained their usual diet. Compliance was assessed by 2-day weighed-diet records and measurement of urea in 24-h urine samples at the end of the second and fourth weeks, as previously described (16). The criterion standard for the estimation of protein intake was 24-h nitrogen output. Dietary macronutrients and micronutrients were analyzed using the Nutrabase '98 Clinical Nutritional Manager software (Cybersoft, Phoenix, AZ) (17). The primary outcome measures were UAER and GFR. Because there were no previous studies examining the role of chicken diet on UAER in microalbuminuric patients with diabetes, the sample size was calculated based on the reduction of albumin clearance corrected by GFR (fractional albumin clearance) after LPD in microalbuminuric patients with type 1 diabetes (18). To obtain a reduction of 3.61 ($\times 10^{-6}$) on the fractional clearance of albumin, it was estimated that 10 microalbuminuric patients had to be included for a significance level of $\alpha = 0.05$ and a power of $1 - \beta = 0.80$.

Laboratory measurements
GFR was measured using the ^{51}Cr-EDTA single-injection technique (coefficient of variation 12%, GFR reference range 72–137.5 ml · min^{-1} · 1.73 m^{-2}). Urinary albumin was measured in 24-h timed sterile urine samples by immunoturbidimetry (Sera-Pak immuno microalbuminuria; Bayer, Tarrytown, NY; mean intra-assay and interassay coefficients of variation 4.5 and 11.0%, respectively).

Microalbuminuria, confirmed at least twice in a 6-month period, was considered to be present when UAER was 20–200 µg/min. Fractional clearance of albumin was calculated by dividing albumin clearance by GFR. Serum albumin level was determined by the bromocresol green technique, glucose level was determined by a glucose oxidase method, creatinine level was measured by the Jaffé reaction, HbA$_{1c}$ was determined by an ion-exchange high-performance liquid chromatography procedure (Merck-Hitachi L-9100 glycated hemoglobin analyzer, reference range 2.7–4.3%; Merck, Darmstadt, Germany), and fructosamine was determined by a colorimetric method (normal range 1.87–2.87 mmol/l). Urinary urea was measured by an enzymatic ultraviolet method (mean intra-assay coefficient of variation 3.8%). The 24-h nitrogen output was obtained according to the following formula: nitrogen intake = urinary urea nitrogen (urea/2) + nonurinary nitrogen (0.031 g/kg). Protein intake was calculated as nitrogen intake × 6.25 (19). Triglycerides and total cholesterol were measured by enzymatic colorimetric methods (Merck Diagnostika, Darmstadt, Germany; Boehringer Mannheim, Buenos Aires, Argentina), and HDL cholesterol was measured by a precipitation method using magnesium chloride and heparin. LDL cholesterol was calculated from the Friedewald equation (20). Apolipoprotein B was determined by immunoturbidimetric method (Unimate 3; Roche Diagnostic System, Basel, Switzerland; intra-assay coefficient of variation 4.2%).

Statistical analysis
The characteristics of normoalbuminuric and microalbuminuric patients were analyzed using the unpaired Student's *t* test or Mann-Whitney's test or Fisher's exact test and χ^2 test, as appropriate. Differences among the three types of diets were tested either by repeated-measures ANOVA and Student-Newman-Keuls post-hoc test or by Friedman's ANOVA and least significant differences post-hoc test. *P* values <0.05 were considered statistically significant. Results were expressed as means ± SD unless otherwise stated. SPSS software (SPSS, Chicago, IL) was used for the analyses.

RESULTS

Patient characteristics
Of the 53 eligible patients, 20 were excluded from the study for various reasons, and 33 (16 normoalbuminuric and 17 microalbuminuric patients) were randomized to follow one of the six diet sequences described in Fig. 1. Five of the randomized patients (one normoalbuminuric and four microalbuminuric patients) did not complete the study protocol; therefore, 28 patients (15 normoalbuminuric and 13 microalbuminuric) were included in the final analysis. One patient was excluded from the GFR analysis due to technical problems in the measurement of GFR, and one patient was excluded from the UAER analysis because the 24-h urine sample collected after LPD was lost. The main clinical and laboratory characteristics of normoalbuminuric and microalbuminuric patients with type 2 diabetes are reported in Table

Table 2—*Dietary intake during the usual diet, the chicken diet, and the low-protein diet, according to weighed-diet records of patients with type 2 diabetes*

	Usual diet	Chicken diet	Low-protein diet	P
Energy (kcal/kg weight)	26.6 ± 6.3	26.0 ± 6.8	23.3 ± 7.4	0.013*
Protein (g/kg weight)	1.43 ± 0.3	1.35 ± 0.3	0.66 ± 0.2	<0.0001†
Carbohydrate (g/kg weight)	2.99 ± 1.1	3.25 ± 1.0	3.53 ± 1.3	0.049‡
Fat (g/kg weight)	0.92 ± 0.23	0.81 ± 0.28	0.86 ± 0.3	0.068
Fatty acids (g/kg weight)				
Saturated	0.26 ± 0.09	0.22 ± 0.1	0.20 ± 0.08	0.0057§
Polyunsaturated	0.28 ± 0.09	0.30 ± 0.11	0.31 ± 0.13	0.26
Monounsaturated	0.30 ± 0.09	0.27 ± 0.11	0.25 ± 0.11	0.048‡
Polyunsaturated saturated	1.15 ± 0.47	1.56 ± 0.61	1.76 ± 0.91	0.0015§
Cholesterol (mg/kg weight)	3.24 ± 1.13	3.03 ± 1.02	0.60 ± 0.43	<0.001*
Calcium (mg)	691 ± 186	733 ± 317	732 ± 250	0.64
Phosphorus (mg)	1,315 ± 321	1,216 ± 329	890 ± 290	<0.0001§
Iron (mg)	15.4 ± 4.8	13.1 ± 4.2	12.0 ± 3.9	<0.0001§
Zinc (mg)	16.1 ± 7.9	10.9 ± 2.9	5.2 ± 1.8	<0.0001‖
Fibers (g/kg weight)	0.31 ± 0.14	0.33 ± 0.15	0.39 ± 0.17	0.015*

Data are means ± SD. *P* refers to repeated-measures ANOVA. *Student-Newman-Keuls: low-protein diet versus usual and chicken diets (*P* < 0.05); †Student-Newman-Keuls: low-protein diet versus usual and chicken diets (*P* < 0.001); ‡Student-Newman-Keuls: low-protein diet versus usual diet (*P* < 0.05); §Student-Newman-Keuls: usual diet versus chicken and low-protein diets (*P* < 0.01); ‖Student-Newman-Keuls: low-protein diet versus usual and chicken diets; usual diet versus chicken diet (*P* < 0.001).

1. All women were postmenopausal, but none was taking hormone replacement therapy. Most of these patients were treated with calcium channel blockers. One patient in each group was being treated with a combination of thiazide and calcium channel blockers. The oral antidiabetic agents used were sulfonylurea and metformin. Two normoalbuminuric and four microalbuminuric patients were taking metformin.

Characteristics of the diets
The characteristics of the diets followed by the patients, as assessed by the weighed record method, are described in Table 2. The energetic, protein, carbohydrate, total fat, calcium, and fiber intake was the same for patients after either the CD or the UD; however, the intake of saturated fatty acids, phosphorus, iron, and zinc was lower in the CD. Carbohydrate intake was higher in the LPD, but the total intake of energy and fat, and the intake of saturated and monounsaturated fatty acids, cholesterol, phosphorus, iron, and zinc was lower. The calcium intake in the LPD was the same as in the UD.

The total protein intake (grams per kilogram body weight), as assessed by nitrogen output in the UD (1.31 ± 0.3), in the CD (1.35 ± 0.4), and in the LPD (0.62 ± 0.2), was similar (*P* > 0.05) to that estimated by weighed-diet records

(UD 1.43 ± 0.3, CD 1.35 ± 0.3, LPD 0.66 ± 0.2).

Effect of the diets on renal function
Renal function parameters after the diets are shown in Table 3. GFR values in normoalbuminuric patients were lower after the LPD and the CD than after the UD; there was no difference between GFR values after the LPD and the CD. In microalbuminuric patients, the GFR values were lower only after the LPD as compared with the CD and the UD. No difference was observed between UD and CD GFR values.

In normoalbuminuric patients, UAER levels were similar after the diets. However, in microalbuminuric patients, UAER levels were lower after the CD as compared with the levels observed after the UD and the LPD. No difference was observed in UAER levels after the UD and the LPD. The same was observed for fractional clearance of albumin (median × 10⁻⁶, range): CD 7.35 (1.04–42.04), LPD 12.04 (2.72–42.49), UD 13.25 (6.22–44.16); *P* < 0.05.

Effect of the diets on serum lipids
Lipid levels after the diets are shown in Table 3. In normoalbuminuric patients, the diets did not affect the lipid profile. In microalbuminuric patients, apolipoprotein B and total cholesterol were lower

after the LPD and the CD than after the UD. No difference was observed between the CD and the LPD. The reduction in LDL levels after CD and LPD did not reach conventional statistical significance (*P* = 0.097). Triglyceride and HDL levels were not different after the diets.

Effect of the diets on glycemic control, blood pressure levels, and body weight
Glucose control, assessed by fasting plasma glucose and fructosamine, was similar (*P* > 0.05) after the UD (3.22 ± 0.55 mmol/l), CD (3.14 ± 0.49 mmol/l), and LPD (3.24 ± 0.52 mmol/l). Mean blood pressure levels were also comparable (*P* = 0.299) after the UD (96.8 ± 7.6 mmHg), CD (96.9 ± 9.2 mmHg), and LPD (94.9 ± 8.6 mmHg). Body weight did not differ after the UD (70.8 ± 8.9 kg) and CD (70.9 ± 8.9 kg), but there was a small but significant decrease (*P* = 0.025) after the LPD (70.0 ± 9.0 kg).

CONCLUSIONS — In this study, we observed a significant reduction of 36% (95% CI 15.8–56.4) in the UAER levels of patients with type 2 diabetes and microalbuminuria after the CD when compared with their usual diet. It was also observed that both the LPD and the CD reduced total cholesterol, LDL, and apolipoprotein B levels in microalbuminuric

Table 3—*Glomerular filtration rate, urinary albumin excretion rate values, and lipid profile after diets in normoalbuminuric and microalbuminuric patients with type 2 diabetes*

	Usual diet	Chicken diet	Low-protein diet	P
GFR (ml · min^{-1} · 1.73 m^{-2})				
Normoalbuminuric	113.4 ± 31.4	101.3 ± 22.9	93.8 ± 20.5	0.0029*
Microalbuminuric	107.1 ± 20.1	102.8 ± 22.5	93.5 ± 8.5	0.0129†
UAER (µg/min)				
Normoalbuminuric	2.9 (0.48–8.2)	3.8 (0.17–8.6)	3.9 (0.1–14.2)	0.247
Microalbuminuric	63.8 (26.4–193.1)	34.3 (3.03–162.8)	52.3 (13.4–167.7)	0.001‡
Cholesterol (mmol/l)				
Normoalbuminuric	4.56 ± 0.92	4.63 ± 0.74	4.51 ± 0.92	0.76
Microalbuminuric	5.20 ± 1.02	4.56 ± 1.18	4.51 ± 0.69	0.0234*
HDL (mmol/l)				
Normoalbuminuric	1.32 ± 0.28	1.32 ± 0.38	1.25 ± 0.29	0.503
Microalbuminuric	1.18 ± 0.21	1.09 ± 0.37	1.06 ± 0.30	0.265
LDL (mmol/l)				
Normoalbuminuric	2.59 ± 0.82	2.74 ± 0.46	2.53 ± 0.72	0.336
Microalbuminuric	3.27 ± 0.73	2.79 ± 0.60	2.69 ± 0.49	0.0976
Apolipoprotein B (mg/dl)				
Normoalbuminuric	120.2 ± 38.4	104.1 ± 32.2	98.9 ± 29.4	0.0561
Microalbuminuric	134.3 ± 30.7	113.5 ± 36.0	103.7 ± 40.1	0.0129*
Triglycerides (mmol/l)				
Normoalbuminuric	1.30 (0.49–3.63)	1.13 (0.43–3.65)	1.31 (0.32–4.29)	0.247
Microalbuminuric	1.34 (0.59–5.11)	1.17 (0.69–2.48)	1.87 (0.71–3.92)	0.761

Data are means ± SD or median (range). *Repeated-measures ANOVA, Student-Newman-Keuls: usual diet versus low-protein and chicken diets ($P < 0.05$); †repeated-measures ANOVA, Student-Newman-Keuls: low-protein diet versus usual and chicken diets ($P < 0.05$); ‡Friedman's ANOVA, least significance differences: chicken diet versus usual and low-protein diets ($P < 0.05$).

patients and GFR in normoalbuminuric patients. In microalbuminuric patients, only the LPD decreased GFR.

Changes in the amount or source of protein can influence renal function. The reduction of GFR observed in our normoalbuminuric patients after the CD and the LPD confirms our previous observation in patients with type 1 diabetes (13,21). Other authors have also reported reduction of GFR in normoalbuminuric patients with type 1 diabetes after protein restriction (22) or replacement of animal protein with vegetarian protein (23). The mechanism behind this effect is still unknown; it might result from hemodynamic glomerular factors related to reduction of renal plasma flow (24). However, we did not observe a decrease in UAER after the CD and the LPD in our normoalbuminuric patients with type 2 diabetes, as reported by others in patients with type 1 diabetes. This absence of effect could be related to the lower levels of UAER (median ~2.9–3.9 µg/min) in our patients, which could be masquerading an eventual effect of these diets. Furthermore, patients with type 2 diabetes may be less responsive to the effect of conditions that affect renal function.

The reduction of UAER in microalbuminuric patients after the CD is unlikely to have been caused entirely by hemodynamic factors, because the decline in GFR in these patients was not significant. Furthermore, the decrease of UAER after the CD was still observed when albuminuria was corrected by GFR (fractional albumin clearance). The lower levels of total cholesterol and of apolipoprotein B in microalbuminuric patients may contribute to the reduction of UAER after the CD. A reduction in the levels of these lipid components was also observed after the LPD. Such a reduction was probably related to the lower dietary content of saturated fatty acids. The magnitude of this reduction (~18%) is clinically substantial and was only observed in patients with microalbuminuria, probably because of the higher levels of serum cholesterol that are characteristic of this group of patients (5). It is well known that the amount of saturated fatty acids in the diet are predictive of serum cholesterol levels and that replacement of saturated fat with unsaturated fatty acids reduces cholesterol levels (25). In a typical North American diet, replacement of saturated fatty acids with monounsaturated fat (derived from mac-

adamia nuts) has been shown to induce a significant reduction (~5%) of total and LDL cholesterol (26). High levels of serum cholesterol have been considered a risk factor for development of diabetic nephropathy in patients with type 2 diabetes (5), and high ingestion of saturated fat has been associated with the presence of microalbuminuria in patients with type 1 diabetes (27). Nevertheless, the role of reducing cholesterol levels in the progression of microalbuminuria is still controversial. Administration of simvastatin was associated with a reduction of UAER in microalbuminuric patients with type 2 diabetes in one study (6) but not in another (7).

One intriguing aspect of our study was the observation that the LPD reduced GFR and cholesterol levels, but the reduction of UAER did not reach statistical significance. Other authors observed that a moderate protein restriction was associated with a reduction of UAER in patients with type 2 diabetes (10,11). This discrepancy may be explained by the reported improvement in metabolic control (10,11) and blood pressure levels (11) in these studies, or it could be that a longer period of LPD would be necessary to in-

duce a reduction in UAER. The lower effect of the LPD on UAER in comparison to the CD suggests that some component of chicken meat might have a specific beneficial effect on renal function. This hypothesis is supported by a recent study in which patients with type 1 diabetes and high intake of fish fat and protein (white meat) showed a reduction in the risk for microalbuminuria (28).

Although this study was not designed to analyze the effect of individual fatty acids, chicken meat has a lower amount of saturated fat and a higher proportion of polyunsaturated fatty acids than red meat, namely linoleic acid (1.5 vs. 0.21 g/100 g), linolenic acid (0.3 vs. 0.2 g/100 g), and arachidonic acid (0.12 vs. 0.04 g/100 g) (17). Polyunsaturated fatty acids have been shown to have a beneficial effect on endothelial function, and this could reduce UAER (29).

The present study followed a crossover design, and there is a possibility that the effect of one diet carried over into the next diet, thus influencing the results. However, a significant carryover effect is unlikely, because the diets were given in a random order, and the 4-week washout period was enough to wean patients from the previous diet. Plasma lipids and lipoproteins reach a stable level after a period of 3–4 weeks of dietetic modification (30). Outpatient feeding studies may present compliance problems. These difficulties were not remarkable in our study. According to the assessment by weighed-diet records and urea measurements performed during and at the end of each diet period, the diets that were actually consumed by the patients were very similar to those that had been prescribed. We had already observed this compliant behavior in a similar group of patients (16). The interpretation of our results should take into account that the patients included in this study were relatively well controlled and compliant. These patients were selected to avoid the interference of possible changes in blood pressure and metabolic parameters during the study on analyzed variables. Furthermore, the effect of the CD on UAER and lipid levels observed in this short-term study and its acceptability should be confirmed in long-term studies, ideally with assessment of outcomes such as progression to renal failure and cardiovascular mortality.

In conclusion, a diet in which red meat is replaced with chicken might represent an alternative or additional strategy for the treatment of microalbuminuric patients with type 2 diabetes.

References
1. Jager A, Kostense PJ, Nijpels G, Heine RJ, Bouter LM, Stehouwer CDA: Microalbuminuria is strongly associated with NIDDM and hypertension, but not with the insulin resistance syndrome: the Hoorn Study. *Diabetologia* 41:694–700, 1998
2. Mogensen CE: Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. *N Engl J Med* 310: 356–360, 1984
3. Panzram G: Mortality and survival in type II (non-insulin-dependent) diabetes mellitus. *Diabetologia* 30:123–131, 1987
4. Mogensen CE: Microalbuminuria, blood pressure and diabetic renal disease: origin and development ideas. *Diabetologia* 42: 263–285, 1999
5. Ravid M, Brosh D, Ravid-Safran D, Levy Z, Rachmani R: Main risk factors for nephropathy in type 2 diabetes mellitus are plasma cholesterol levels, mean blood pressure, and hyperglycemia. *Arch Intern Med* 158:998–1004, 1998
6. Tonolo G, Ciccarese M, Brizzi M, Puddu L, Secchi G, Calvia P, Atzeni MM, Melis MG, Maioli M: Reduction of albumin excretion rate in normotensive microalbuminuric type 2 diabetic patients during long-term simvastatin treatment. *Diabetes Care* 20:1891–1895, 1997
7. Nielsen S, Schmitz O, Möller N, Pöksen N, Klausen IC, Alberti KGMM, Mogensen CE: Renal function and insulin sensitivity during simvastatin treatment in type II (non-insulin-dependent) diabetic patients with microalbuminuria. *Diabetologia* 36: 1079–1086, 1993
8. Ravid M, Lang R, Rachmani R, Lishner M: Long-term renoprotective effect of angiotensin-converting enzyme inhibition in non-insulin dependent diabetes mellitus: a 7-year follow-up study. *Arch Intern Med* 156:286–289, 1996
9. Morris AD, Boyle DIR, McMahon AD: ACE inhibitor use is associated with hospitalization for severe hypoglycemia in patients with diabetes. *Diabetes Care* 20: 1363–1367, 1997
10. Pomerleau J, Verdy M, Garrel DR, Nadeau MH: Effect of protein intake on glycaemic control and renal function in type II (non-insulin-dependent) diabetes mellitus. *Diabetologia* 36:829–834, 1993
11. Pijls LTJ, de Vries H, Donker AJM, van Eijk JTM: The effect of protein restriction on albuminuria in patients with type 2 diabetes mellitus: a randomized trial. *Nephrol Dial Transplant* 14:1445–1453, 1999
12. Pedrini MT, Levey AS, Lau J, Chalmers TC, Wang PH: The effect of dietary protein restriction on the progression of diabetic and non-diabetic renal disease: a meta-analysis. *Ann Intern Med* 124:627–632, 1996
13. Pecis M, Azevedo MJ, Gross JL: Chicken and fish diet reduces glomerular hyperfiltration in IDDM patients. *Diabetes Care* 17:665–672, 1994
14. Rudberg S, Persson B, Dahlquist G: Increased glomerular filtration rate as a predictor of diabetic nephropathy: an 8-year prospective study. *Kidney Int* 41:822–828, 1992
15. Franz MJ, Horton ES, Bantle JP, Beebe CA, Brunzell JD, Coulston AM, Henry RR, Hoogwerf BJ, Stacpoole PW: Nutrition principles for the management of diabetes and related complications (Technical Review). *Diabetes Care* 17:490–518, 1994
16. Moulin CC, Tiskievicz F, Zelmanovitz T, Oliveira J, Azevedo MJ, Gross JL: Use of weighed diet records in the evaluation of diets with different protein contents in patients with type 2 diabetes. *Am J Clin Nutr* 67:853–857, 1998
17. United States Department of Agriculture, Agriculture Research Service: U.S. Department of Agriculture Nutrient Data Base for Standard Reference. Release 12. Washington, DC: US Department of Agriculture, 1998 (USDA handbook no 8)
18. Cohen D, Dodds R, Viberti GC: Effect of protein restriction in insulin dependent diabetics at risk of nephropathy. *BMJ* 294: 795–798, 1987
19. Maroni BJ, Steinman TI, Mitch WE: A method for estimating nitrogen intake of patients with chronic renal failure. *Kidney Int* 27:58–65, 1985
20. Friedewald WT, Levy RI, Fredrickson DS: Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin Chem* 18:499–502, 1972
21. Azevedo MJ, Padilha LM, Gross JL: Short-term low-protein diet reduces glomerular filtration rate in insulin-dependent diabetes mellitus patients. *Braz J Med Biol Res* 23:647–654, 1990
22. Wiseman MJ, Hunt RE, Dodds R, Keen H,

Viberti GC: Changes in renal function in response to protein restricted diet in type 1 (insulin-dependent) diabetic patients. *Diabetologia* 30:154–159, 1987

23. Kontessis P, Bossinakou I, Sarika L, Iliopoulou E, Papantoniou A, Trevisan R, Roussi D, Stipsanelli K, Grogorakis S, Souvatzoglou A: Renal, metabolic, and hormonal responses to proteins of different origin in normotensive, nonproteinuric type I diabetic patients. *Diabetes Care* 18:1233–1240, 1995

24. Brenner BM, Lawler EV, Mackenzie HS: The hyperfiltration theory: a paradigm shift in nephrology. *Kidney Int* 49:1774–1777, 1996

25. Mensing RP, Katan MB: Effect of dietary fatty acids on serum lipids and lipoproteins: a meta-analysis of 2 trials. *Arterioscler Thromb* 338:12911–12919, 1992

26. Curb JD, Wergowske G, Dobbs JC, Abbott RD, Huang B: Serum lipid effects of a high-monounsaturated fat diet based on macadamia nuts. *Arch Intern Med* 160: 1154–1158, 2000

27. Riley M, Dwyer T: Microalbuminuria is positively associated with usual dietary saturated fat intake and negatively associated with usual dietary protein intake in people with insulin-dependent diabetes mellitus. *Am J Clin Nutr* 67:50–57, 1998

28. Möllsten AV, Dahlquist GG, Stattin EL, Rudberg S: Higher intakes of fish protein are related to a lower risk of microalbuminuria in young Swedish type 1 diabetic patients. *Diabetes Care* 24:805–810, 2001

29. De Caterina R, Liao JK, Libby P: Fatty acid modulation of endothelial activation. *Am J Clin Nutr* 70 (Suppl.):213S–223S, 2000

30. Kris-Etherton P, Dietschy J: Design criteria for studies examining individual fatty acid effects on cardiovascular disease risk factors: human and animal studies. *Am J Clin Nutr* 65 (Suppl.):1590S–1596S, 1997