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The Role of Dietary Proteins among Persons with Diabetes

Jeannette M. Beasley, PhD, MPH, RD and Judith Wylie-Rosett, EdD

Albert Einstein College of Medicine, Bronx, NY

Abstract

Examining the role of dietary protein and establishing intake guidelines among individuals with diabetes is complex. The 2013 American Diabetes Association (ADA) standards of care recommend an individualized approach to decision making with regard to protein intake and dietary macronutrient composition. Needs may vary based on cardiometabolic risk factors and renal function. Among individuals with impaired renal function, the ADA recommends reducing protein intake to 0.8–1.0 g/kg per day in earlier stages of chronic kidney disease (CKD) and to 0.8 g/kg per day in the later stages of CKD. Epidemiological studies suggest animal protein may increase risk of diabetes; however, few data are available to suggest how protein sources influence diabetes complications.

Keywords

diabetes; dietary protein; amino acids

I. Introduction

Current protein recommendations are very wide (10–35% of kilocalories) and were set by the difference after accounting for carbohydrate and fat needs¹. The median protein intake in the United States is approximately 15% of kilocalories, varying little by age and gender². This is well below the upper limit set by the Institute of Medicine of 35% of kilocalories from protein, but exceeds the Recommended Dietary Allowance of 0.8 g/kg protein (i.e. 1.0 g/kg for a 70 kg person consuming 2,000 kilocalories per day).

Protein is the major functional and structural component of all the cells of the body. The chemical composition and physical structure of dietary and body proteins varies considerably. However, all proteins are comprised of amino acid chains which contain a requisite amino (or imino) nitrogen group. Amino acids function as precursors of many coenzymes, hormones, and nucleic acids in addition to the role of the diverse protein structures in the body. Because amino acids also contain carbon, oxygen, and hydrogen, their remnants can enter the tricarboxylic acid cycle to be used for energy after deamination.

Examining the role of dietary protein and establishing intake guidelines among individuals with diabetes is complex. The 2013 American Diabetes Association (ADA) standards of care recommend an individualized approach to decision making with regard to protein

Corresponding Author: Jeannette Beasley, PhD, MPH, RD, 1300 Morris Park Avenue Suite 1312c, Bronx, NY 10461, Jeannette.beasley@einstein.yu.edu, Phone: (718) 430-3089.

Conflict of Interest

Jeannette M. Beasley declares that she has no conflict of interest.

Judith Wylie-Rosett declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

intake and dietary macronutrient composition.³ Factors to be considered include the metabolic status of the patient (e.g., lipid profile, renal function) and/or food preferences.

II. Role of Proteins in Achieving Metabolic Goals

IIa. Quantity of Protein

Recently, a systematic review⁴ and meta-analysis⁵ have summarized the evidence regarding the range of dietary protein intake appropriate for individuals with diabetes. Wheeler and colleagues concluded that a diet higher in protein (defined as 30% of calories) may or may not improve A1C but appears to improve one or more cardiovascular risk factors⁴. Likewise, based upon a combination of two studies, Ajala et al reported a significant decrease in the percentage of HbA1c in participants who consumed high-protein diets (weighted mean difference: -0.28% (95% CI: -0.38%, -0.18%; $P < 0.00001$, $I^2 = 60\%$).

While high protein intake does not necessarily lead to weight loss, in some cases, higher protein intake may influence diabetes risk through weight loss. For individuals with type 2 diabetes (T2D), studies have demonstrated that moderate weight loss (5% of body weight) is associated with decreased insulin resistance, improved measures of glycemia and lipemia, and reduced blood pressure.³ A meta-analysis including 38 studies for weight change (2,326 participants), 16 for BMI (887 participants) and 15 for waist circumference (1,214 participants) summarized the standardized effect sizes for changes in weight loss as (-0.36, 95% CI = -0.56 to -0.17), BMI (-0.37, 95% CI -0.56 to -0.19) and waist circumference (-0.43, 95% CI = -0.69 to -0.16), representing statistically significant small to moderate effects.⁶ Clifton summarized that high protein diets increase the loss of fat relative to lean mass but suggested that saturated fat intake be minimized to consider effects on lipid levels.⁷

Of note, however, are the emerging reports from cohort studies suggesting higher protein intake is associated with an increased risk of T2D (Table 1). In particular, two prospective studies (WHI and MALMO) including thousands of T2D incident cases over 8–12 years of follow-up both reported ~20% increased risk of T2D among those with higher versus lower protein intake in their respective populations.

IIb. Amino Acids and Qualitative Aspects of Protein

The ADA provides no guidance regarding optimal type of protein intake or amino acid composition of the diet. As reported in a recent meta-analysis by Feskens and colleagues⁸, studies on meat consumption and complications among people with diabetes are scarce: no studies on meat consumption and microvascular diabetes complications were identified. However, per 100 g of total meat, the pooled relative risk (RR) for incident diabetes was 1.15 (95 % CI=1.07–1.24), for (unprocessed) red meat, 1.13 (95 % CI=1.03–1.23), and for poultry 1.04 (95 % CI = 0.99–1.33); per 50 g of processed meat, the pooled RR is 1.32 (95 % CI=1.19–1.48). Furthermore, emerging data suggest the branched chain amino acids leucine, isoleucine, and valine are positively associated with insulin resistance, as measured by HOMA and HbA1C (Table 1). These data, primarily from metabolomics research, suggest there is much that can be learned about the pathways by which amino acid intake may influence both diabetes risk and sequelae.

III. Role of Proteins in Achieving Treatment Goals for Renal and Other Complications of Diabetes

IIIa. Complications of Diabetes that may alter dietary protein needs

The ADA estimates that diabetic nephropathy occurs in 20–40% of patients with diabetes, making it the leading cause of renal failure.³ Diabetic kidney disease (DKD), which is defined as chronic kidney disease (CKD) that is presumed to be caused by diabetes, has increased dramatically with the global increases in obesity and diabetes.⁹ CKD is diagnosed clinically on the basis of persistent abnormal urine albumin excretion (defined as at least two abnormal specimens within a 3- to 6-month period) and decreased estimated glomerular filtration rate (eGFR). Historically, an albumin:creatinine ratio of 30–300 mg/d was classified as microalbuminuria, and macroalbuminuria was defined as a urine albumin:creatinine ratio >300 mg/d. eGFR is estimated using the Chronic Kidney Disease Epidemiology Collaboration formula.⁹

The stages of CKD on the basis of GFR are:

Stage 1 - Kidney damage with normal GFR ≥ 90 mL/min/1.73 m²

Stage 2 - Kidney damage with mild decreased GFR 60–89 mL/min/1.73 m²

Stage 3 - Moderately decreased GFR 30–59 mL/min/1.73 m²

Stage 4 - Severely decreased GFR 15–29 mL/min/1.73 m²

Stage 5 - Kidney failure <15 mL/min/1.73 m² or dialysis

Renal biopsy may be used to identify early kidney damage as estimated GFR alone can only accurately identify CKD stages 3 or higher. Although transient microalbuminuria may be unrelated to kidney function, the presence of persistent macroalbuminuria is associated with the deterioration of renal function. Advances in the medical management of DKD have slowed the deterioration in renal function, and it is important to recognize that the evidence base regarding the role of dietary protein intake is largely older research that has had mixed findings.^{3,4,10}

IIIb. Quantity of Protein

The goal of recommendations regarding restriction of protein intake is to improve measures of renal function (urine albumin excretion rate, eGFR). The ADA recommendations include reducing protein intake to 0.8–1.0 g/kg per day in patients with diabetes and earlier stages of CKD and to 0.8 g/kg per day in the later stages of CKD. The ADA recommendations are general with regard to CKD stages without specification of the cut point for greater restriction. Referral to renal specialists is recommended for care of kidney disease, uncertainty about the etiology of kidney disease, difficult management issues, or advanced kidney disease. However, the extent to which referrals are needed with respect to restricting protein intake is not indicated. The 2013 National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines update on diabetes and CKD focused on new research related to HbA1c targets, treatments to lower low-density lipoprotein cholesterol (LDL-C) levels, and use of angiotensin-converting enzyme inhibitor (ACE-I) and angiotensin receptor blocker (ARB) and endorsed its KDOQI 2007 guidelines with respect to the role of nutrition in DKD.^{10,11} The guidelines refer to the RDA for dietary protein intake. However, tailoring is also suggested with regard to the CKD and diabetes status. For CKD stages 1 and 2, a protein intake of 0.8 g/kg or 10% of energy intake is recommended for patients with diabetes whereas up to 1.4 g/kg or 18% of energy intake is recommended in the absence of diabetes. For CKD stages 3–4, a protein intake of 0.6–0.8 g/kg or ~8–10% of energy intake irrespective of diabetes status.

Trend data from the National Health and Nutrition Examination Survey (NHANES) indicate that the protein intake of individuals with diabetes is similar to that of the general population, which is ~ 18–20% of energy intake.¹² A 2012 American Diabetes Association systematic review concluded that in the absence of diabetic kidney disease, higher protein eating patterns (30% of calories) may or may not improve HbA1c but may improve CVD risk measures such as triglyceride and HDL cholesterol.⁴ For individuals with diabetic kidney disease in the presence of either micro- or macroalbuminuria, reducing the amount of protein from normal levels does not appear to alter glycemic measures, CVD risk measures, or the course of renal deterioration.¹³

A 2007 Cochrane review of twelve studies (randomized controlled trials (RCT) = 9 and pre-post design studies = 3), which addressed protein restriction in DKD, pooled results using random-effects models.¹⁰ The level of protein restriction achieved in the intervention groups varied considerably, ranging from 0.7 to 1.1 g/kg/day. With respect to type 1 diabetes, pooling of the seven RCTs resulted in a non-significant reduction in the decline of eGFR of 0.1 ml/min/month (95% CI = -0.1 to 0.3) for the protein restriction intervention. The Cochrane review included no pooling of results for type 2 diabetes, due to differences in study design and participant characteristics. Trend results of the Cochrane review suggest that reducing protein intake may achieve a slight slowing of the progression to renal failure, but the trend was not statistically significant. Noted research challenges included difficulty in achieving the protein restriction intervention goals and the lack of longer-term studies conducted in large representative groups of patients for both type 1 and type 2 diabetes. Although the 2007 Cochrane review called for more research to address the role of protein restriction in DKD, research advances have addressed the potential clinical benefits of lowering HbA1c, LDL cholesterol and blood pressure.¹⁰

Reviewing findings from intervention trials of dietary protein restriction and renal function can help guide future research in this area. A four-year RCT by Hansen et al (Table 2) found that restricting dietary protein intake (0.89 g/kg/d for low protein treatment arm versus 1.02 g/kg/d for the usual diet treatment arm) reduced the risk of CKD stage 5 or death by 77% in patients who had type 1 diabetes and CKD stage 2.¹⁴ However, both treatment arms had a similar decline in mean eGFR when all CKD stages were evaluated. Studies by Meloni et al (Table 2)^{15,16} have yielded mixed results. In the 2002 one-year trial by Meloni *et al*¹⁵ diabetic patients randomized to the severe dietary protein restriction (0.6 g/kg/d) had a decrease in serum prealbumin, which raised questions about the risk of malnutrition. However, the study treatment arms did not differ with respect to decline in renal function. In the 2004 one-year trial by Meloni *et al* randomizing both non-diabetic and diabetic groups to 0.6 g/kg/d protein or control, there were no differences in prealbumin between groups, but renal function decline was slower in the intervention group among individuals without diabetes.^{15,16}

Metabolic byproducts of protein are excreted by the kidney, which increases the rate of glomerular filtration when protein intake is high. Presumably high-protein diets can increase albuminuria and may thereby accelerate loss of kidney function in the presence of kidney damage. Hyperfiltration and increased intraglomerular pressure are suggested mechanisms through which further damage to the kidney may occur. Having diabetes may exacerbate the effects of high protein intake on kidney hemodynamics. The American Diabetes Association recommends monitoring renal function in patients, who are on low-carbohydrate diets that may be higher in dietary protein.³ However, a concomitant increase in the proportion of energy from protein would occur with restriction of carbohydrate without an increase in the absolute quantity of protein (number of gram of protein consumed) if total energy intake decreases. In addition, the ADA recommends adding monitoring of protein intake in patients who are on restricted carbohydrate diets and have nephropathy. The National Kidney

Foundation cautions that people with diabetes and CKD should avoid high-protein diets (20% of total daily calories).^{11,17,18} The rationale for the cautionary note is research associating higher protein intake (20%) with loss of kidney function in women with mild renal insufficiency (defined as estimated GFR < 80 and > 55 mL/min/1.73 m²).¹⁹

IIIC. Amino Acids and Qualitative Aspects of Protein

The National Kidney Foundation recommends “50% to 75% of the protein should be of high biological value, derived predominantly from lean poultry, fish, and soy- and vegetable-based proteins.”¹¹ Clinical observations have led to the soy-protein hypothesis that “substitution of soy protein for animal protein results in less hyperfiltration and glomerular hypertension...”²⁰ Proposed beneficial components of soy protein include specific peptides, amino acids, and isoflavones. Several small studies have reported improvement in cardiorenal biomarkers when soy protein is substituted for animal protein in patients with DKD, but the hypothesis has not been conclusively proven.^{21,22,23}

Conclusions

The evidence base to guide recommendations for dietary protein intake in relation to the prevention and management of diabetes is mixed. Higher protein intake may reduce risk of developing diabetes and improve metabolic control only when weight loss is achieved. However, an isocaloric high protein diet and higher branched-chain amino acid intake may increase insulin resistance, which could adversely affect metabolic parameters. The 2013 American Diabetes Association (ADA) standards of care recommendations include using an individualized approach in diabetes medical nutrition therapy with regard to protein intake and dietary macronutrient composition. Factors to consider in tailoring advice include cardiometabolic risk status and renal function. The ADA has recommended reducing protein intake to 0.8–1.0 g/kg per day in earlier stages of CKD and to 0.8 g/kg per day in the later stages of CKD. These recommendations for protein intake are similar to those of the National Kidney Foundation.

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•• Of major importance

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Table 1**Observational Studies Evaluating Protein and risk of T2D**

Author and Year	Study/Design	Study Population	Findings
Batch 2012 ^{24***}	Cross-sectional	MURDOCK: 3 cohorts (1872 men and women (410 lean, 610 overweight, 852 obese)	“BCAA” factor (phe, leu/ile, val, tyr, met, ala, his) distinguished metabolically well from unwell individuals with a high degree of statistical significance, particularly in obese individuals
Ericson 2013 ²⁵	MALMO	1709 diabetes cases among 27,140 over 12 years of follow-up	Higher protein intake was associated with increased risk of T2D (HR 1.27 for highest compared with lowest quintile; 95 % CI 1.08, 1.49; P for trend = 0.01).
Feskens 2013 ⁸	Meta-analysis of 14 cohort studies		Per 100 g of total meat, the pooled RR for incident T2D was 1.15 (95 % CI 1.07–1.24), for (unprocessed) red meat 1.13 (95 % CI 1.03–1.23), and for poultry 1.04 (95 % CI 0.99–1.33); per 50 g of processed meat, the pooled RR was 1.32 (95 % CI 1.19–1.48)
Huffman 2009 ²⁶	Cross-sectional	STRIDE, n=73 (mean age 51, BMI 25–35)	“BCAA” factor (phe, leu/ile, val, tyr, met, pro, tyrosine, uric acid, histidine) inversely associated with insulin sensitivity ($r^2=0.26$)
Linn 2000 ²⁷	Comparison of habitual high protein (HP)(1.9 ± 0.3 g/kg/day) vs. low protein(LP) 0.7 ± 0.08 g/kg/day)	26* men and women (mean age 30 and BMI 23) Insulin secretion, Glucose output, gluconeogenesis	HP insulin secretion (516 ± 45 vs. 305 ± 32 pmol/l, p=0.01), reduced glucose disposal (1.21 ± 0.1 vs. 1.69 ± 0.2, p=0.04, stimulated gluconeogenesis by 40%
Newgard 2009 ²⁸	Cross-sectional	73 obese and 67 lean men and women (median age 52 and BMI 36.6)	Through PCA, identified BCAA-related metabolite (leucine, isoleucine, valine, methionine, glutamate/ glutamine, phenylalanine, tyrosine) and HOMA were correlated ($r=0.58$, $p<0.0001$) (partial Spearman $r=0.36$, $p=0.002$ after adjusting for obesity)
Papakonstantinou 2005	ATTICA	N=210 participants with diabetes and N=2,832 participants without diabetes	Protein intake was not associated with blood glucose, insulin, or insulin sensitivity, irrespective of diabetes status.
Shah 2012 ^{29***}	Prospective	WLM random sample (n=500); validation cohort of gastric bypass patients	“BCAA” factor (phe, leu/ile, val, tyr, met, ala, pro, glx, orn) significantly correlated with HOMA-IR and improvement in HOMA-IR among overweight/obese independently of weight loss in both cohorts; only weakly correlated with dietary intake ($r=0.14$, $p=0.003$)
Sluijs 2010 ³⁰	EPIC	918 cases among 38,094 participants over a 10-y follow-up of European men and women	Higher total (and animal) protein was associated with 2.2 times the risk of T2D (95% CI 1.8–2.6)
Tai 2010 ³¹	Cross-sectional	Non-obese Asian-Indian and Chinese men, n=263	“BCAA” factor (phe, leu/ile, tyr, met, pro, glutamate/ glutamine, alanine) positively associated with HOMA
Tinker 2011 ³²	WHI	3,319 cases among 74,155 over an 8-y follow-up of postmenopausal women	A 20% increase in biomarker-calibrated protein intake was associated with a 19% (95% CI 7–32%) increased risk of diabetes
Wang 2010 ³³	MASALA	146 South Asian Indians; cross-sectional	70% increase in the odds of diabetes per standard deviation in gram of protein intake/day (OR 1.70 [95% CI 1.08, 2.68]).
Ware 2011 ³⁴	Nested case control ; 12 years of follow-up	Framingham Offspring Study (n=189 T2D, 189 controls); MALMO diet and cancer replication cohort (n=163 cases, 163 controls)	Baseline amino acid concentrations; adjusted OR and 95%CI Q4 vs. Q1) isoleucine (3.0, 1.2–7.4), leucine (4.1, 1.5–11.3), valine (2.9, 1.1–7.7), tyrosine(2.9,1.0–8.3), and phenylalanine (2.1, 0.8–5.8) predicted diabetes

Abbreviations: MURDOCK=Measurement to Understand the Reclassification of Disease in Cabarrus/Kannapolis; BCAA=Branched Chain Amino Acid; T2D=type 2 diabetes, HR=hazard ratio; RR=relative risk; STRIDE= Studies of Targeted Risk Reduction Interventions through Defined Exercise; BMI=Body Mass Index; EPIC=European Prospective Investigation in Cancer; WHI=Women’s Health Initiative; WLM=Weight Loss Maintenance

Table 2
Intervention studies of high vs. control protein diets among individuals with T2D

Author and Year	Study Design and Duration	Participants N	Intervention Arms	Outcome Variables	Findings
Brinkworth 2004 ^{35,36}	RCT; 12 mo	Obese adults 66 (38 completers)	30% prot; 40% CHO; 30% fat vs. 15% prot; 55% CHO; 30% fat	Weight, lipids, HbA1c, FPG	NS
Gannon 2003 ^{37,38}	Crossover study 5 wks with 2-5 wk washout between periods	Adults with T2D N=12	30% prot, 40% kcal CHO, 30% kcal vs. 15% prot, 55% CHO 30% fat (food provision)	HbA1c, lipids	HbA1c decrease from $8.1 \pm 0.3\%$ $\rightarrow$ $7.3 \pm 0.2\%$ for hi pro ($P < 0.05$), NS for control. Triglycerides were lower after 5 wks of hi pro diet as compared to control (161 ± 23 mg/dL vs. 199 ± 20 mg/dL), $P = 0.03$
Hansen 2002 ¹⁴	RCT; 4 yr	Adults with T1D with diabetic nephropathy (N=82)	Low protein (0.6 g/kg/day) (LPD) versus usual protein intake (Control)	Renal function; mortality	Decline in renal function similar between groups, but LPD had lower ESRD or death (RR=0.23; 95% CI 0.07 to 0.72)
Krebs 2002 ³⁹	Crossover trial of AA	7 healthy men (mean age 27 yr and BMI 23)	Aminoplasma 0.94 g/kg body weight vs. saline infusion	Glucose turnover rate; intracellular glycogen, G6P; plasma metabolites	A 2.1-fold elevation of plasma AAs reduced whole-body glucose disposal by 25% ($P < 0.01$). Rates of muscle glycogen synthesis decreased by 64% ($P < 0.01$), which was accompanied by a reduction in G6P starting at 130 min $P < 0.05$).
Krebs 2012 ⁴⁰	RCT 12 mo intervention/12 maintenance	Overweight adults (BMI > 27) 419 (294 completers)	30% prot; 40% CHO; 30% fat vs. 15% prot; 55% CHO; 30% fat	Weight, waist circumference, fat mass, glycemia, lipid profile, blood pressure, renal function	NS
Larsen 2011 ⁴¹	RCT 12 mo	Overweight/obese adults 108 (99 completers)	26.5% prot vs. 19% protein	Weight, lipids, HbA1c	NS
Meloni 2002 ^{15,16}	RCT; 1 yr	Adults with T1D (N=32) and T2D (N=37) with diabetic nephropathy and hypertension	Low protein (0.6 g/kg/day) (LPD) versus usual protein intake (Control)	Renal function, nutritional status	Decline in renal function similar between groups, but prealbumin and albumin was lower in the LPD vs. control at the end of the intervention.
Meloni 2004 ^{15,16}	RCT; 1 yr	Adults with hypertension and: chronic renal failure (N=89), diabetic nephropathy (N=24 with T1D and 56 with T2D)	Diabetic and non-diabetic patients randomly divided into 2 groups: Low protein (0.8 g/kg/day) (LPD) versus usual protein intake (Control)	Renal function, nutritional status	Decline in renal function similar between diabetic groups, but LPD nondiabetic group had a lower decrease in renal function compared with control; prealbumin and albumin were stable and didn't differ by treatment group
Parker 2002 ⁴²	RCT; 8 wk energy restriction + 4 wk energy balance	54 obese adults	28% prot, 42% CHO, 28% fat (HP) vs. 16% prot, 55% CHO, 26% fat (NP)	Weight loss, fat mass, HbA1c, lipids	LDL reduction was significantly greater on the HP (5.7%) vs. NP (2.7%) diet ($P < 0.01$). Both diets lost similar amounts of weight; in women only, those on HP lost more total (5.3 vs. 2.8 kg, $P = 0.0009$) and abdominal (1.3 vs. 0.7 kg, $P = 0.006$) fat compared with NP diet.
Pijls 2002 ⁴³	RCT; duration of intervention and	131 patients with type 2 diabetes and	Protein restriction to 0.8 g/kg/day (n=63) vs. control (n=68)	eGFR	Protein intake differed only by 0.08 g/kg/day between study groups

Author and Year	Study Design and Duration	Participants N	Intervention Arms	Outcome Variables	Findings
Sargrad 2005	follow-up was 28 ± 7 months RCT; 8 wk	microalbuminuria or at least detectable albuminuria, or a diabetes duration >5 years 12 obese adults	27% prot, 51% CHO, 30% fat (HP) vs. 15% prot, 45% CHO, 30% fat	Weight, blood pressure, insulin sensitivity, HbA1c	In the high-carbohydrate group, HbA1c decreased (from 8.2% to 6.9%, P=0.03), FPG decreased (from 8.8 to 7.2 mmol/L, P<0.02), and insulin sensitivity increased (from 12.8 to 17.2 µmol/kg/min, P<0.03). No significant changes in these parameters occurred in the high-protein group, instead systolic and diastolic blood pressures decreased (10.5±2.3 mm Hg, P=0.003 and 18±9.0 mm Hg, P<0.05, respectively).
Solerte 2004 ⁴⁴⁻⁴⁶	Crossover study; 16 wk periods with 2 week washout	34 older adults (age range 65–85, BMI 18–23)	8g EAA vs. placebo	Fasting and postprandial glucose; HOMA-IR	EAA decreased fasting insulin, fasting and postprandial glucose, HbA1c and HOMA as well as HDL-cholesterol
Teixeira 2004 ⁴⁷	Crossover trial, 2 mo with 1 mo lead-in and 1 mo washout period	14 males with diabetic nephropathy	0.5 g/kg isolated soy protein vs. 0.5 g/kg casein	Urinary albumin excretion, lipids	Consumption of 0.5 g/(kg · d) of ISP instead of casein reduced urinary albumin excretion 9.5% in type 2 diabetic patients.
Wycherley 2010 ⁴⁸	RCT 2×2 factorial 4 mo	Overweight/obese sedentary men and women 83 (59 completers)	33% prot*; 43% CHO; 22% fat +/- resistance training 3× per week vs. 19% prot; 53% CHO; 26% fat +/- resistance training 3× per week (NP +RT)	Weight, fat mass, waist circumference, blood pressure, lipids, HbA1c	HP+RT had 3.3 kg greater weight and fat loss and 21% greater reduction in waist circumference. There were no between group differences in blood pressure, lipids, or HbA1c.

RCT=Randomized, Controlled Trial; Prot=protein; CHO=carbohydrate; HbA1c=hemoglobin A1c; FPG=fasting plasma glucose; wk=weeks; T2D=type 2 diabetes; HR=hazard ratio; RR=relative risk; STRIDE= Studies of Targeted Risk Reduction Interventions through Defined Exercise; BMI=Body Mass Index; EPIC= European Prospective Investigation in Cancer; WHI=Women's Health Initiative; WLM=Weight Loss Maintenance; EAA=essential amino acids