Title: Effects of pork vs. chicken/fish in a DASH diet on blood pressure regulation in older adults with hypertension – **NPB #11-154** Final

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Industry Summary

Hypertension, or high blood pressure, is the most commonly treated condition in primary care settings and is a major and modifiable risk factor of cardiovascular and kidney diseases [1]. The most recent evidence suggests that nearly one-third of American adults have high blood pressure and the condition is especially prevalent in older adults, with 65% of those older than 60 years being affected [2]. Lifestyle modifications such as the adoption of the Dietary Approaches to Stop Hypertension (DASH) diet have been proven effective for decreasing blood pressure in adults with high blood pressure [3, 4]. The DASH emphasizes increased consumption of fruits/vegetables, whole-grains, lowfat dairy, nuts, and poultry/fish and reduced intakes of sodium, sugar, and red meats (including pork). However, the effects of incorporating pork into the DASH diet pattern have not been previously studied. We therefore designed a DASH diet intervention study to test whether including a large amount of pork in the DASH diet had an effect on the expected improvements in blood pressure in older adults with high blood pressure. Nineteen study participants (13 women and 6 men) completed the 18-week study. On average, participants were older (61 years), obese (BMI 31.2 kg/m^2), and had elevated blood pressure (130/85 mm Hg). During weeks 1-2, participants were counseled to continue following their normal eating pattern and baseline measurements of blood pressure, body composition (weight, % body fat, and waist circumference), fasting blood glucose, insulin, and lipid concentrations, and food intake were collected. Participants were then randomly assigned to consume the DASH diet with either pork (DASH-P) or chicken/fish (DASH-CF) as the major protein source for 6 weeks (weeks 3-8). Measurements of blood pressure, body composition, and fasting blood samples were repeated during weeks 7-8 to evaluate changes in these study outcomes. Participants were counseled to return to their normal pattern for a "wash-out" period (weeks 9-12) and then consumed the alternate protein source during weeks 13-18. Measurements of blood pressure, body composition, and fasting blood samples were repeated again during weeks 11-12 and 17-18. Systolic and diastolic blood pressure were assessed manually (seated and laying down) and with a 24hr blood pressure monitoring system. After DASH-CF, manual systolic and diastolic blood pressure both decreased 6 mmHg, and 24hr systolic blood pressure decreased 8 mm Hg and diastolic blood pressure decreased 5 mm Hg. After DASH-P, manual systolic blood pressure decreased 8 mm Hg and diastolic blood pressure decreased 5 mm Hg, and 24hr systolic blood pressure decreased 7mmHg and diastolic blood pressure decreased 3 mm Hg. Our

statistical analyses confirmed that changes in blood pressure were significant and were not different for DASH-P vs. DASH-CF. These results indicate that substitution of lean pork for chicken and fish as the major source of protein does not influence the effectiveness of a DASH diet to improve blood pressure control in older adults with high blood pressure. For additional information contact Wayne W. Campbell, PhD, Professor, Department of Nutrition Science, Purdue University, 765-494-8236, campbeww@purdue.edu.

Key Words: DASH diet; hypertension; older adults; protein source; pork; chicken; fish

Scientific Abstract

Hypertension is a major, modifiable risk factor for cardiovascular and kidney disease and mortality that is improved by the Dietary Approaches to Stop Hypertension (DASH) diet. The DASH diet emphasizes increased consumption of fruits/vegetables, whole-grains, lowfat dairy, and poultry/fish and reduced intakes of sodium and red meats (including pork). In a randomized crossover study, 13 women and 6 men, aged 61±2 y (mean±SEM), BMI 31.2±1.4 kg/m^2, with high blood pressure (BP) consumed the DASH diet for 2, 6-wk periods (with a 4-wk diet washout) with either chicken/fish (DASH-CF, control diet) or lean pork (DASH-P) as the major protein source (55% of protein intake). Systolic (S) and diastolic (D) BP were assessed manually (seated and supine) and with a 24h BP monitoring system on 3 days prior to and at the end of each diet period. After DASH-CF, manual SBP and DBP decreased 6±2 and 6±1 mm Hg, respectively, and 24h SBP and DBP decreased 8±2 and 5±1 mm Hg. After DASH-P, manual SBP and DBP decreased 8±2 and 5±1 mm Hg, and 24h SBP and DBP decreased 7±2 and 3±1 mm Hg. All changes in BP were statistically confirmed at $p<0.05$ and were not different for DASH-P vs. DASH-CF ($p>0.05$). These results indicate that substitution of lean pork for chicken and fish as the predominant source of protein does not influence the effectiveness of a DASH diet to improve blood pressure control in older adults with hypertension.

Introduction from Original Proposal

Hypertension is a major risk factor for mortality and is a global public health issue affecting 50 million people in the United States and one billion people world-wide [5]. Despite progress in the detection, evaluation, and treatment of hypertension, most of the adult population is classified as pre-hypertensive or hypertensive, resulting in an increased risk of cardiovascular disease [6]. In fact, by 2025 the number of adults with hypertension is expected to increase to about 60% of the world's population totaling 1.5 billion people. Nutrition is an important environmental determinant of blood pressure and changes in dietary patterns may be an effective line of defense against this formidable disease [6-8]. Dietary protein intake is considered an important factor in BP control. Among more than 25 cross-sectional or population studies, about two-thirds reported higher protein intake was associated with lower BP (i.e. an inverse relationship existed [8].

The proposal is submitted in response to the NPB solicitation for research to address the question, **"**What is the effect of including lean pork products in place of poultry and fish in a DASH (Dietary Approaches to Stop Hypertension) diet to control blood pressure?" The DASH diet is a well-documented diet plan to effectively improve BP regulation in hypertensive adults [9, 10].

Objectives from Original Proposal

To examine the impact of protein source (pork vs. chicken/fish), as part of a DASH diet on blood pressure control in older adults with hypertension.

<u>Hypothesis:</u> Consumption of pork vs. chicken/fish as the primary source of protein for 6 weeks will not influence the expected reduction in blood pressure due to consumption of a DASH diet.

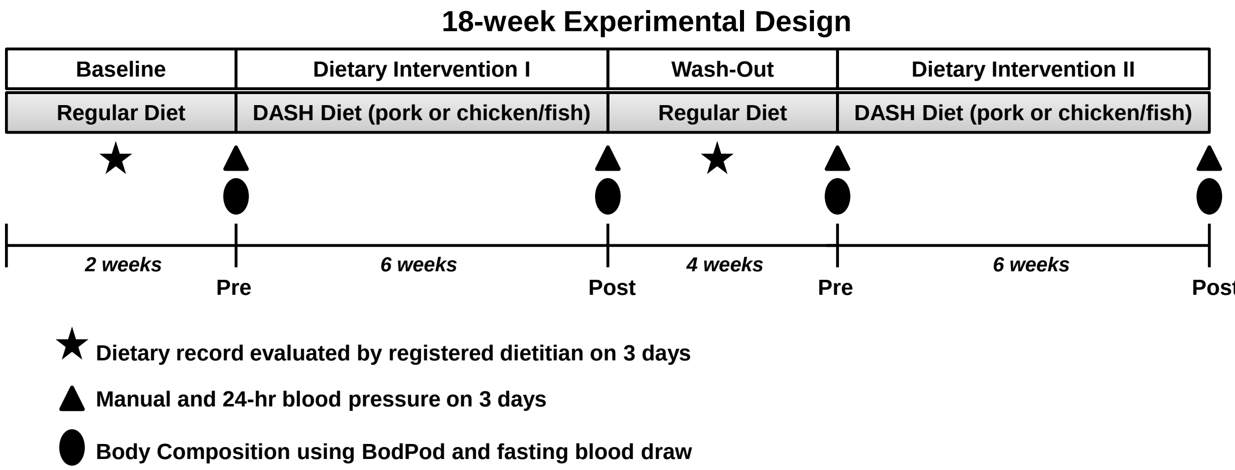
Objectives from 2014 Extension

To examine the impact of a protein source (pork vs. chicken/fish), as part of a DASH diet on inflammatory status.

Hypothesis: Consumption of a DASH-style diet will improve markers of systemic inflammation (TNFα, IL-6, MCP-1, IGF-1, and adiponectin) and protein source will not influence these results.

Materials & Methods

Experimental Design: Participants completed two 6-week periods of dietary control, separated by a 4-week wash-out period. In random order, each participant consumed the DASH diet with a majority of protein from pork or chicken/fish. Testing was performed before and during the final 2 weeks of both dietary intervention periods. Two weeks prior to the start of the first 6-week intervention and for 4 weeks between trials, participants consumed their normal diet, which was evaluated for energy and nutrient contents by a registered dietitian using a three-day dietary records and Nutrition Data System for Research software (Nutrition Coordinating Center, University of Minnesota). The design of the 18-wk protocol is divided into 4 phases as shown in the schematic.



Subjects and Recruitment: Twenty-nine individuals (20 women and 9 men) were recruited from the greater Lafayette, IN, community for participation in the study. Nineteen participants (13 women and 6 men) completed all study procedures. The initial inclusion criteria included: male or female; age ≥ 60-75 y, body mass index: 30-40 kg/m^2, systolic BP between 130 and 160 mm Hg and diastolic BP <100 mm Hg; no acute illness; not diabetic; not currently (or within the past 3 months) following a vigorous exercise regimen or weight loss program; willingness to eat study foods; ability to travel to testing facility; and urinary continence. Due to difficulty in meeting recruitment goals, inclusion criteria for age, BMI, and blood pressure were changed (with the approval of the NPB) to 21-75 y, no specific BMI criteria, and systolic blood pressure ≥ 120 mm Hg or diastolic blood pressure ≥ 80 mm Hg. The original study protocol and all revisions were approved by the Purdue University Biomedical Institutional Review Board.

Diet Intervention: Participants consumed a DASH diet during the two controlled feeding periods with a macronutrient distribution of ~55% carbohydrate, 27% fat, and 18% protein, as previously described [9, 10]. Sodium intake was controlled at 2500 mg/day, which corresponds to the "Intermediate Sodium Level" as described by Sacks et al. [4] and Svetkey et al. [10]. Participants were randomly assigned to consume either pork (DASH-P) or chicken/fish (DASH-CF) as the primary protein source during Dietary Intervention 1, and the opposite primary protein source during Dietary Intervention 2. During each intervention, 55% of total protein intake was derived from either pork or chicken/fish. The remaining 45% of dietary protein was obtained through dairy, vegetable, and other animal (beef) sources. No chicken or fish was consumed during DASH-P and no pork was consumed during DASH-CF. The dietary controls were accomplished using dietary counseling to follow a prescribed menu (7-day cycle) of specific foods and beverages to achieve the desired energy, macronutrient, and micronutrient intakes. All meat products were provided to participants and included fresh pork tenderloin and uncured ham trimmed of visible fat during DASH-P and boneless, skinless chicken breast and tilapia fillets during DASH-CF. Two servings of beef tenderloin were provided per week during both DASH interventions. Other items including some snacks and condiments were also provided to control sodium intake. The remaining items on the menu were purchased by the participant at a local grocery store using a detailed, brand-specific shopping list provided by the research dietitian. The 6-week DASH diet interventions (DASH-P and DASH-CF) were designed to meet 100% of the participants' estimated daily energy requirement based on the Institute of Medicine energy requirement equations for overweight and obese adults [11]. All menus were developed using Pronutra software (Viocare, Inc. Princeton, NJ). All diet-related activities and assessments were performed in conjunction with the Indiana Clinical Research Center Bionutrition Facility at Purdue University. As a measure of dietary adherence, 24hr urine volumes (weight divided by specific gravity [Digital Probe Refractometer, Misco Products Division, Cleveland, OH]) were obtained from three 24hr urine collections and aliquots were stored at -20°C for subsequent analyses of urea nitrogen (COBAS Integra 400; Roche Diagnostic Systems, Indianapolis, IN). Blood urea nitrogen (BUN) was assessed using the COBAS Integra 400 analyzer [Roche Diagnostic Systems, Indianapolis, IN]. Both methods were utilized during the study as crude markers of protein intake before and after each phase of the intervention.

Body Weight and Composition: Body weight and composition (% body fat and fat-free mass) were determined using the BOD POD Gold Standard Body Composition Tracking System (COSMED USA, Inc., Concord, CA). Waist circumference was measured at the level of the umbilicus in triplicate by the same research staff.

Blood Pressure Assessment: Blood pressure was assessed manually (HEM-780, Omron Healthcare, Inc., Lake Forest, IL) and using a 24-hour ambulatory blood pressure monitoring system (Oscar2, SunTech Medical Inc., Morrisville, NC) on 3 separate days before and during the final 2 weeks of each DASH diet intervention period. Automated blood pressure measurements were programmed at 30-minute intervals during the day (8am – 9pm) and at 90-minute intervals during the night (9pm – 8am). 24-hour blood pressure measurements were considered to be valid if ≥80% of scheduled measurements were obtained without error. If the error rate exceeded 20%, participants were asked to wear the monitor for an additional 24 hours. Manual blood pressure was measured in seated and supine positions in the morning after 15 min of rest. Two manual blood pressure measurements were obtained in each position and a third reading was obtained if the blood pressure values differed by ≥3 mm Hg.

Blood Collections: Fasting state blood samples were collected on 1 day before and during the last week of each dietary intervention. Blood samples were collected into serum-separator tubes and centrifuged for 15 minutes at 4400rpm and 4ºC to obtain serum. Serum samples were stored at -80ºC until analysis. Fasting glucose, total cholesterol (Total-C), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), triglycerides (TG), and blood urea nitrogen (BUN) were analyzed by enzymatic colorimetry using an oxidase method on a COBAS Integra 400 analyzer (Roche Diagnostic Systems, Indianapolis, IN). Fasting serum insulin was analyzed by electrochemiluminescence immunoassay method on the Elecsys 2010 analyzer (Roche Diagnostic Systems). Tumor necrosis factor-alpha (TNFα), interleukin-6 (IL-6), monocycte chemoattactant protein-1 (MCP-1), insulin-like growth factor (IGF-1), and adiponectin concentrations were analyzed using ELISA kits (Cayman Chemical: TNFα and IL-6; Sigma-Aldrich: MCP-1, IGF-1, and adiponectin).

Statistical Analysis: All statistical analyses were completed using SAS Version 9.2 and data are presented as mean ± SEM. Analyses were completed using data from the 19 subjects that completed all study procedures. Doubly repeated measures ANOVA (MIXED Procedure) was used to assess main effects of time (Pre vs Post intervention), diet (DASH-P vs DASH-CF), gender, and intervention order (first vs second intervention period) as well as interactions on changes in BP, indices of the metabolic syndrome, markers of inflammatory status, and diet composition. A Tukey-Kramer adjustment for multiple comparisons was used as necessary for post hoc analyses.

Results

Subject Characteristics: Baseline subject characteristics are presented in Table 1. Nineteen participants (13 female/6 male) completed all study procedures. On average, participants were 61 ± 2 years and obese (BMI 31.2 ± 1.4 kg/m^2). The average manual systolic BP obtained at baseline in the seated position was 130 mm Hg and the average diastolic BP was 85 mm Hg. Average values for serum glucose, insulin, Total-C, LDL-C, HDL-C, TG, and BUN were within the normal reference range (Table 1).

Diet Analysis: Analysis of 3-day diet records completed during Baseline and Wash-Out periods and menu checklists completed during the last 2 weeks of DASH-P and DASH-CF indicate that total energy consumed did not differ between study phases (Table 2). Compared to baseline and wash-out, participants reported greater consumption of carbohydrate, protein, fiber, calcium, potassium and magnesium and decreased total fat and sodium consumption during DASH-P and DASH-CF interventions (Table 2). No differences in energy, macronutrient distribution, and micronutrient consumption were detected between Baseline and Wash-Out periods, indicating that participants returned to their usual eating patterns during the Wash-Out period. Similarly, energy, macronutrient distribution, and micronutrient consumption during DASH-P and DASH-CF were not different (Table 2).

Body Composition: Body mass and composition were determined before and during the last week of each diet intervention. Significant changes in body composition were observed despite a prescription for weight maintenance and no reported differences in daily energy intake (Table 3). Body mass decreased by approximately 2 kg and % body fat decreased approximately 1.5% during DASH-P and DASH-CF. Changes in body mass and % body fat were not different between DASH-P and DASH-CF (p = 0.86 and p = 0.33, respectively). A significant decrease in waist circumference was also observed during DASH-CF, but not DASH-P. However, the change in waist circumference was not different between DASH-CF and DASH-P (-1.3 ± 0.3 cm vs. -1.5 ± 0.6 cm, p = 0.87).

Blood Pressure: Manual and 24-hr blood pressure were measured on 3 days prior to (Baseline and Wash-Out) and during the last 2 weeks of the DASH-P and DASH-CF. Significant reductions in manual and 24-hr SBP and DBP were observed following both DASH-P and DASH-CF diet interventions (Figure 1 and Figure 2). Seated manual SBP decreased 8 ± 2 mm Hg and DBP decreased 5 ± 1 mm Hg after DASH-P. Seated manual SBP decreased 6 ± 2 mm Hg and DBP decreased 6 ± 1 mm Hg after DASH-CF. Supine manual SBP decreased 8 ± 2 mm Hg and DBP decreased 5 ± 1 mm Hg after DASH-P. Supine manual SBP decreased 6 ± 2 mm Hg and DBP decreased 6 ± 1 mm Hg after DASH-CF. Changes in SBP and DBP were not different between DASH-P and DASH-CF (Figure 1). Total 24-hr SBP and DBP decreased 7 ± 2 mm Hg and 3 ± 1 mm Hg after DASH-P and 8 ± 2 mm Hg and 5 ± 1 mm Hg after DASH-CF. The 24-hr blood pressure assessment period was further analyzed during the day (8am to 9pm) and the night (9pm to 8am). Daytime SBP and DBP decreased 7 ± 2 mm Hg and 3 ± 1 mm Hg following DASH-P and 7 ± 2 mm Hg and 4 ± 1 mm Hg following DASH-CF. Nighttime SBP and DBP decreased 7 ± 2 mm Hg and 3 ± 2 mm Hg after DASH-P and 9 ± 2 mm Hg and 5 ± 1 mm Hg after DASH-CF. The decrease in nighttime DBP of 3 ± 2 mm Hg following DASH-P was not significant. However, changes in total, daytime, and nighttime SBP and DBP were not different between DASH-P and DASH-CF (Figure 2).

Blood and Urine Collections: Fasting state blood samples were collected on 1 day prior to (Baseline and Wash-Out) and during the last week of DASH-P and DASH-CF. Twenty-four hour urine samples were collected on 3 days prior to (Baseline and Wash-Out) and during the last 2 weeks of the DASH-P and DASH-CF. Significant reductions in Total-C, LDL-C, and HDL-C of 27 ± 6 mg/dL, 18 ± 5 mg/dL, and 6 ± 1 mg/dL, respectively were observed following DASH-P. Significant reductions in Total-C (13 ± 6 mg/dL) and HDL-C (3 ± 1 mg/dL) and a significant increase in UUN (1259 ± 525 mg/day) were observed following DASH-CF (Table 4). No significant changes in fasting glucose, insulin, TG, or BUN were observed after DASH-P or DASH-CF. Changes in UUN during DASH-P and LDL-C after DASH-CF were also non-significant. However, no changes in fasting serum parameters or 24-hr UUN were significantly different between DASH-P and DASH-CF (Figure 4). Consumption of the DASH-style diet did not influence IL-6, MCP-1, IGF-1 or adiponectin concentrations (data not shown). However, TNFα increased during DASH-P and DASH-CF in men (Pre-DASH: 2.00 ± 1.25 pg/mL, Post-DASH: 4.36 ± 1.13, $P < 0.05$), but not women (Pre-DASH: 3.74 ± 0.34 pg/mL, Post-DASH: 4.24 ± 0.40 pg/mL). Changes in TNFα were not influenced by intervention order or protein source.

Discussion

The primary outcome of this randomized cross-over diet intervention was to evaluate whether the predominant protein source (pork vs. chicken/fish) in a DASH diet would affect changes in blood pressure in older adults. Significant reductions in both manual and 24-hr SBP and DBP were observed following both DASH-P and DASH-CF that were not different between the diet interventions. These data support our hypothesis that protein source would not influence the expected reduction in blood pressure due to consumption of a DASH diet.

The 19 participants that completed all study procedures were, on average, older (61 ± 2 years) and would be classified as stage I obese (31.2 ± 1.4 $kg/^2$) and pre-hypertensive (BP: 130/85) according to the 7th report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [12]. As indicated by the fasting serum parameters at baseline (Table 1), these participants were otherwise apparently healthy. As expected, we observed significant alterations in reported intakes of macronutrients and micronutrients but not total energy between Baseline/Wash-Out periods and the DASH interventions. Three-day diet records suggest that participants consumed greater amounts of carbohydrate, protein, fiber, potassium, magnesium, and calcium while decreasing total fat and sodium intake during the DASH interventions with no differences between DASH-P and DASH-CF. Increased intakes of fiber, potassium, and magnesium are consistent with increased consumption of fruits, vegetables, and whole grains while increased calcium intake suggests higher dairy consumption as is recommended in the DASH diet pattern. Observed decreases in sodium and total fat during DASH-P and DASH-CF are also consistent with sodium restriction and low-fat guidelines of the DASH diet pattern. Despite a prescription for energy balance and no reported differences in total energy intake, study participants lost approximately 2kg during DASH-P and DASH-CF, with no difference between the diet interventions. Given the well-established problems with underreporting of energy intake by food records [13], it is possible that participants were consuming more than reported during the Baseline and Wash-Out periods. We will continue to investigate these data as we make final preparations for the manuscript.

The addition of the analysis of systemic inflammatory markers was included as part of a project extension in 2014. With the exception of TNFα, consumption of a DASH-style diet did not influence inflammatory status. Contrary to our hypothesis, we found that TNFα concentrations increased after the DASH-style diet intervention in men, but this effect was not seen in women. This effect was not influenced by the predominant protein source in the diet (pork vs chicken/fish). It is important to emphasize that this study was powered to detect changes in blood pressure and therefore results on secondary outcomes should be considered as exploratory and interpreted with caution.

Tables and Figures

Table 1: Participant characteristics at baseline (n = 19).

Parameter	Mean ± SEM
Age (y)	61 ± 2
# Female/Male	13/6
Body Mass (kg)	87.2 ± 3.6
BMI (kg/m^2)	31.2 ± 1.4
Waist Circumference (cm)	104.1 ± 3.9
% Body Fat	41.7 ± 2.1
Systolic Blood Pressure (mm Hg)[1]	130 ± 2
Diastolic Blood Pressure (mm Hg)[1]	85 ± 2
Glucose (mg/dL)	93 ± 2
Insulin (µU/mL)	12.61 ± 2.10
Total Cholesterol (mg/dL)	199 ± 9
LDL-Cholesterol (mg/dL)	120 ± 8
HDL-Cholesterol (mg/dL)	54 ± 2
Triglycerides (mg/dL)	121 ± 11
Blood Urea Nitrogen (mg/dL)	15 ± 1
Urinary Urea Nitrogen (mg/day)	10,428 ± 677

[1] Manual blood pressure measured in the seated position at baseline.

Table 2: Average daily dietary intake using dietary records on 3 days during each study phase.

	Baseline	DASH-P	Wash-Out	DASH-CF
Energy (kcal)	2160 ± 148^{A}	2309 ± 112^{A}	2149 ± 142^{A}	2372 ± 85^{A}
Carbohydrate (g)	246 ± 22^{B}	347 ± 16^{A}	259 ± 24^{B}	350 ± 15^{A}
Protein (g)	82 ± 6^{B}	102 ± 4^{A}	81 ± 5^{B}	108 ± 3^{A}
Fat (g)	92 ± 7^{A}	67 ± 4^{B}	86 ± 6^{A,B}	71 ± 3^{B}
Fiber (g)	22 ± 3^{C}	41 ± 2^{A}	23 ± 3^{B,C}	35 ± 2^{A,B}
Sodium (mg)	3229 ± 254^{A}	2527 ± 102^{B}	3380 ± 258^{A}	2518 ± 100^{B}
Calcium (mg)	946 ± 95^{B}	1638 ± 125 ^{A}	980 ± 87^{B}	1739 ± 77^{A}
Potassium (mg)	2934 ± 335^{B}	4967 ± 226^{A}	3040 ± 323^{B}	4848 ± 180^{A}
Magnesium (mg)	324 ± 33^{B}	499 ± 23^{A}	336 ± 30^{B}	473 ± 100^{A}

Values with different superscript letters are significantly different (p<0.05).

Table 3: Changes in body composition during DASH-P and DASH-CF

	DASH-P	DASH-CF	p-value[1]
∆ Body Mass (kg)	-2.3 ± 0.3*	-2.3 ± 0.3*	0.86
∆ % Body Fat	-1.3 ± 0.4*	-1.8 ± 0.4*	0.33
∆ Waist Circumference (cm)	-1.3 ± 0.6	-1.5 ± 0.6*	0.87

[1] Difference between diet interventions (DASH-P vs. DASH-CF).

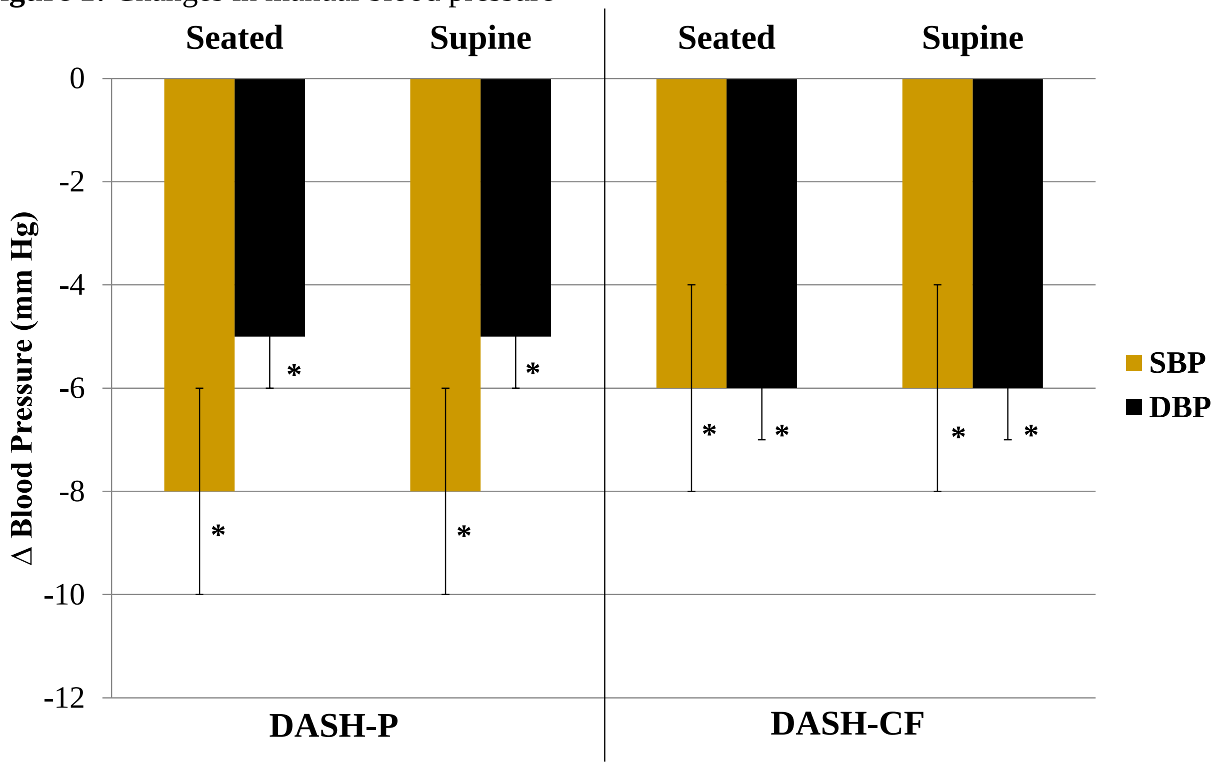
* Indicates significant change from pre to post diet intervention (p < 0.05).

Table 4: Changes in fasting serum and 24-hr urine parameters

	DASH-P	DASH-CF	p-value[1]
Glucose (mg/dL)	-1 ± 2	+2 ± 2	0.22
Insulin (µU/mL)	-1.62 ± 2.25	-3.72 ± 2.25	0.50
Total Cholesterol (mg/dL)	-27 ± 6*	-13 ± 6*	0.09
LDL-Cholesterol (mg/dL)	-18 ± 5*	-8 ± 5	0.12
HDL-Cholesterol (mg/dL)	-6 ± 1*	-3 ± 1*	0.10
Triglycerides (mg/dL)	-9 ± 8	-10 ± 8	0.97
Blood Urea Nitrogen (mg/dL)	+1 ± 1	0 ± 1	0.11
Urinary Urea Nitrogen (mg/day)	+741 ± 525	+1259 ± 525*	0.43

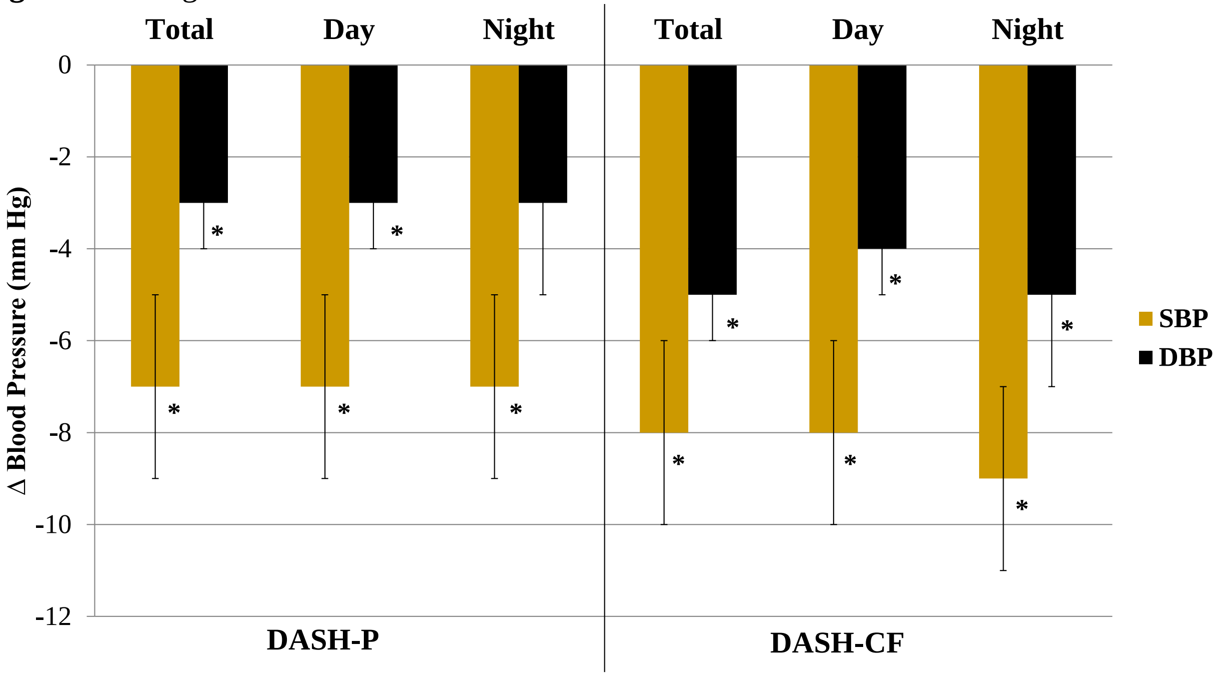
[1] Difference between diet interventions (DASH-P vs. DASH-CF).
* Indicates significant change from pre to post diet intervention (p < 0.05).

Figure 1: Changes in manual blood pressure



* Indicates significant change from pre to post diet intervention (p < 0.05).

Figure 2: Changes in 24-hr Blood Pressure



* Indicates significant change from pre to post diet intervention ($p < 0.05$).

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