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Effect of soy nuts and equol status on blood pressure, lipids and inflammation in postmenopausal women stratified by metabolic syndrome status☆

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ABSTRACT

Objective. Soy has been associated with lower risk of cardiovascular disease in Asian countries which consume daily soy. Our study examined whether production of equol, an estrogen metabolite, affected the ability of soy nuts to improve cardiovascular risk factors.

Materials/Methods. Sixty postmenopausal women participated in a randomized, controlled, crossover trial of a Therapeutic Lifestyle Changes (TLC) diet alone and a TLC diet in which 0.5 cup of soy nuts (25 g of soy protein and 101 mg of aglycone isoflavones) replaced 25 g of nonsoy protein daily. Each diet was followed for 8 weeks at the end of which blood pressure (BP), lipid levels, adhesion molecules and inflammatory markers were measured.

Results. Women with MetS had significantly higher baseline body mass index (BMI), BP, triglycerides (TG), and soluble intercellular adhesion molecule (sICAM) than women without MetS. In women with MetS on the soy diet, significant reductions in diastolic BP (7.7%; $P = 0.02$), TG (22.9%; $P = 0.02$), C-reactive protein (CRP) (21.4%; $P = 0.01$) and sICAM (7.3%; $P = 0.03$) were noted among equol producers compared to levels on the TLC diet. No significant changes were noted in equol nonproducers. Similarly, in women without MetS, only equol producers had significant reductions in diastolic BP (3.3%, $P = 0.02$) and CRP (30%, $P = 0.04$). In contrast to women with MetS, TG and sICAM levels were not affected in women without MetS, a finding possibly related to lower baseline levels.

Conclusions. Cardiovascular risk reduction with soy nuts is not uniform and may be greater among producers of equol.

Abbreviations: CVD, cardiovascular disease; CHD, coronary heart disease; MetS, metabolic syndrome; TLC, therapeutic lifestyle changes; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Total-C, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; IL-6, interleukin-6; MMP-9, matrix metalloproteinase 9; apoB, apolipoprotein B-100; sVCAM-1, vascular cell adhesion molecule-1; sICAM-1, soluble intercellular adhesion molecule-1; CRP, C-reactive protein.

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1. Introduction

Coronary heart disease (CHD) is the leading cause of death among women aged 60 years and older. The incidence rises in postmenopausal women presumably due to loss of estrogen, which has vascular protective effects [1,2]. Hormone replacement therapy has been associated with increased risk of cardiovascular disease (CVD), cancer and dementia [3]; therefore, alternative vasoactive agents have been studied for their potential to decrease cardiovascular morbidity and mortality. Daily soy food intake has been associated with a reduction in CHD risk factors in Chinese women [4,5] and was inversely proportional to serum cholesterol level in Japanese adults [6]. Higher intake of dietary soy has been associated with lower cardiovascular mortality in Japanese women [7].

The metabolic syndrome (MetS) is comprised of a cluster of closely related risk factors, including visceral adiposity, insulin resistance, hypertension and dyslipidemia that increase cardiovascular risk [8]. The risk of CHD attributed to MetS is more than twice in women compared to men and more than half of all cardiovascular events in women are related to MetS [9]. Postmenopausal status is independently associated with a 60% additional risk of MetS after adjusting for age, body mass index (BMI), lifestyle-related factors and socioeconomic status [10]. This may be at least partly due to decline in circulating estrogen levels, which may increase cardiovascular risk through effects on adiposity, blood pressure (BP), lipid metabolism and prothrombotic state [11,12].The prevalence of MetS in postmenopausal women aged 50–59 years is around 35% and increases to around 45% for women aged ≥60 [13].

We previously reported that substituting a whole soy food (soy nuts) for nonsoy protein in a therapeutic lifestyle changes (TLC) diet lowered systolic and diastolic BP in hypertensive, prehypertensive and normotensive women [14] and that the beneficial effect may be mediated via an effect on inflammation [15]. Since our original study design, the potential role of equol, an estrogen metabolite which can be formed from the soy isoflavone daidzein, in mediating beneficial effects of soy has become apparent [16]. Equol might be predicted to lower cardiovascular risk via potent inhibition of inflammation and oxidation [17]. Therefore, we performed a post-hoc analysis of our data stratified by equol production and metabolic syndrome status to test the hypothesis that equol production status affects the ability of soy nuts to lower BP and improve lipid levels and inflammatory markers in postmenopausal women.

2. Material and methods

2.1. Subjects

Sixty healthy postmenopausal women (absence of menses for at least 12 months or irregular periods and hot flashes) without atherosclerosis or diabetes participated in this study. These are the same women in our prior report in which inclusion and exclusion criteria were described [14]. The institutional review board of the Beth Israel Deaconess Medical Center approved the protocol, and all participants gave informed consent.

2.2. Study design

This was a randomized controlled crossover trial of the effect of one-half cup of soy nuts daily for 8 weeks on cardiovascular risk factors in postmenopausal women with and without MetS. A registered dietitian instructed the participants to consume a TLC diet, which consisted of 30% of energy from total fat (≤7% saturated fat, 12% monounsaturated fat, and 11% polyunsaturated fat), 15% from protein and 55% from carbohydrate; less than 200 mg of cholesterol per day [18]; and 1200 mg of calcium and 2 fatty fish meals per week. Those ingesting suboptimal dietary calcium were given calcium carbonate supplementation.

After a 4-week diet run-in, participants adherent to the TLC diet (from review of two 3-day food records) were randomized in a crossover design between 2 diet sequences for 8-week periods: the TLC diet without soy or the TLC diet with prepackaged daily allowances of one-half cup of unsalted soy nuts (Genisoy, Fairfield, CA) containing 25 g of soy protein and 101 mg of aglycone isoflavones divided into 3 or 4 portions spaced throughout the day. Detailed nutritional composition of one-half cup of soy nuts has been previously published [14]. We chose a whole soy food, dry-roasted soybeans, which were administered 3 times daily to mimic Asians who consume whole soy food or fermented soy products high in aglycone isoflavones at several times throughout the day.

After a 4-week washout on the TLC diet alone, participants crossed over to the other arm for an additional 8 weeks. Participants were individually advised from which sources to decrease their protein intake to compensate for the 25 g of soy protein in the soy diet arm to keep protein amounts similar on both diet arms. At the end of each 8-week period, fasting blood was collected for measurement of lipid levels, and participants collected a 24-h urine sample for measurement of isoflavone and creatinine levels. Dietary assessment (from 3-day food records) and exercise assessment was as previously described [14].

2.3. MetS criteria and blood pressure measurements

The assessment of MetS was based on the presence of three of its five components according to a modified version of the Adult Treatment Panel III guidelines [18] for women: 1. BMI ≥ 28.8 kg/m^2; 2. triglyceride levels of 150 mg/dL or greater; 3. High-density lipoprotein cholesterol (HDL-C) level less than 50 mg/dL; 4. BP of 130/85 mm Hg or higher; and 5. abnormal glucose metabolism as identified by a fasting blood glucose level of 100 mg/dL or higher. Because waist circumference was not available at baseline, a cutpoint for obesity of BMI (calculated as the ratio of body mass expressed in kilograms to the square of height expressed in meters) of 28.8 kg/m^2 or higher was used as a surrogate. A similar modification has been previously used [19]. BP measurements were performed with cycling dynamaps (GE Medical Systems Information Technologies, Inc, Milwaukee, WI) at the end of each diet period as previously described [14,20,21].

2.4. Laboratory measurements

Fasting blood samples and 24-h urines were obtained at screening and at the end of each diet period. Lipids, glucose, apolipoprotein B-100 (apoB), serum soluble vascular cell