



## Effects of non-fat dairy products added to the routine diet on vascular function: A randomized controlled crossover trial

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### KEYWORDS

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**Abstract** *Background and aims:* High consumption of low- and non-fat dairy products is associated with reduced risk of high blood pressure (BP) and central arterial stiffness. However, interventional studies to determine if the addition of non-fat dairy products to the diet is capable of reducing central BP and improving vascular function are lacking. The aim of this study was to determine if the solitary addition of non-fat dairy products to the normal routine diet would reduce central BP and improve vascular function in middle-aged and older adults with elevated BP.

*Methods and results:* Using a randomized, crossover intervention study design, forty-nine adults (44% men,  $53 \pm 2$  years,  $170 \pm 2$  cm,  $88 \pm 3$  kg; mean  $\pm$  SEM) with elevated BP ( $134 \pm 1/81 \pm 1$  mm Hg) underwent a High Dairy condition (+4 servings/day of conventional non-fat dairy products) and No Dairy condition (+4 servings/day fruit products) in which all dairy products were removed. Both dietary conditions lasted 4 weeks with a 2-week washout before crossing over into the alternate condition. The High Dairy condition produced reductions in central systolic BP ( $-3 \pm 1$  mm Hg) and carotid-femoral pulse wave velocity ( $-0.5 \pm 0.1$  m/sec), with a concomitant increase in brachial flow-mediated dilation ( $+1.1 \pm 0.4\%$ ) and cardiovagal baroreflex sensitivity ( $+5 \pm 1$  ms/mm Hg) ( $P < 0.05$  for all vs. baseline). In the No Dairy condition, brachial flow-mediated dilation was reduced ( $-1.0 \pm 0.1\%$ ,  $P < 0.05$  vs. baseline).

*Conclusions:* The solitary manipulation of conventional dairy products in the normal routine diet modulates levels of central BP and vascular function in middle-aged and older adults with elevated BP.

*Clinical trial registration:* [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: [NCT01577030](https://clinicaltrials.gov/ct2/show/study/NCT01577030).

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### Introduction

This rise in arterial blood pressure (BP), particularly systolic BP, with age is a major contributor to age-associated increases in risk of cardiovascular disease (CVD) [1]. The physiological mechanisms by which BP increases with age

are not known. However, structural and functional alterations of the walls of large arteries, including arterial stiffening, have been implicated [2]. Increases in arterial stiffness are associated with reductions in arterial endothelial function and baroreflex sensitivity (BRS), an important short-term mechanism for regulating arterial BP [3–5], further contributing to elevated CVD risk.

To reduce CVD incidence, it is of paramount importance to identify treatments that can lower BP and improve vascular function. In most individuals at risk of CVD, the initial treatment approach is the adoption of healthy

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lifestyle modifications [6]. Indeed, lifestyle changes such as regular exercise and salt restriction have reported reductions in systolic BP and improvements in vascular function in middle-aged and older adults [7,8]. We and others have reported that the consumption of a diet high in low- and non-fat dairy products are associated with the reductions in BP [9–12]. Information concerning the physiological mechanisms by which dairy consumption lowers arterial BP is extremely limited [13,14]. It is plausible to hypothesize that improved vascular function in general and de-stiffening of large arteries in particular may play an important role in producing the hypotensive effects of dairy products [7,8]. Currently, it is not known if the addition of conventional non-fat dairy products to the routine diet is capable of improving vascular function and whether such improvements are associated with reductions in BP, particularly central BP [15].

Accordingly, the primary aims of the present study were to determine if the solitary addition of conventional non-fat dairy products to the routine diet would reduce central BP and improve vascular function in middle-aged and older adults with elevated BP. We hypothesized that the addition of non-fat dairy products would reduce central BP and be accompanied by improvements in vascular function. To maximally differentiate the dietary dairy intake, all dairy products were removed from the routine diet in the control condition.

## Methods

### Study population

All subject had seated brachial systolic BP 120–159 mm Hg with a diastolic BP < 100 mm Hg. Detailed description of subjects and inclusion criteria have been described previously [12]. Five subjects were taking antihypertensive medications, and dosages and routines were maintained throughout the study. All subjects underwent a 2-week “run-in period” that included 3 screening visits to ensure that all subjects demonstrated stable BP within the appropriate range. The University of Texas at Austin Institutional Review Board reviewed and approved the study. All volunteers gave their written informed consent before participation.

### Experimental design

This study is part of a randomized trial with two 4-week dietary conditions and a washout period of 2 weeks (Fig. 1), reported in detail previously [12]. Briefly, the two dietary conditions were: High Dairy condition, in which subjects added four daily servings of non-fat dairy products in addition to their baseline dietary dairy intake and No Dairy condition, in which all dairy products were removed from the diet and four daily servings of fruit products were added. Each dietary condition had its own baseline and endpoint. All measurements were taken at the same time of day and after having abstained from food, alcohol, caffeine, and exercise for at least 12 h. In

premenopausal women, measurements were performed during the early follicular phase of the menstrual cycle.

### Central arterial stiffness and BP

After 10 min of supine rest, brachial and ankle BP, carotid and femoral pressure waveforms, and heart rate were simultaneously measured by an automated vascular testing device (Colin VP-2000, Omron Healthcare, Kyoto, Japan) [16]. Carotid-femoral pulse wave velocity (cfPWV) was calculated as travel distance divided by the transit time, as described previously [17]. Analog output of carotid pressure waveforms was recorded (WinDaq 2000, Dataq Instruments, Akron, OH) for determination of central systolic BP and PP, as described previously [18]. Day-to-day coefficients of variation are  $3.2 \pm 0.2\%$  for cfPWV in our laboratory [19].

### Cardiovagal BRS

After 10 min in the seated upright position, cardiovagal BRS was determined using the Valsalva maneuver [18] by having subjects forcibly exhale against a closed airway, while R–R interval and beat-by-beat BP (Pilot 9200, Colin Medical Instruments, San Antonio, TX) were measured continuously. Data were analyzed during the phase IV overshoot (WinDaq 2000, Dataq Instruments, Akron, OH) [4,20]. The coefficient of variation for repeated assessment of cardiovagal BRS was  $10 \pm 2\%$  [20].

### Flow-mediated dilation (FMD)

Brachial artery FMD was assessed after 10 min of supine rest using a Doppler ultrasound machine equipped with a high-resolution linear array transducer (Philips iE33 Ultrasound System, Bothel, WA) positioned 5–10 cm proximal to the antecubital fossa [21]. After baseline arterial diameter determination, a pneumatic cuff positioned 3–5 cm distal to the antecubital fossa was inflated to >100 mm Hg systolic BP for 5 min (E20 Rapid Cuff Inflator, D.E. Hokanson, Bellevue, WA). To capture peak diameter, brachial artery diameter was monitored until 3 min past cuff deflation. Ultrasound-derived diameter data were analyzed using automated image analysis software (Brachial Analyzer, Coralville, IA).

### Dietary analyses

Subjects were given detailed instructions on how to keep weekly 3-day dietary records (i.e., two weekdays and one weekend day) by the research bionutritionist, described previously [12]. Study compliance during each dietary condition was assessed by having each subject complete daily dietary surveys that indicated consumption of the food products provided and any dairy products consumed in their normal diet.

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