

2012

Relations between dairy food intake and arterial stiffness: Pulse wave velocity and pulse pressure

Georgina E. Crichton
University of South Australia

Merrill F. Elias
University of Maine, mfelias@maine.edu

Gregory A. Dore
University of Maine

Walter P. Abhayaratna

Michael A. Robbins
University of Maine, michael.robbins@umit.maine.edu

Follow this and additional works at: http://digitalcommons.library.umaine.edu/longitudinal_papers

Repository Citation

Crichton, Georgina E.; Elias, Merrill F.; Dore, Gregory A.; Abhayaratna, Walter P.; and Robbins, Michael A., "Relations between dairy food intake and arterial stiffness: Pulse wave velocity and pulse pressure" (2012). *Maine-Syracuse Longitudinal Papers*. 67.
http://digitalcommons.library.umaine.edu/longitudinal_papers/67



Published in final edited form as:

Hypertension. 2012 May ; 59(5): 1044–1051. doi:10.1161/HYPERTENSIONAHA.111.190017.

RELATIONS BETWEEN DAIRY FOOD INTAKE AND ARTERIAL STIFFNESS: PULSE WAVE VELOCITY AND PULSE PRESSURE

Georgina E. Crichton^{a,*}, Merrill F. Elias^{b,c}, Gregory A. Dore^b, Walter P. Abhayaratna^d, and Michael A. Robbins^{b,c}

^aNutritional Physiology Research Centre, University of South Australia, Adelaide, Australia

^bDepartment of Psychology, University of Maine, Orono, Maine, USA

^cGraduate School of Biomedical Sciences, University of Maine, Orono, Maine, USA

^dCollege of Medicine, Biology and Environment, Australian National University, Canberra, Australia

Abstract

Modifiable risk factors, such as diet, are becoming increasingly important in the management of cardiovascular disease, one of the greatest major causes of death and disease burden. Few studies have examined the role of diet as a possible means of reducing arterial stiffness, as measured by pulse wave velocity, an independent predictor of cardiovascular events and all-cause mortality. The aim of this study was to investigate whether dairy food intake is associated with measures of arterial stiffness including carotid-femoral pulse wave velocity and pulse pressure. A cross-sectional analysis of a subset of the Maine Syracuse Longitudinal Study sample was performed. A linear decrease in pulse wave velocity was observed across increasing intakes of dairy food consumption (ranging from never/rarely to daily dairy food intake). The negative linear relationship between pulse wave velocity and intake of dairy food was independent of demographic variables, other cardiovascular disease risk factors and nutrition variables. The pattern of results was very similar for pulse pressure, while no association between dairy food intake and lipid levels was found. Further intervention studies are needed to ascertain whether dairy food intake may be an appropriate dietary intervention for the attenuation of age-related arterial stiffening and reduction of cardiovascular disease risk.

Keywords

pulse wave velocity; arterial stiffness; blood pressure; dairy food

Introduction

Cardiovascular disease (CVD) is one of the leading causes of death and disease burden in Europe, the United States, and Australia. As populations age, the risk, prevalence and cost of CVD is likely to increase further. Positive modifiable risk factors for CVD, including diet, will become increasingly important to alter the course of this disease.

*Corresponding author: Georgina Crichton, Nutritional Physiology Research Centre, University of South Australia, GPO Box 2471, Adelaide, South Australia 5001, AUSTRALIA, whige003@mymail.unisa.edu.au, Phone: +61-8-83021452, Fax: +61-8-83022178.

Disclosures

None.

Dairy foods and milk products have received a negative reaction in the media in the recent past, largely due to the association between saturated fatty acids (SFA) and CVD risk, and the high SFA content in dairy foods. However, a number of recent reviews of milk and dairy consumption and CVD have concluded that dairy foods are not associated with a higher risk of CVD, and indeed may offer some benefit. The Dietary Approaches to Stop Hypertension study (DASH), was one of the first studies to show that a diet high in low-fat dairy can have beneficial effects on blood pressure (BP)¹. Following the DASH diet, high in fruit, vegetables, and low-fat dairy products (approximately three serves per day), for six months was associated with greater reduction in systolic BP (SBP) and diastolic BP (DBP) than either a control diet or a weight-reducing diet, among men and women. These reductions were in the range of 11 to 12 mmHg for SBP and 6 to 7 mmHg for DBP¹. Although the individual contributions of low-fat dairy on BP could not be determined from this combination diet, the DASH researchers attributed the beneficial BP effect to the high intake of dairy-rich calcium and potassium in the DASH diet. Evidence with respect to consumption of milk and dairy products in relation to BP reduction has been summarized in a recent review of the literature². Based on results from 11 cross-sectional and eight prospective studies, it was concluded that increased dairy food consumption is associated with lower SBP and lower risk for hypertension, particularly for low-fat dairy food. A recent intervention study has also demonstrated a reduction in SBP following an intake of three serves of low-fat dairy products per day for two months³.

Traditionally, BP is measured by assessing the pressure in the brachial artery in the upper arm and arterial stiffness is assessed by way of pulse pressure (PP; SBP - DBP). However it is becoming increasingly recognised that measures of central arterial function, i.e. measures of arterial stiffness, are more valuable predictors of vascular health outcomes⁴. The central arteries slowly stiffen with age, with the rate influenced by hypertension, diabetes and atherosclerosis⁵. Pulse wave velocity (PWV) is now considered the gold standard non-invasive method for measuring arterial stiffness, and is an independent predictor of cardiovascular events and all-cause mortality^{6,7}.

There have been few studies on the role of micronutrients in the treatment of arterial stiffness. A recent review showed support for the intake of omega-3 fish oils, and soy isoflavones, as well as consumption of fermented milk products containing bioactive peptides⁸. Studies evaluating the relationship between milk and dairy products and holistic markers of CVD risk, such as arterial stiffness have been recommended⁹, as has research to examine the role of micronutrients in the treatment of arterial stiffness⁸. The aim of our study was to examine dairy food intake *per se*, in relation to measures of arterial stiffness via carotid-femoral PWV (cfPWV), PP, and other indices of cardiovascular health including SBP and DBP.

Methods

Participants

Participants were obtained from the Maine-Syracuse Longitudinal Study (MSLS), a study designed to examine cardiovascular risk factors in relation to cognitive performance in community-dwelling individuals. The MSLS consists of five cohorts defined by time of entry into the study (1975–2000). Recruitment and data collection procedures for the MSLS have been previously described in detail¹⁰. The data for the present study were obtained from those participants returning for the seventh study wave, as both cfPWV and dietary intake measures were both obtained at this examination for the first time.

From an initial sample of 626 individuals with cfPWV data at wave 7, participants were excluded in the following order: history of stroke ($n = 14$), probable dementia ($n = 2$),

inability to read English ($n = 1$), missing data on dairy consumption ($n = 3$), or suboptimal quality of data on arterial stiffness as defined *a priori* as a cfPWV error of estimate $>20\%$ ($n = 19$). Dementia and stroke were reasons for exclusion because we were interested in examining relationships between diet and arterial stiffness in a community-dwelling, relatively healthy study population. The characteristics of the final sample with complete data ($N = 587$) are presented in Table 1.

The University of Maine Institutional Review Board approved this study, and the use of de-identified MSLS data was approved by the University of South Australia Human Ethics Committee. All participants provided informed consent for data collection, and all procedures followed were in accordance with institutional guidelines.

Procedure

Within two weeks of the laboratory visit, participants completed the Center for Epidemiologic Studies Depression Scale (CES-D)¹¹, the Nurses' Health Study Activity Questionnaire¹², and the Nutrition and Health Questionnaire¹³. At this visit, a blood sample, brachial artery BP, and pulse wave measures were obtained prior to breakfast, following an overnight fast. Standard assay methods were employed^{10,14} to obtain total cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol, triglycerides, fasting plasma glucose, and plasma homocysteine. After a light breakfast, including decaffeinated tea or coffee, participants underwent a medical interview including a detailed medical history.

BP and cfPWV assessment

Brachial artery pressures were measured in accordance with the procedure at prior MSLS waves, taken five times each in reclining, sitting and standing after a supine rest for 10 minutes, with a five minute rest between each set of measures. Measures were taken using the traditional pressure-cuff method (Critikon Dinamap ProCare 100, oscillometric method). In a supine position, cfPWV was assessed non-invasively using the SphygmoCor system (AtCor Medical) with applanation tonometry. The carotid-femoral path length was estimated as the surface distances joining the suprasternal notch, the umbilicus, and the femoral pulse subtracted from distance between the suprasternal notch and the carotid pulse. Carotid-femoral transit time was estimated in 8 to 10 sequential ECG-gated femoral and carotid waveforms as the average time difference between the onset of the femoral and carotid waveforms. The intersecting tangent method was employed to identify the foot of the pulse wave. PWV was calculated as the carotid-femoral path length divided by the carotid-femoral transit time, a reproducible measure of central arterial stiffness⁶.

Dietary assessment

Diet was assessed using The Nutrition and Health Questionnaire, which comprises 41 questions about dietary intake, smoking history, physical activity, marital status, medical history, self-reported health, and medication and supplement use^{13,15}. The questionnaire has been used in a large investigation of cancer and nutrition and its acceptable validity has been demonstrated by comparison with dietary recall, protein excretion and total energy expenditure data¹⁶. The dietary component questions participants about their frequency of consumption of meat, fish, dairy products, eggs, breads, cereals, and beverages including tea, coffee, carbonated drinks, water, fruit juice, and alcohol. A comprehensive list of 37 foods follows, and participants are required to stipulate how frequently they consume each food, with six response options: never; seldom; once a week; 2 to 4 times a week; 5 to 6 times a week; or once or more a day. These six response options were used to form the five level categorization of total dairy food consumption, with the never and seldom respondents grouped together due to the low numbers in each category. Dairy products included were

milk, cheese, yoghurt and dairy desserts (grouped together), ice-cream and cream (grouped together), and total dairy foods. Milk was the only dairy food for which participants were asked to stipulate the fat content of milk consumed (whole fat, reduced fat, or skim). Milk intake included milk on cereal and in other beverages such as tea and coffee. Soy milk intake was not included in any analyses of dairy and cFPWV.

The median score within each response option was used to estimate total intakes per week for each food in the questionnaire; for example, 2 to 3 times per week was estimated at 2.5. These totals were used to determine mean daily intakes for each food. As portion sizes were not stipulated, the totals are an estimate of the number of *times* each food was consumed on a daily basis. Individual foods were grouped into five major food categories (in addition to dairy products) - grains, fruits, vegetables, protein foods, and fats/sweets/other (empty calories) - based on the USDA MyPlate¹⁷. Intakes of individual foods and beverages within each food group were summed to give an estimate of total intake for each group, and intakes for all food groups were added to estimate total energy intake. The primary predictor variable in this study was the five level categorization of total dairy food consumption.

Covariates

Variables that were measured at the physical examination and were considered as candidates for inclusion in the covariate sets included height, weight, body mass index (BMI), waist circumference, and prevalent obesity, diabetes, hypertension, and CVD. BMI was calculated from height and weight (kg/m^2), and obesity was defined as BMI of $30 \text{ kg}/\text{m}^2$ or above. Waist circumference was measured over light clothing, using a non-extendable tape at the level of the iliac crest. Diabetes mellitus was defined as treatment with insulin, oral antidiabetic agents, or by fasting glucose level of $7 \text{ mmol}/\text{L}$ or above. Hypertension was defined as treatment for hypertension or a BP of $140/90 \text{ mmHg}$. Prevalent CVD was defined by the self-reported presence of coronary artery disease, myocardial infarction, congestive heart failure, transient ischemic attack, or angina pectoris, and confirmed by medical records. Where necessary, diagnostic determinations were confirmed by chart review with permission.

Statistical analyses

Data were analysed with SPSS (Version 18, Chicago, IL, USA). Preliminary analyses were performed to assess any significant correlations between dairy intake, cFPWV and other demographic, health, nutrition and lifestyle factors. The dairy intakes in the sample were calculated and the demographic, health and dietary characteristics of those who consume dairy food at least once per day and those who consume less than this were tested for differences using ANOVA or chi-square tests where appropriate. For the primary analyses, univariate ANCOVA was used to compare cFPWV across increasing intakes of dairy food consumption, ranging from never/seldom to at least once per day, and polynomial trend analyses were performed across the five levels of dairy food intake only after the ANCOVA test of the dairy intake main effect was found to be statistically significant ($p < 0.05$). If the omnibus test of overall differences among groups was observed, any significant trends were reported. Adjustments for multiple comparisons among dairy food intake groups were made and reported in terms of the Bonferroni adjustment.

An age-adjusted model was first performed, and then analyses followed using four covariate sets. The extended covariate sets were as follows: (1) basic covariate set: age, sex, education and race; (2) extended covariate set 1: basic set + height, weight, heart rate, antihypertensive drug treatment (yes/no) and mean arterial pressure (MAP); (3) extended covariate set 2: extended covariate set 1 + waist circumference, total cholesterol, HDL-cholesterol, and LDL-cholesterol; (4) extended covariate set 3: extended covariate set 2 + depressive

symptoms (CES-D raw score), intake of grains, vegetables, protein foods, empty calories (sweets/fats/others), and total intake from all food groups (all in times per day).

As adjustment for height when assessing cfPWV has been recommended¹⁸, height and weight were used in the basic set instead of BMI. However, alternative analyses (reported in results) were done with height and weight removed and with waist circumference substituted.

Variables were required to meet 1 of 2 criteria to be included as an additional covariate: 1) significantly related ($p < 0.05$) to dairy food intake (the predictor) and cfPWV (the primary outcome variable) to be included in the second extended model, or 2) differed significantly between low (less than once per day) and high (at least daily) dairy consumers to be included in the third extended model. Preliminary correlational analyses were performed to ensure that MAP had the same relationship to cfPWV in each dairy intake category. MAP was calculated as $DBP + 1/3 (DBP - DBP)$. cfPWV was significantly correlated with MAP for both low dairy consumers (<1 time per day, $n=371$), and high dairy consumers (1 time/day, $n=216$), indicating that MAP has the same relationship to PWV regardless of dairy intake. Additional analyses were performed with the inclusion of a dairy intake x MAP interaction term.

Supplemental Table 1 shows those health and dietary variables that were significantly correlated with both dairy food intake and cfPWV (please see <http://hyper.ahajournals.org>, Table S1). While PWV and MAP, SBP and PP were highly correlated, they were used as dependent variables in the current study. For all the models employed, covariates were entered simultaneously with the predictor variables.

Results

The self-reported intakes of dairy foods (milk, cheese, yoghurt and dairy desserts, cream and ice-cream) are shown in Table 1. Slightly over one-third of the sample (36.1%) reported eating dairy food at least once per day. Half of participants (50.5%) reported eating dairy foods between two and six times per week. The remaining participants (13.4%) reported eating dairy foods no more than once per week. For individual foods, milk was the dairy product consumed most frequently on a daily basis. Nearly one-third of the sample reported drinking at least 600 mL of milk per day, equating to just over two serves per day. A similar proportion of the sample consumed less than 150 mL per day, with the remaining participants (37.9%) drinking between 150 and 450 mL per day. Of those that drank milk, the majority reported drinking skim or reduced fat milk (80%). Cheese was most often consumed between two and four times per week. Yoghurt, dairy desserts, cream and ice-cream were consumed infrequently.

In Table 2, the demographic, health and nutritional characteristics of participants who consumed dairy food at least daily (36.8%) are compared with those who consumed dairy food less frequently than this (63.2%). Participants who consumed dairy on a daily basis consumed more vegetables and protein foods, but fewer grains and empty calories (sweets/fats), adjusting for total energy intake, compared to those who ate dairy less frequently than this. They also had a higher number of years of education, lower body weight and waist circumference, lower SBP and DBP, and fewer depressive symptoms (all $P < 0.05$). More females than males consumed dairy food on a daily basis.

There was a decrease in cfPWV, PP and SBP for participants across increasing intakes of dairy food, ranging from never/seldom, to at least one time per day (Table 3). Table 3 shows the 95 percent confidence limits associated with each mean for each group, and summarizes the results of statistical analyses for the age-adjusted, basic and the most extended models. A

table describing results for each covariate set for each dependent variable may be seen in the supplemental data (please see <http://hyper.ahajournals.org>, Table S2).

For the age-adjusted model, the lowest cfPWV values (mean value 9.9 m/s) were observed for those who consumed dairy products at least 5 to 6 times per week, and daily (mean value 10.0 m/s). With the addition of demographic variables, other cardiovascular risk factors and nutrition variables, this significant linear trend across increasing intakes of dairy food remained (extended covariate set 3). The cfPWV of those in the lowest three intake categories (eat dairy 0 to 4 times per week) was significantly higher than the cfPWV for those in the highest two intake categories (eat dairy at least 5 to 7 times per week) ($P=0.001$). No associations between individual dairy foods (milk, cheese, yoghurt and dairy desserts, cream and ice-cream) and cfPWV were found (all $P>0.30$).

The pattern of results was very similar for PP and SBP (Table 3). For all fully extended models, PP and SBP decreased in a linear fashion as dairy food intake increased. Contrasts performed between categories of intake showed that those who consumed dairy food at least 5 to 6 times per week had significantly lower PP and SBP than those who never or rarely consumed dairy foods, after adjustment for demographic, cardiovascular and dietary factors. Figure S1 (please see <http://hyper.ahajournals.org>) shows the reductions in cfPWV, PP and SBP across increasing intakes of dairy food.

No significant differences among dairy intake groups were observed for DBP, waist circumference, total cholesterol, HDL and LDL cholesterol, or triglyceride measures for either the basic or extended models. These results are displayed in the supplemental data (please see <http://hyper.ahajournals.org>, Table S2).

Additional analyses

The pattern of significant results remain unchanged when the following additional regression models were employed: waist circumference was substituted for height and weight, a MAP x dairy intake interaction was used in the model with MAP, and the addition of physical activity to the extended covariate sets.

The analyses were repeated for participants not on any medication ($n=218$). Comparing those who eat dairy less than daily ($n=137$) with those who eat dairy food at least daily ($n=81$), the pattern of results for cfPWV were the same as for the whole sample, with the high dairy consumers having a lower cfPWV in all covariate models (data not shown).

Discussion

Dairy product intake was inversely associated with cfPWV and SBP, with adjustment for demographic, cardiovascular, and dietary factors. cfPWV, PP and SBP all decreased in a linear fashion as dairy food intake increased across categories of intake from never/seldom to 5 to 6 times per week or more. Importantly, we have also shown that dairy food intake is not adversely associated with higher levels of cholesterol (total, HDL and LDL cholesterol) or increased abdominal obesity (as measured by waist circumference). Moreover, our results for cfPWV, the gold standard measure of arterial stiffness, were supported by our findings for PP and SBP, surrogate hemodynamic indices of arterial stiffness.

These findings are consistent with research examining the effects of different milk-derived proteins on BP and arterial stiffness. Peptides derived from milk protein, including casokinins (casein-derived) and lactokinins (whey-derived) have been shown to inhibit angiotensin-I-converting enzyme (ACE) activity, an important enzyme involved in BP regulation^{19,20}. Beneficial effects on BP and augmentation index have been reported for

both fermented milk rich in casein^{21–23}, and rich in whey protein^{24,25}. A more recent study found that ionic calcium, in addition to lactic acid bacteria, released during milk fermentation also contributed to ACE-inhibitory activity²⁶. This small collection of research does provide evidence for the role of probiotic dairy products in BP modification. Further research is needed to determine their role in the treatment of arterial stiffness.

Our data supports one of the first intervention studies to examine the effects of low-fat dairy product consumption on BP, in addition to other risk parameters of the metabolic syndrome³. Consumption of three serves of low-fat dairy foods in overweight individuals for eight weeks resulted in a significant reduction in SBP (2.9 ± 7.4 mmHg). The high dairy diet showed no relationship with total cholesterol, LDL cholesterol or triglycerides.

Our findings also support studies that have examined dairy products without added probiotics in relation to measures of CVD. These include a number of recent reviews, including a meta-analysis by Elwood et al²⁷ who found significant reductions in the relative risk (RR) of ischemic heart disease, ischemic and hemorrhagic stroke in those who consume the most milk, and other reviews of prospective studies which have failed to find a consistent relationship between dairy food intake and coronary heart disease^{28,29}. Most recently, an increased consumption of yoghurt has been associated with carotid artery intima-media thickness³⁰, a marker of atherosclerotic vascular disease and predictor of future cardiovascular and cerebrovascular events³¹. This study showed that women aged over 70 years who consumed more than 100g of yoghurt per day had a significantly lower carotid artery intima-media thickness than those with lower yoghurt intakes, after adjustment for baseline, dietary and lifestyle risk factors. Higher milk, cheese or total dairy intakes were not associated with carotid artery intima-media thickness, or with SBP or DBP. An earlier prospective study found that yoghurt intake was associated with a lower risk of acute myocardial infarction³², a clinical consequence of atherosclerotic vascular disease.

Little is known about the mechanisms by which dairy foods may improve BP or arterial stiffening, a slow process resulting from changes in the extracellular matrix of the arterial walls. The strongest evidence surrounds the role of bioactive peptides derived from dairy protein, released during digestion, to inhibit ACE, modulate endothelial function and cause vasodilatation³³. Additional components of dairy are likely to play a role. High levels of potassium have been associated with lower BP in numerous observational studies and clinical trials³⁴. Dietary potassium is thought to cause vasodilatation by stimulating the sodium pump and opening potassium channels, as well as reducing vasoconstrictive sensitivity to angiotensin II³⁴. Magnesium modulates vascular tone and reactivity, stimulates the production of vasodilators, improving blood flow and decreasing vascular resistance, thereby lowering BP and increasing arterial function³⁵. Phosphorus from dairy products has recently been associated with lower BP and a reduced risk of incident hypertension in a large prospective study³⁶. Without a known mechanism on how dairy phosphorus may reduce BP, it may be the combination of a range of nutrients in dairy foods that are effective in modulating BP. Finally, dietary calcium has been linked with low BP, working in combination with sodium, potassium and magnesium to ensure ionic balance, stabilise vascular cell membranes and increase vasodilatation³⁴. BP reduction may also be mediated by body weight or fat reductions, as substantial evidence exists for an anti-obesity effect of dairy^{37–39}, and any positive effect on weight loss will be of benefit to BP.

Studies have reported that consumption of caffeinated tea and coffee affects PWV if consumed immediately before PWV analyses^{40,41}. Our participants consumed non-caffeinated tea and coffee on the day of the examination. Coffee and tea consumption as a routine part of the diet was not related to cfPWV, PP or BP.

Although the differences in cfPWV and SBP according to dairy food intake in this study were relatively small (difference of 1.0 m/s and 4.5 mm Hg between never/seldom and 5–6 times/week groups for cfPWV and SBP, respectively), the differences are likely to be clinically significant. In a recent meta-analysis, it was estimated that for every 1 m/s increase in cfPWV, there was an age-, sex- and risk factor-adjusted increase of 14%, 15% and 15% in total CVD events, CVD mortality and all-cause mortality, respectively⁷. Clearly, hypertension represents a modifiable risk factor with U.S. data suggesting that even small reductions in BP can have a great public health impact and translate into substantial reductions in coronary heart disease and stroke events^{42,43}. It has been estimated that a reduction in SBP by 2 mm Hg may reduce the risk for stroke and myocardial infarction by approximately 4%⁴⁴.

A limitation to the study can be regarded as the lack of detailed information regarding quantities of foods, including dairy food, consumed. Participants were asked ‘how often do you eat the following foods?’, but not required to estimate portion or serving sizes. Quantities are therefore likely to differ substantially amongst individuals as well as the same individual on different occasions. Additionally, the range of responses to indicate how often a food is consumed was limited in the high intake range, i.e. there was not a more specific measure of intake beyond ‘once or more a day’. We are also unable to stipulate the fat content of dairy food consumed based on information provided (with the exception of milk). The study was cross-sectional and dietary measurement at only one point in time may not reflect long-term consumption patterns. Secondly, the cross-sectional nature of the study does not enable us to come to any conclusions regarding causality. We are unable to infer that increasing dairy intake may decrease arterial stiffness. The age range in the present study was wide, but we adjusted for age in our statistical analytic procedures because we did not have sufficient numbers of subjects to examine results for multiple age groups over a narrower range of ages. Finally, the MAP in this study was estimated using SBP and DBP, and was not a true measure of MAP.

This study has a number of strengths. This is the first cross-sectional study that has examined dairy food intake (not limited to fermented dairy products) and cfPWV as a measure of arterial stiffness. We have examined this relationship in a large, community-dwelling, healthy sample across a wide age span, and controlled for relevant demographic, health and dietary variables.

Perspectives

Higher dairy food intake was associated with lower cfPWV and accompanying reductions of PP and SBP. Further evidence from long-term longitudinal or intervention studies is needed before the incorporation of dairy foods into a balanced diet for the attenuation of arterial stiffening can be recommended, but this initial analysis of dairy consumption in relation to arterial stiffness indicates that dairy consumption is not associated with a worsening of traditional risk factors such as hypercholesterolemia and hypertension and may indeed have benefits in reducing arterial stiffness.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank Amanda Goodell and Suzanne Brennan, Maine Syracuse Longitudinal Study, University of Maine, for their help with data acquisition, and data management.

Sources of funding

The research was supported by the Maurice de Rohan International Scholarship (University of South Australia), and in part by the National Heart, Lung, and Blood Institute (grants HL67358 and HL81290) and the National Institute on Aging (grant AG03055) of the National Institutes of Health. Conclusions expressed in the paper are those expressed by the authors, not by the institutions providing support.

References

1. Azadbakht L, Mirmiran P, Esmailzadeh A, Azizi T, Azizi F. Beneficial effects of a Dietary Approaches to Stop Hypertension eating plan on features of the metabolic syndrome. *Diabetes Care*. 2005; 28:2823–2831. [PubMed: 16306540]
2. Kris-Etherton PM, Grieger JA, Hilpert KF, West SG. Milk products, dietary patterns and blood pressure management. *J Am Coll Nutr*. 2009; 28 (Suppl 1):103S–119S. [PubMed: 19571168]
3. van Meijl LEC, Mensink RP. Low-fat dairy consumption reduces systolic blood pressure, but does not improve other metabolic risk parameters in overweight and obese subjects. *Nutr Metab Cardiovasc Dis*. 2011; 21:355–361. [PubMed: 20153619]
4. Yasmin, Brown MJ. Similarities and differences between augmentation index and pulse wave velocity in the assessment of arterial stiffness. *QJM*. 1999; 92:595–600. [PubMed: 10627881]
5. Benetos A, Waeber B, Izzo J, Mitchell G, Resnick L, Asmar R, Safar M. Influence of age, risk factors, and cardiovascular and renal disease on arterial stiffness: clinical applications. *Am J Hypertens*. 2002; 15:1101–1108. [PubMed: 12460708]
6. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I, Struijker-Boudier H. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J*. 2006; 27:2588–2605. [PubMed: 17000623]
7. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2010; 55:1318–1327. [PubMed: 20338492]
8. Pase MP, Grima NA, Sarris J. The effects of dietary and nutrient interventions on arterial stiffness: a systematic review. *Am J Clin Nutr*. 2011; 93:446–454. [PubMed: 21147858]
9. Givens DI. Milk in the diet: good or bad for vascular disease? *Proc Nutr Soc*. 2011:1–7.
10. Elias MF, Robbins MA, Budge MM, Elias PK, Brennan SL, Johnston C, Nagy Z, Bates CJ. Homocysteine, folate, and vitamins B6 and B12 blood levels in relation to cognitive performance: the Maine-Syracuse study. *Psychosom Med*. 2006; 68:547–554. [PubMed: 16868263]
11. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Applied Psychological Measures*. 1977; 1:385–401.
12. Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, Rosner B, Kriska A, Willett WC. Reproducibility and validity of a self-administered physical-activity questionnaire. *Int J Epidemiol*. 1994; 23:991–999. [PubMed: 7860180]
13. Kaaks R, Riboli E. Validation and calibration of dietary intake measurements in the EPIC project: methodological considerations. *European Prospective Investigation into Cancer and Nutrition*. *Int J Epidemiol*. 1997; 26 (Suppl 1):S15–25. [PubMed: 9126530]
14. Elias MF, Robbins MA, Budge MM, Elias PK, Dore GA, Brennan SL, Johnston C, Nagy Z. Homocysteine and cognitive performance: modification by the ApoE genotype. *Neurosci Lett*. 2008; 430:64–69. [PubMed: 18023533]
15. Riboli E, Kaaks R. The EPIC Project: rationale and study design. *European Prospective Investigation into Cancer and Nutrition*. *Int J Epidemiol*. 1997; 26 (Suppl 1):S6–14. [PubMed: 9126529]
16. Kroke A, Klipstein-Grobusch K, Voss S, Moseneder J, Thielecke F, Noack R, Boeing H. Validation of a self-administered food-frequency questionnaire administered in the European Prospective Investigation into Cancer and Nutrition (EPIC) Study: comparison of energy, protein, and macronutrient intakes estimated with the doubly labeled water, urinary nitrogen, and repeated 24-h dietary recall methods. *Am J Clin Nutrition*. 1999; 70:439–447. [PubMed: 10500011]

17. United States Department of Agriculture. ChooseMyPlate.gov; 2011. <http://www.choosemyplate.gov/>
18. Smulyan H, Marchais SJ, Pannier B, Guerin AP, Safar ME, London GM. Influence of body height on pulsatile arterial hemodynamic data. *J Am Coll Cardiol*. 1998; 31:1103–1109. [PubMed: 9562014]
19. FitzGerald RJ, Meisel H. Milk protein-derived peptide inhibitors of angiotensin-I- converting enzyme. *Br J Nutr*. 2000; 84 (Suppl 1):S33–37. [PubMed: 11242444]
20. FitzGerald RJ, Murray BA, Walsh DJ. Hypotensive peptides from milk proteins. *J Nutr*. 2004; 134:980S–988S. [PubMed: 15051858]
21. Hata Y, Yamamoto M, Ohni M, Nakajima K, Nakamura Y, Takano T. Placebo- controlled study of the effect of sour milk on blood pressure in hypertensive subjects. *Am J Clin Nutrition*. 1996; 64:767–771. [PubMed: 8901799]
22. Seppo L, Jauhiainen T, Poussa T, Korpela R. A fermented milk high in bioactive peptides has a blood pressure-lowering effect in hypertensive subjects. *Am J Clin Nutrition*. 2003; 77:326–330. [PubMed: 12540390]
23. Jauhiainen T, Ronnback M, Vapaatalo H, Wuolle K, Kautiainen H, Groop PH, Korpela R. Long-term intervention with *Lactobacillus helveticus* fermented milk reduces augmentation index in hypertensive subjects. *Eur J Clin Nutr*. 2010; 64:424–431. [PubMed: 20145666]
24. Kawase M, Hashimoto H, Hosoda M, Morita H, Hosono A. Effect of administration of fermented milk containing whey protein concentrate to rats and healthy men on serum lipids and blood pressure. *J Dairy Sci*. 2000; 83:255–263. [PubMed: 10714858]
25. Pal S, Ellis V. The chronic effects of whey proteins on blood pressure, vascular function, and inflammatory markers in overweight individuals. *Obesity (Silver Spring)*. 2010; 18:1354–1359. [PubMed: 19893505]
26. Gonzalez-Gonzalez CR, Tuohy KM, Jauregi P. Production of angiotensin-I- converting enzyme (ACE) inhibitory activity in milk fermented with probiotic strains: Effects of calcium, pH and peptides on the ACE-inhibitory activity. *Int Dairy J*. 2011; 21:615–622.
27. Elwood PC, Pickering JE, Givens DI, Gallacher JE. The consumption of milk and dairy foods and the incidence of vascular disease and diabetes: an overview of the evidence. *Lipids*. 2010; 45:925–939. [PubMed: 20397059]
28. Gibson RA, Makrides M, Smithers LG, Voevodin M, Sinclair AJ. The effect of dairy foods on CHD: a systematic review of prospective cohort studies. *Br J Nutr*. 2009; 102:1267–1275. [PubMed: 19682399]
29. Mente A, de Koning L, Shannon HS, Anand SS. A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. *Arch Intern Med*. 2009; 169:659–669. [PubMed: 19364995]
30. Ivey KL, Lewis JR, Hodgson JM, Zhu K, Dhaliwal SS, Thompson PL, Prince RL. Association between yogurt, milk, and cheese consumption and common carotid artery intima-media thickness and cardiovascular disease risk factors in elderly women. *Am J Clin Nutrition*. 2011; 94:234–239. [PubMed: 21613553]
31. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction - The Rotterdam Study. *Circulation*. 1997; 96:1432–1437. [PubMed: 9315528]
32. Tavani A, Gallus S, Negri E, La Vecchia C. Milk, dairy products, and coronary heart disease. *J Epidemiol Community Health*. 2002; 56:471–472. [PubMed: 12011208]
33. Clare DA, Swaisgood HE. Bioactive milk peptides: a prospectus. *J Dairy Sci*. 2000; 83:1187–1195. [PubMed: 10877382]
34. Houston MC, Harper KJ. Potassium, magnesium, and calcium: their role in both the cause and treatment of hypertension. *J Clin Hypertens (Greenwich)*. 2008; 10:3–11. [PubMed: 18607145]
35. Sontia B, Touyz RM. Role of magnesium in hypertension. *Arch Biochem Biophys*. 2007; 458:33–39. [PubMed: 16762312]
36. Alonso A, Nettleton JA, Ix JH, de Boer IH, Folsom AR, Bidulescu A, Kestenbaum BR, Chambless LE, Jacobs DR Jr. Dietary phosphorus, blood pressure, and incidence of hypertension in the

- atherosclerosis risk in communities study and the multi-ethnic study of atherosclerosis. *Hypertension*. 2010; 55:776–784. [PubMed: 20083730]
37. Zemel MB. Role of calcium and dairy products in energy partitioning and weight management. *Am J Clin Nutrition*. 2004; 79:907S–912S. [PubMed: 15113738]
 38. Zemel MB, Teegarden D, Van Loan MD, Schoeller DA, Matkovic V, Lyle RM, Craig BA. Dairy-rich diets augment fat loss on an energy-restricted diet: a multicenter trial. *Nutrients*. 2009; 1:83–100. [PubMed: 22253969]
 39. Zemel MB, Thompson W, Milstead A, Morris K, Campbell P. Calcium and dairy acceleration of weight and fat loss during energy restriction in obese adults. *Obes Res*. 2004; 12:582–590. [PubMed: 15090625]
 40. Mahmud A, Feely J. Acute effect of caffeine on arterial stiffness and aortic pressure waveform. *Hypertension*. 2001; 38:227–231. [PubMed: 11509481]
 41. Vlachopoulos C, Hirata K, Stefanadis C, Toutouzas P, O'Rourke MF. Caffeine increases aortic stiffness in hypertensive patients. *Am J Hypertens*. 2003; 16:63–66. [PubMed: 12517685]
 42. Cook NR, Cohen J, Hebert PR, Taylor JO, Hennekens CH. Implications of small reductions in diastolic blood-pressure for primary prevention. *Arch Intern Med*. 1995; 155:701–709. [PubMed: 7695458]
 43. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM. Dietary approaches to prevent and treat hypertension - A scientific statement from the American Heart Association. *Hypertension*. 2006; 47:296–308. [PubMed: 16434724]
 44. Selmer RM, Kristiansen IS, Haglerod A, Graff-Iversen S, Larsen HK, Meyer HE, Bonna KH, Thelle DS. Cost and health consequences of reducing the population intake of salt. *J Epidemiol Community Health*. 2000; 54:697–702. [PubMed: 10942450]

Novelty and Significance

1) What is new?

- First study to examine the relationship between dairy food intake and arterial stiffness, as measured by PWV.

2) What is relevant?

- Studies evaluating the relationship between dairy products and holistic markers of cardiovascular disease risk, such as arterial stiffness have been recommended.

3) Summary

- Higher dairy food intake is associated with lower cfPWV, and lower SBP.
- Further intervention studies are needed to ascertain whether dairy food intake may be an appropriate dietary intervention for management of arterial stiffening, hypertension, and reducing cardiovascular disease risk.

Table 1

Self-reported intakes of cheese, yoghurt/dairy desserts, cream/ice-cream, total dairy food, and milk (N=587)

Dairy product	Dairy food intake					
	Never/seldom n (%)	1 time/wk n (%)	2-4 times/wk n (%)	5-6 times/wk n (%)	1 time/day n (%)	600 mL/day
Cheese	92 (15.7)	147 (25.0)	245 (41.8)	70 (11.9)	33 (5.6)	
Yoghurt & dairy desserts	275 (46.8)	98 (16.7)	130 (22.1)	44 (7.5)	40 (6.8)	
Cream & ice-cream	294 (50.1)	164 (28.0)	100 (17.0)	21 (3.6)	8 (1.4)	
Total dairy food	37 (6.3)	40 (6.8)	141 (24.0)	153 (26.1)	216 (36.8)	
	0-150 mL/day	150 mL/day	300 mL/day	450 mL/day	600 mL/day	
Milk	180 (30.7)	67 (11.4)	151 (25.7)	32 (5.5)	157 (26.7)	
Whole fat* (5.9%)	13 (40.6)	3 (9.4)	6 (18.8)	1 (3.1)	7 (21.9)	
Skim/reduced fat* (80.4%)	126 (28.7)	53 (12.1)	103 (23.5)	27 (6.2)	124 (28.3)	
Other (e.g. soy)* (13.7%)	28 (37.3)	7 (9.3)	12 (16.0)	3 (4.0)	23 (30.7)	

* % from within milk group.

Demographic variables, health characteristics, and dietary intake of sample, comparing those who consume dairy food at least once per day compared to less than this (N=587)

Table 2

Demographic/health characteristic	Dairy food < 1 time/day (n=371)		Dairy food at least 1 time/day (n=216)		P*
	Mean	SD	Mean	SD	
Age, y	63.0	12.7	65.2	11.6	.039
Education, y	14.4	2.7	15.0	2.9	.019
Physical activity, MET hours/wk	21.2	27.9	24.6	26.2	NS
Smoking, cigarettes/wk	9.3	36.8	5.5	32.2	NS
Waist circumference, cm	95.1	15.1	91.8	16.5	.015
Weight, kg	84.3	19.6	80.8	18.7	.035
BMI, kg/m ²	29.9	6.8	29.1	6.0	NS
cPWV, m/s	10.4	2.9	10.1	2.7	NS
SBP, mm Hg	130.9	20.6	126.8	18.6	.016
DBP, mm Hg	78.2	10.2	75.8	9.5	.005
MAP, mm Hg	95.8	12.4	92.8	11.3	.004
PP, mm Hg	52.7	16.2	51.0	14.7	NS
Heart rate, bpm	60.2	9.6	59.9	8.9	NS
Total cholesterol, mmol/L	4.8	1.0	4.9	1.0	NS
HDL cholesterol, mmol/L	1.4	0.4	1.4	0.4	NS
LDL cholesterol, mmol/L	2.9	0.8	2.9	0.8	NS
Triglycerides, mmol/L	1.3	0.9	1.3	0.8	NS
Glucose, mmol/L	5.5	1.4	5.4	1.2	NS
Depression, CES-D [§]	8.6	7.6	7.1	7.4	.017

	n	% (within <1 time/day group)	n	% (within 1 time/day group)	P [†]
Gender					
Males	154	41.5	70	32.4	.029
Females	217	58.5	146	67.6	.029
Race					
White	301	81.1	203	94.0	<.001

Demographic/health characteristic	Dairy food < 1 time/day (n=371)		Dairy food at least 1 time/day (n=216)		P*
	Mean	SD	Mean	SD	
Other	70	18.9	13	6.0	<.001
CVD [†]	41	11.1	29	13.4	NS
Diabetes mellitus	57	15.4	30	13.9	NS
Hypertension	238	64.2	122	56.5	NS
Anti-hypertensive medication	204	55.0	113	52.3	NS
Cholesterol-lowering medication	130	35.0	74	34.3	NS
Diabetes medication	50	13.5	29	13.4	NS
	Mean	SEM	Mean	SEM	P [‡]
Grains/day	3.5	0.08	3.2	0.10	.010
Fruit/day	1.5	0.05	1.6	0.07	NS
Vegetables/day	2.6	0.05	2.9	0.07	.002
Protein foods/day	1.8	0.04	1.9	0.05	.024
Other (fats/sweets)/day	2.1	0.08	1.5	0.11	<.001
Alcohol, standard drinks/day	0.4	0.04	0.4	0.05	NS
Total all foods serves/day [¶]	12.0	3.8	13.5	4.1	<.001

BMI indicates body mass index; CES-D, Centre for Epidemiologic Studies Depression Scale; cPWV, carotid-femoral pulse wave velocity; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MAP, mean arterial pressure; MET, metabolic equivalent; PP, pulse pressure; SBP, systolic blood pressure.

* Analysis of variance for continuous variables.

[†] Chi square for categorical variables.

[‡] Analysis of covariance, controlling for total serves per day all food groups.

[§] CES-D: higher score indicates greater number of depressive symptoms.

^{||} CVD was defined as present if there was self-reported history of coronary artery disease, myocardial infarction, congestive heart failure, transient ischemic attack, or angina pectoris.

[¶] Mean and SD, includes alcohol.

Table 3

Results of analysis of covariance, showing associations between cFPWV, PP, and SBP across increasing intakes of dairy food (N=587), for basic and extended covariate set 3

Outcome measure	Covariate set	Dairy food intake						P*				
		Never/seldom n = 37		1 time/week n = 40		2-4 times/week n = 141			5-6 times/week n = 153		1/day n = 216	
		Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	
cFPWV	Age-adjusted	10.8	10.0, 11.5	11.1	10.4, 11.8	10.8	10.4, 11.2	9.9 ^{††}	9.6, 10.3	10.0 ^{††}	9.7, 10.3	.000 [‡]
	Basic	10.6	9.8, 11.4	10.9	10.2, 11.6	10.7	10.3, 11.1	10.0	9.6, 10.3	10.1	9.7, 10.4	.016 [‡]
	Extended 3	11.0	10.3, 11.7	10.8	10.1, 11.5	10.6	10.3, 11.0	10.0	9.6, 10.3	10.1	9.8, 10.4	.018 [‡]
PP	Age-adjusted	56.3	51.9, 60.7	57.8	53.5, 62.1	53.2	50.9, 55.5	51.3	49.1, 53.4	50.2 ^{††}	48.3, 52.0	.003 [‡]
	Basic	56.3	51.9, 60.6	56.6	52.3, 60.9	52.7 [§]	50.5, 55.0	51.4 [§]	49.2, 53.5	50.6 [§]	48.8, 52.4	.035 [‡]
	Extended 3	57.6	54.1, 61.0	53.1	49.8, 56.5	52.4	50.6, 54.1	50.8 [§]	49.2, 52.4	51.6 [§]	50.2, 53.0	.013 [‡]
SBP	Age-adjusted	131.8	125.6, 137.9	138.7	132.7, 144.6	131.7	128.5, 134.8	128.8 ^{††}	125.8, 131.9	126.1 ^{††}	123.6, 128.7	.001 [‡]
	Basic	130.1	124.1, 136.2	135.9	130.1, 141.8	130.4	127.3, 133.4	129.5	126.5, 132.4	127.4	124.8, 129.9	NS
	Extended 3	133.0	130.7, 135.3	130.1	127.8, 132.3	129.6	128.4, 130.7	128.5 [§]	127.4, 129.6	129.1 [§]	128.1, 130.0	.013 [‡]

CES-D indicates Centre for Epidemiologic Studies Depression Scale; cFPWV, carotid-femoral pulse wave velocity; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PP, pulse pressure; SBP, systolic blood pressure; WC, waist circumference.

Age-adjusted: adjusted for age.

Basic set: adjusted for age, education, gender, race.

Extended set 3: adjusted for variables in basic set + height, weight, heart rate, antihypertensive drug treatment, mean arterial pressure, WC, total cholesterol, HDL- and LDL-cholesterol, CES-D raw score + grains/day, vegetables/day, sweets/day, protein/day, total food serves/day.

* P for overall omnibus outcome.

[†] P < 0.05.

[‡] P < 0.01, for statistically significant linear trend.

[§] significantly different from the never/seldom group.

^{††} significantly different from 1 time/week group.

^{†††} significantly different from the 2-4 times/week group.