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Dietary predictors of arterial stiffness in a cohort with type 1 and type 2 diabetes

K.S. Petersen [a], J.B. Keogh [a], P.J. Meikle [b], M.L. Garg [c], P.M. Clifton [a, *]

[a] School of Pharmacy and Medical Sciences & Sansom Institute for Health Research, University of South Australia, GPO Box 2471, Adelaide, SA 5000, Australia
[b] Baker IDI Heart and Diabetes Institute, 75 Commercial Road, Melbourne, VIC 3004, Australia
[c] Nutraceuticals Research Group, 305C Medical Science Building, University of Newcastle, Callaghan, Australia

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ABSTRACT

Objective: To determine the dietary predictors of central blood pressure, augmentation index and pulse wave velocity (PWV) in subjects with type 1 and type 2 diabetes. **Methods**: Participants were diagnosed with type 1 or type 2 diabetes and had PWV and/or pulse wave analysis performed. Dietary intake was measured using the Dietary Questionnaire for Epidemiological Studies Version 2 Food Frequency Questionnaire. Serum lipid species and carotenoids were measured, using liquid chromatography electrospray ionization–tandem mass spectrometry and high performance liquid chromatography, as biomarkers of dairy and vegetable intake, respectively. Associations were determined using linear regression adjusted for potential confounders. **Results**: PWV ($n = 95$) was inversely associated with reduced fat dairy intake ($\beta = -0.01$; 95% CI −0.02, −0.01; $p = 0 < 0.05$) in particular yoghurt consumption ($\beta = -0.04$; 95% CI −0.09, −0.01; $p = 0 < 0.05$) after multivariate adjustment. Total vegetable consumption was negatively associated with PWV in the whole cohort after full adjustment ($\beta = -0.04$; 95% CI −0.07, −0.01; $p < 0.05$). Individual lipid species, particularly those containing 14:0, 15:0, 16:0, 17:0 and 17:1 fatty acids, known to be of ruminant origin, in lysophosphatidylcholine, cholesterol ester, diacylglycerol, phosphatidylcholine, sphingomyelin and triacylglycerol classes were positively associated with intake of full fat dairy, after adjustment for multiple comparisons. However, there was no association between serum lipid species and PWV. There were no dietary predictors of central blood pressure or augmentation index after multivariate adjustment. **Conclusion**: In this cohort of subjects with diabetes reduced fat dairy intake and vegetable consumption were inversely associated with PWV. The lack of a relationship between serum lipid species and PWV suggests that the fatty acid composition of dairy may not explain the beneficial effect.

1. Introduction

The number of people with diabetes is projected to be 7.7% worldwide by 2030, an increase of 54% since 2010 [1]. Individuals with type 1 and type 2 diabetes have approximately double the risk of cardiovascular disease (CVD) compared to the general population [2,3]. Dietary intake is a modifiable risk factor for CVD with studies showing that better dietary quality reduces the risk of CVD [4,5].

Arterial stiffness, which can be measured by carotid femoral pulse wave velocity (PWV) and augmentation index, is a predictor of CVD [6,7]. A meta-analysis of individual participant data from 17 studies (17 635 subjects) showed that PWV independently predicted CVD and CVD mortality such that per 1 standard deviation increase in PWV the hazard ratio was 1.30 (95% CI 1.18, 1.43) and 1.28 (95% CI 1.15, 1.43), respectively, after adjustment for established risk factors. Furthermore, the addition of PWV to conventional Framingham risk factors improved 10 year CVD risk prediction by 13% in those at intermediate risk of CVD [7]. Elevated central blood pressure and a larger augmentation index have also

* Corresponding author.
E-mail addresses: kristina.petersen@mymail.unisa.edu.au (K.S. Petersen), jennifer.keogh@unisa.edu.au (J.B. Keogh), peter.meikle@bakeridi.edu.au (P.J. Meikle), manohar.garg@newcastle.edu.au (M.L. Garg), peter.clifton@unisa.edu.au (P.M. Clifton).

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been shown to increase the risk of a cardiovascular event [6].

The SEARCH for Diabetes in Youth Study, involving children aged ≥10 years with type 1 diabetes, showed that a dietary pattern, determined by reduced rank regression, high in sugar sweetened and diet beverages, eggs, potatoes, high fat meat and low in dairy was associated with higher augmentation index and PWV; however the relationship with PWV did not persist after adjustment for cofounders [8]. Epidemiological studies conducted in cohorts without diabetes suggest that fruit and vegetables [9–11] and dairy [12,13] may be inversely associated with PWV. The aim of this study is to determine the dietary predictors of central blood pressure, augmentation index and PWV in subjects with type 1 and type 2 diabetes.

2. Methods

2.1. Study methods

This is a cross-sectional study of the association between dietary intake and arterial stiffness in subjects with type 1 and type 2 diabetes. One hundred and fifty subjects were recruited by public advertisement between August 2012 and December 2013. Subjects eligible for inclusion were adults (age > 18 years) with diagnosed type 1 or type 2 diabetes for any duration managed with diet, oral hypoglycaemic agents (OHA) and/or insulin. Subjects were excluded if they had cancer, unstable CVD requiring intervention, heart failure, significant renal impairment (eGFR < 30 ml/min) or liver disease. This study includes data from participants who had PWV ($n = 95$) and/or pulse wave analysis measurements ($n = 111$) performed. Thirty nine-participants did not have PWV or pulse wave analysis performed because the equipment was not available and PWV data were available for only 95 participants because of technical difficulty performing the measurement due to obesity. Ethics approval was obtained from the University of South Australia Human Research Ethics Committee and the trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12612001052820).

Subjects attended the clinic after an overnight fast. Anthropometric measurements, pulse wave analysis, PWV and blood pressure were performed by one operator and a blood sample was taken. Participants completed the online version of the Dietary Questionnaire for Epidemiological Studies Version 2 Food Frequency Questionnaire (DQES v2 FFQ) to determine habitual dietary intake.

2.2. Anthropometric measurements

Height was measured using a stadiometer (SECA, Hamburg, Germany) to the nearest 0.1 cm while barefoot or in flat footwear. Weight was measured to the nearest 0.05 kg using calibrated electronic scales (SECA, Hamburg, Germany) while the participants were barefoot or in light footwear and wearing light clothing.

2.3. Blood pressure

Clinic brachial blood pressure was measured using an automated sphygmomanometer (SureSigns VS3; Philips, North Ryde, Australia) once the participant had been seated for 5 min. A normal sleeve (16 × 52 cm) was used for an arm circumference of 24–32 cm and a large sleeve (16 × 70 cm) for an arm circumference of 32–42 cm. A minimum of four consecutive readings were taken at 1 min intervals while subjects were sitting quietly and alone. The first reading was discarded and the following three consistent measurements i.e. systolic blood pressure within a range of 10 mmHg, were used [14].

2.4. Pulse wave analysis

A SphygmoCor® XCEL (AtCor Medical, West Ryde, Australia) was used to perform pulse wave analysis as previously described [15]. Briefly, a cuff was placed over the brachial artery on the right arm to measure central blood pressure, augmentation index and augmented pressure. A normal sleeve (16 × 52 cm) was used for an arm circumference of 23–33 cm and a large sleeve (16 × 70 cm) for an arm circumference of 31–40 cm. After the participants had been quietly resting for 5 min, 3 consecutive measurements were taken. The coefficient of variation (CV) was 11% ($n = 5$).

2.5. Pulse wave velocity

A SphygmoCor® XCEL (AtCor Medical, West Ryde, Australia) was used to measure right carotid femoral PWV as previously described [15]. Three measurements were performed and all of the measurements were taken by one operator with a CV of 4.2% ($n = 28$).

2.6. Laboratory analysis

Serum total cholesterol, HDL cholesterol, triglycerides, C reactive protein (CRP) and glucose were measured using a Konelab 20XTi automatic analyser (Thermo Electron Corporation, Louisville, CO, USA) with reagents from Thermo Fisher Scientific (Melbourne, Australia). LDL cholesterol was calculated using the Friedewald formula ((total cholesterol − HDL cholesterol) − (triglycerides × 0.45)) [16]. Subjects with a serum CRP >10 mg/L were excluded from the analysis. Serum carotenoids were measured by high performance liquid chromatography according to a previously published protocol [17]. Lipid analysis was performed by liquid chromatography, electrospray ionization–tandem mass spectrometry as previously published [18]. Briefly, 333 individual lipid species from 25 classes were measured and the median intra assay CV was 8%.

2.7. Dietary analysis

Habitual dietary intake was measured using the electronic version of the DQES v2 FFQ. This FFQ has been found to have relatively good agreement with a 3 day weight food record [19]. It classifies more than two thirds of subjects within one quintile, for all nutrients, compared with a 3 day weighed food record [20].

2.8. Statistical analysis

Data are presented as mean ± standard deviation or median (interquartile range) depending on the distribution. Data were checked for normality using Shapiro–Wilk and Kolmogorov–Smirnov values. Pearson's correlation was used to determine univariate relationships and stepwise multivariate linear regression was used to determine predictors of central blood pressure, augmentation index and PWV. Variables that were correlated ($p < 0.1$) with the variable of interest in Pearson's correlation were entered into a stepwise linear regression to determine predictors. Linear regression analysis was adjusted for predictors identified in the stepwise linear regression and outliers (±2 standard deviations) were removed. To determine the level of under-reporting the Schofield equation was used to calculate Basal Metabolic Rate [21] and the Goldberg cut-off was applied [22]. Significant under-reporting was observed. Therefore intake is reported as a percentage of total energy intake or units per 1000 kJ. Serum carotenoids and serum lipid concentrations were normalised to their respective interquartile ranges to account for the variation in relative abundance in serum. Therefore the β-coefficients obtained