



Applied nutritional investigation

Associations between major dietary patterns and biomarkers of endothelial dysfunction in two urban midsized cities in Argentina

María Daniela Defagó Ph.D. ^{a,b,c,*}, Natalia Elorriaga M.Sc. ^b, Aldo Renato Eynard Ph.D. ^c,
Rosana Poggio M.Sc. ^b, Laura Gutiérrez M.Sc. ^b, Vilma Edith Irazola M.Sc. ^b, Adolfo Luis Rubinstein Ph.D. ^b

^a Instituto de Investigaciones en Ciencias de la Salud (INICSA), CONICET, Universidad Nacional de Córdoba, Ciudad Universitaria, Córdoba, Argentina

^b Centro de Excelencia en Salud Cardiovascular para el Cono Sur (CESCAS/SACECH), Instituto de Efectividad Clínica y Sanitaria (IECS), Buenos Aires, Argentina

^c Escuela de Nutrición, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Edificio Escuelas, Ciudad Universitaria, Córdoba, Argentina

ARTICLE INFO

Article History:

Received 10 May 2018

Received in revised form 15 May 2019

Accepted 9 June 2019

Keywords:

Diet
Endothelium
Markers
Argentina

ABSTRACT

Objective: We examined whether dietary patterns (DPS) are associated with endothelial dysfunction (ED) markers in an Argentinian population.

Research Methods & Procedures: The sample in this cross-sectional study was derived from 1,983 subjects from two mid-sized cities in Argentina who were involved in the CESCAS I Study. To define DP, a food-frequency questionnaire was applied. In a subsample randomly selected from the primary cohort, serum concentrations of C-reactive protein (hs-CRP), soluble vascular cell adhesion molecule-1 (sVCAM-1), soluble intercellular adhesion molecule-1 (sICAM-1), and soluble E selectin (sSELE) were determined. Correlations and multiple linear regression models were used to assess the relation between each quartile of DP adherence score and ED markers (Q1 lowest adherence; Q4 highest adherence).

Results: Three DPs were identified: Traditional (TDP), Prudent (PDP), and Convenience and processed (CDP). TDP was characterized by higher intake of refined grains, red meat, whole fat dairy products, vegetable oils, and “mate”, a traditional South American infused drink; PDP was characterized by higher intake of vegetables, fruit, low-fat dairy products, whole grains, and legumes; and CDP consisted mainly of processed meat, snacks, pizza, and “empanadas”, a stuffed bread served baked or fried. Lower scores (Q2, Q3) in TDP were inversely associated with concentrations of sSELE ($P < 0.0001$ and $P < 0.05$, respectively). In PDP, higher scores were inversely associated with hs-CRP, whereas lower scores showed a positive relation with sSELE ($P < 0.05$). Contrariwise, higher scores in CDP were directly associated with sSELE concentrations ($P < 0.05$).

Conclusion: Adherence for each DP identified is differentially related to ED markers in the studied population.

© 2019 Elsevier Inc. All rights reserved.

Introduction

Cardiovascular diseases (CVDs) have become an omnipresent cause of morbidity and a leading contributor of mortality in most countries. For example, in Argentina, CVDs represent 34.2% of deaths [1]. The World Health Organization estimates there will be about 20 million deaths from CVD in 2015, accounting for 30% of all deaths worldwide [2]. Nowadays, CVD is the largest single

contributor to global mortality and will continue to dominate mortality trends in the future [3].

The endothelial system is integrated by a number of powerful vasoconstrictor peptides and their receptors, secreted by endothelial cells such as EDN1 (endothelin-1) and NOS₃ (endothelial NO synthase). These molecules participate in the contraction and relaxation processes of vascular smooth muscle cells [4]. Furthermore, elevated levels of endothelial adhesion molecules such as soluble vascular cell adhesion molecule 1 (sVCAM-1) in blood and E-selectin (sSELE) are related to increased blood pressure [5]. These endothelial adhesion molecules have been implicated in the pathogenesis of the early stages of the atherosclerotic process [6]. The concentrations of soluble endothelial adhesion molecules could be elevated in patients who do not have yet clinically manifested CVD but have well-known coronary risk factors, such as smoking, hypertension, and hypercholesterolemia. In addition, markers of systemic inflammation and endothelial dysfunction are predictors of CVD [7].

The National Heart, Lung, and Blood Institute grant number HHSN268200900029 C and SeCyT-UNC (Universidad Nacional de Córdoba, Argentina, RHCS 313/16) supported this work. MDD, NE, and ALR were responsible for conception and design of study. MDD and NE collected, analyzed, and interpreted data with assistance from RP, VEI, ARE, and LG. MDD wrote the manuscript with contribution from NE, RP, ALR, and ARE. All authors approved of the final version of the manuscript.

* Corresponding author. Tel./Fax: (+54-351)433-4021.

E-mail addresses: danieladefago@hotmail.com, ddefago@iecs.org.ar (M.D. Defagó).

The expression *endothelial dysfunction* (ED) refers to any pathophysiological alteration of the endothelium, usually chronic and subtle, that produces a progressive imbalance of regulatory functions. ED is considered the main cause of development and progression of the atherosclerotic process. ED is influenced by several risk factors that are also associated with the CVD, such as hypertension and prothrombotic status [8,9].

The relationship between dietary factors and CVD has been studied extensively, and ED is one of the mechanisms linking diet and the risk of CVD. There is strong evidence that dietary patterns (DP) with high intakes of vegetables, legumes, fruits, nuts, whole-grain products, cheese or yoghurt, and monounsaturated rather than saturated fats (also called “prudent diets”) offer protection against CVD. DPs have shown a relation to some plasma markers of CVD risk. Actually, results of recent studies suggest that eating a prudent type of diet with abundant fruits and vegetables is associated with lower concentrations of C-reactive protein (a reliable marker of low and persistent levels of inflammation related to CVD risk) and other inflammatory parameters [10–12]. However, information about the possible interactions between dietary factors and markers of endothelial dysfunction and inflammation is still limited.

The aim of the present study was to examine whether food patterns built using principal component analysis are associated with markers of endothelial dysfunction.

Materials and methods

Participants

This research is nested study in the CESCAS I (Centro de Excelencia en Salud Cardiovascular para América del Sur). CESCAS I is the first longitudinal study to estimate the CVD trend and risk factors in Argentina, Chile, and Uruguay. This study entails a probabilistic sample of 7524 non-institutionalized mainly urban men and women between the ages of 35 and 74 y representing the general adult population in these countries. Four midsize cities have been selected: two in Argentina (Bariolche and Marcos Paz), one in Chile (Temuco), and one in Uruguay (Pando-Barros Blancos). The methodology of this research has been published elsewhere [13]. For the present study, only the Argentinian sample included in CESCAS study ($n = 1983$) was considered.

This study was conducted in accordance with the guidelines laid down in the Declaration of Helsinki, and all procedures involving human participants were approved by the institutional review boards (IRBs) in all participating centers in Argentina, Chile, Uruguay, and the United States, as well as by the National Heart, Lung and Blood Institute of the National Institutes of Health. Written informed consent was obtained from all participants.

Assessment of dietary intake

Dietary information was collected via a food frequency questionnaire (FFQ), which evaluated the usual consumption. We employed the National Cancer Institute Diet History Questionnaire, adapted and validated for the purposes of our research [14]. The paper-based and self-administered FFQ queries the frequency of intake for 126 separate food items during the last 12 mo and asks the portion size for most of these by providing a choice of three sizes, including major traditional foods and key foods available in stores. Food items were grouped in 19 major food and beverage categories on the basis of nutrient profiles or culinary practice. With the help of real-size pictures, the selected frequency category and portion size for each food item was converted to a daily intake. Nutrient intakes were estimated by summing up the nutrient contribution of all items. The nutrient content and portion size of each item were obtained from a nutrient database derived from the Argenfoods Database and Latinfood Database, data compiled for the National Health and Nutrition Survey in Argentina [15–17].

Assessment of other variables

During the home survey, information was obtained on demographic characteristics, including age, sex, and personal history of CVD and risk factors. Physical activity was evaluated using the International Physical Activity Questionnaire–Long Form [18]. Information about current and former cigarette smoking was assessed using the Global Adult Tobacco Survey, and alcohol consumption by using cross-culturally adapted questionnaires from the Hispanic Community Health Study/Study of Latinos [19,20].

Anthropometric measurements were obtained by trained and certified observers using standard protocols and techniques. During the health center visit, three

blood pressure measurements were obtained with the participant in the seated position after 5 min of rest using a standard mercury or aneroid sphygmomanometer, and the mean of three readings was used for analysis [21]. Body weight and height were measured twice during the examination and the average of two measurements was used in all analyses. Weight was measured in light indoor clothing without shoes, in kilograms to one decimal place, using standing scales. Height was measured without shoes, in centimeters to one decimal place using a wall-mounted stadiometer. The body mass index (BMI) was calculated by weight divided by height in meters squared (kg/m^2).

Laboratory tests

A subsample of 187 participants was randomly selected from the primary Argentinian cohort. Participants with previous cardiovascular events or on lipid-lowering and antiplatelet treatments were excluded.

Blood samples were obtained by venipuncture after a 12-h overnight fast. Measurement of high-sensitivity C-reactive protein (hs-CRP) was carried out using the turbidometric hs-CRP test (Wiener Lab).

Concentrations of sSELE, soluble intercellular adhesion molecule (sICAM-1), and sVCAM-1 were measured by using a commercial enzyme-linked immunosorbent assay (R&D Systems).

Statistical analysis

In the subsample, baseline demographic characteristics were calculated as means and SD for continuous variables or as numbers and percentages for categorical variables.

The procedure for deriving DPs by using food consumption data from the FFQ has been described in detail elsewhere [22]. Derived DPs were calculated with the complete Argentinian sample including in CESCAS study. We performed principal component analysis to derive DPs based on food groups. The number of factors retained was based on the following criteria: components with an eigenvalue > 1 , scree plot test, and the interpretability of the factors. Food items were considered to load on a factor if they had an absolute correlation ≥ 0.35 . Three main factors with eigenvalues > 0.30 , which together accounted for 25% of the total variation, were extracted after orthogonal (varimax) rotation.

The factor score for each DP was designed by summing observed intakes of the component food items weighted by factor loadings, so each person received a factor score for each identified DP. Relationships among the DPs and studied variables were examined across quartiles of each factor. The first quartile represented the participants who had the lowest adherence to the DP and the fourth quartile represented the participants who had the highest. Linear regression was used to calculate unadjusted means of participant characteristics and biochemical markers related to inflammation and endothelial activation in each quartile of DP score.

Two multivariate models were used to assess the relation between each DP score and hs-CRP, sICAM, sVCAM, and sSELE concentrations. We used log-transformed serum concentrations of biomarkers to achieve normal distributions. In model 1, adjustments were made for age, sex, current smoking, alcohol drinking, and physical activity. Model 2 included the variables in model 1 plus BMI.

Tests for trend across DP were conducted within multivariable regression models by using DP score as a continuous variable. All analyses were performed with Stata statistical software package Version 11.0 ($P < 0.05$).

Results

Table 1 shows the basic characteristics of the study participants. The mean age was 52 y for men and 51 y for women. Heavy and moderate drinkers accounted for 58% of men and 33% of women, and current smokers represented 31% of men and 30% of women. Men and women had a similar average BMI (29.7 versus 29.5 kg/m^2). The physical activity level was low in both men and women (93.2% versus 93.6%). E-selectin and diastolic blood pressure were significantly higher in men than in women ($P < 0.01$).

Three DP were identified by factor analysis (Table 2). The first factor (traditional dietary pattern [TDP]), was characterized by a high intake of refined grains, red meat, whole-fat dairy products, vegetable oils, and mate, a traditional South American infused drink commonly consumed in Argentina, Uruguay, and to a lesser degree, also in Chile; the second factor (prudent dietary pattern [PDP]) was characterized by a high intake of vegetables, fruit, low-fat dairy products, whole grains, and legumes; the third factor (convenience and processed food dietary pattern [CDP]) consisted

Table 1
Characteristics of study participants

Characteristic	Men (n = 77)	Women (n = 110)	P
Age (y), mean	51.6	52.1	0.76
SD	1.3	0.9	
Alcohol, n (%)			
Non-drinker	32 (43.2)	73 (66.4)	0.003
Moderate drinker	37 (50.0)	36 (32.8)	
Heavy drinker	5 (6.8)	1 (0.9)	
Smoking, n (%)			
Never smoker	28 (36.4)	66 (60.0)	<0.0001
Former smoker	26 (33.8)	12 (10.9)	
Current smoker	23 (29.8)	32 (29.1)	
Body mass index (kg/m ²), mean	29.7	29.5	0.76
SD	5.2	6.2	
Physical activity level, n (%)			
Low physical activity	69 (93.2)	103 (93.6)	0.67
Moderate physical activity	8 (6.8)	7 (6.4)	
hs-CRP (ng/mL), mean	4.06	4.04	0.70
SD	1.76	1.67	
sICAM-1 (ng/mL), mean	405.4	403.4	0.93
SD	20.5	15.9	
sVCAM-1 (ng/mL), mean	781.1	787.2	0.99
SD	45.1	34.4	
sSELE (pg/mL), mean	52.8	41.1	<0.0001
SD	2.02	1.8	
Systolic blood pressure (mm Hg), mean	127.6	127.1	0.85
SD	2.3	2.10	
Diastolic blood pressure (mm Hg), mean	84.6	80.4	0.008
SD	1.3	0.9	

hs-CRP, high-sensitivity C-reactive protein; sICAM-1, soluble intercellular adhesion molecule 1; sSELE, soluble E-selectin; sVCAM-1, soluble vascular cell adhesion molecule 1

P values for sex differences are based on *t* tests for continuous variables and χ^2 tests for categorical variables. Values are mean and standard deviations (SD) for continuous variables and number (percentage) for categorical variables.

mainly of processed meat, snacks, pizza, and empanadas, a baked or fried meat-stuffed bread.

Table 3 shows the characteristics of participants according to quartiles of three DP scores. In TDP, serum concentrations of sSELE were lower in individuals with intermediate quartiles (Q2 and Q3) compared with quartiles (Q1 and Q4, $P < 0.001$). On the other hand, serum concentrations of hs-CRP were lower with higher PDP scores ($P = 0.05$).

The results of multivariate analyses are presented in Table 4. Lower scores in the TDP were inversely correlated to serum concentrations of sSELE ($P < 0.0001$). In PDP, higher scores were inversely associated with hs-CRP, whereas lower scores had a positive relation with sSELE ($P < 0.05$). On the contrary, higher scores in CDP were directly associated with sSELE concentrations ($P < 0.05$). We did not see important differences between the β coefficients before and after adjustment for BMI.

Discussion

During the last decades, the study of DP has become more linked to nutritional epidemiology and several articles have been published on the association between diet and several chronic disease risks [23]. The present report is the first cross-sectional study of DPs in an Argentinian population and their influence on markers of endothelial function. Analysis of our findings revealed some similarities and some differences with previous reports in other countries. In our population, men had higher sSELE levels than women. A number of previous studies have reported higher sSELE levels in men compared with women [24–26]. One potential explanation for this result could be the protective effect of female

Table 2
Factor-loading matrix for dietary patterns from food frequency questionnaires*

Foods	Traditional dietary pattern Factor 1	Prudent dietary pattern Factor 2	Convenience and processed food dietary pattern Factor 3
White bread and crackers	0.63		
Sugar/marmalade/jam	0.58		
Red meat (beef)	0.58		0.31
Other fat spreads (margarine/lard/butter)	0.55		
Vegetable oils	0.47		
Pasta/refined cereals/rice	0.47		
High-fat dairy products	0.44		
Poultry	0.43		
Mate	0.40		
Potatoes and other tubers	0.38	0.30	
Egg	0.37		
Cookies	0.34		
Mayonnaise	0.33		
Other vegetables		0.72	
Dark-yellow vegetables		0.67	
Green leafy vegetables		0.64	
Fruits		0.61	
Legumes and whole grains		0.44	
Low-fat dairy products		0.39	
Cereal bars/breakfast cereal		0.36	
Tomatoes		0.35	
Processed meats	0.35		0.66
Snacks			0.54
Other meats			0.52
Pizza and empanadas			0.47
Confectionery	0.32		0.34
Organ meat			0.33
Sweets and desserts			0.33
Variance explained (%)	13.04	6.33	5.75

*Varimax rotation. Foods or food groups with factor loadings <0.30 were not listed.

sex hormones against endothelial dysfunction [27,28]. Other authors propose that BMI is an influencing factor for sSELE concentration [29]. However, although a high percentage of our population were overweight, we did not find differences between sex and BMI. Besides, men presented a higher intake of alcohol and tobacco (especially in the former smokers group, both being risk factors for ED) [30,31]. In this sense, these facts could explain the higher level of diastolic blood pressure also identified in men.

A large proportion of the sample had low levels of physical activity (<600 mets/min per week). Physical inactivity is an established risk factor for CVD, and it is related to an increased risk of obesity, diabetes, and hypertension [32]. The third National Survey of Risk Factors in Argentina (2015) established a lower prevalence of low physical activity than in our study (54.7%), similar to the data from the second survey, carried out in 2009 [33]. In the Southern Cone, a recent report from the CESCAS I study found that about 35.2% of adults had low physical activity, and it is strongly related with obesity [34].

In our study, three DPs were identified by factor analysis. The PDP (higher intakes of vegetables, fruit, whole food), TDP (higher intakes of meat, eggs, and fats), and CDP (processed meat, snacks, pizza, and empanadas) identified in our study are analogous to similar patterns described in previous studies of South American populations [35–37]. The immigration and cultural influences in Argentina, combined with the availability and accessibility of the market, among other factors, conform to the DP. In 2004 to 2005 the National Nutrition and Health Survey was conducted in Argentina. It was found that the national DP included cereals and derivatives (39% of total energy intake), sweets and beverages (19%), meat and eggs (16%), fats or oils (11%), dairy products (8%), and

Table 3
Characteristics of study participants according to quartiles (Q) of dietary pattern score for three empirically derived dietary patterns

	Traditional dietary pattern				Prudent dietary pattern				Convenience and processed food dietary pattern			
	Q1 (n=47)	Q2 (n=46)	Q3 (n=46)	Q4 (n=48)	Q1 (n=46)	Q2 (n=45)	Q3 (n=47)	Q4 (n=49)	Q1 (n=47)	Q2 (n=46)	Q3 (n=47)	Q4 (n=47)
Age, mean	51.6	52.3	50.3	52.3	49.3	51.3	51.2	54.5	50.2	52.9	51.1	52.1
SD	10.9	13.1	10.9	9.6	9.1	12.7	11.1	10.9	10.4	10.3	11.4	12.2
BMI, mean	30.8	29.5	29.4	28.8	29.3	29.7	29.2	30.4	28.5	28.8	30.2	30.6
SD	6.8	4.9	6.1	5.4	6.8	5.7	5.2	5.7	5.8	5.7	5.9	5.9
hs-CRP (mg/L), mean	3.9	4.8	4.6	5.2	5.51	5.67	3.66	3.83	4.6	5.6	4.7	3.44
SD	0.19	0.43	0.44	0.49	0.41	0.84	0.46	0.39	0.47	0.74	0.44	0.85
sVCAM-1 (ng/mL), mean	402.5	397.5	384.4	457.5	419.1	461.4	377.7	382.2	404.7	421.5	390.1	423.2
SD	17.5	14.7	15.4	19.2	18.4	61.6	71.3	15.2	18.2	17.6	12.9	18.7
sVCAM-1 (ng/mL), mean	790.1	764.5	740.9	810.1	825.8	881.3	742.9	734.1	815.2	780.6	807.4	814.2
SD	36.7	33.2	33.8	43.3	36.9	40.9	34.7	35.8	39.6	38.4	27.8	41.1
sSELE (pg/mL), mean	51.9	38.9	43.9	48.4	53.3	45.3	42.5	42.5	40.9	45.3	47.5	39.7
SD	2.8	1.8	2.2	6.7	7.5	9.4	8.3	6.7	7.1	7.4	9.6	9.7
Systolic blood pressure (mm Hg), mean	127.6	129.5	128.4	123.5	124.2	129.7	126.9	128.8	125.6	127.1	130.4	128.7
SD	27.8	17.5	21.1	15.4	21.7	20.4	19.0	21.7	19.6	18.4	21.4	22.7
Diastolic blood pressure (mm Hg), mean	81.4	82.8	83.1	81.2	81.8	84.4	80.8	81.5	81.5	82.4	82.6	81.9
SD	8.6	10.4	10.2	11.8	10.3	9.4	10.4	11.1	8.9	11.8	10.3	10.5

BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein; sVCAM-1, soluble intercellular adhesion molecule 1; sSELE, soluble E-selectin; sVCAM-1, soluble vascular cell adhesion molecule 1. P value for linear trend.

fruit and vegetables (7%) [38]. The detected TDP was similar to the National Nutrition and Health Survey information, with a high prevalence of refined grain, red meat, whole-fat dairy product, vegetable oil, and mate intake. Although the PDP was detected, including some healthy components reported by other authors in their definition of DP, the fruit and vegetable intake remains very low in Argentina [39–41]. Regarding CDP, several researchers have reported a high intake of processed food, and their consumption is now rapidly increasing [42–44].

We found several statistical differences in endothelial markers concentrations and blood pressure across quartiles of DP score. Intermediate quartiles of TDP were inversely associated with sSELE serum concentrations. In addition, we found an inverse association between lower scores of TDP and sSELE. Westernized DP (high intakes of processed meats, eggs, red meats, high-fat dairy products and refined grains; similar in some aspects to our TDP) have been related to higher concentrations of CRP, sSELE, sICAM-1, and sVCAM-1 [45–47]. This DP contains the biggest food sources of saturated and trans fatty acids, and they may perturb endothelial function. The systemic level of soluble adhesion molecules varies with the consumption of different fatty acids. The intake of diets rich in saturated fatty acids is associated with increased postprandial vascular reactivity. For example, the degree of saturation of the fatty acid influences the ability of reconstituted HDL to inhibit VCAM-1 expression by activated endothelial cells [48,49]. A higher intake of saturated fatty acids is associated with lower number of hepatic LDL lipoprotein receptors and elevated concentrations of total cholesterol and low-density lipoprotein cholesterol [50]. Furthermore, trans fatty acids are incorporated into endothelial cell membranes and may alter cellular and macromolecular components of the blood vessel wall. This alteration may affect the antihemostatic properties, triggering altered vascular tone, hyperadhesiveness of blood leukocytes, and increased cytokine and growth factor production [51].

We found lower levels of hs-CRP in higher scores of PDP. Moreover, in the multivariate model, higher scores—more adherence to a prudent diet—were inversely associated with hs-CRP. On the contrary, lower scores—less adherence—were directly related to more elevated sSELE concentrations. Diets higher in fruits, vegetables, and fish, rich in antioxidant vitamins and ω -3 fatty acids, have beneficial effects on vascular endothelial function improving the endothelium-dependent vasodilation [45]. Our results are similar to those of other authors [46,47,52]. CRP is an acute-phase protein involved in inflammation, and elevated blood levels of CRP are associated with age, obesity, smoking, and alcohol intake and a lower level of physical activity. Also, elevated concentrations of CRP have been found to predict the development of type 2 diabetes mellitus, and this fact is corroborated in spontaneous diabetic rats [53,54]. sSELE molecules are expressed in vascular endothelium and on immune and inflammatory cells and mediate the adhesion and transmigration of leukocytes to vascular endothelium [55]. A healthy diet has been related to reduced inflammation markers, such as CRP and interleukin-6 [56,57]. We also found a direct association between higher scores of CDP and sSELE levels. CDP includes processed food products, some of them heavily industrialized and containing elevated amounts of saturated fat, sugar, sodium, or additives, which are related to increased risk for chronic diseases [58]. In this context, growing evidence exists about the negative effects of processed food intake—especially red meat—on CVD and type 2 diabetes [59,60].

Some limitations of the present study must be considered. First, it is of cross-sectional design; therefore, we cannot infer

Table 4**β** Coefficients regression for the relation between dietary patterns scores and log-transformed endothelial biomarkers

	Traditional dietary pattern				Prudent dietary pattern				Convenience and processed food dietary pattern			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Standardized score*	-1.03	-0.45	0.14	1.40	-1.12	-0.46	0.24	1.36	-1.34	-0.12	0.40	1.07
Model 1 (β)												
Log hs-CRP	Ref.	0.07	-0.10	-0.17	Ref.	0.44	-0.72 [†]	-0.56	Ref.	0.65	0.13	-0.10
Log sICAM-1	Ref.	-0.001	-0.04	0.09	Ref.	0.11	-0.10	-0.10	Ref.	-0.05	0.03	-0.05
Log sVCAM-1	Ref.	-0.06	-0.09	0.06	Ref.	-0.008	-0.08	-0.22	Ref.	-0.03	0.01	0.09
Log sSELE	Ref.	-0.37*	-0.19 [†]	-0.11	Ref.	0.21 [†]	0.03	-0.02	Ref.	0.12	0.23 [†]	0.19 [†]
Model 2 (β)												
Log hs-CRP	Ref.	0.05	-0.08	0.13	Ref.	0.42	-0.74 [‡]	-0.54	Ref.	0.66	0.22	-0.07
Log sICAM-1	Ref.	-0.003	-0.04	0.08	Ref.	0.11	-0.10	-0.10	Ref.	-0.05	0.04	-0.05
Log sVCAM-1	Ref.	-0.06	-0.09	0.04	Ref.	-0.01	-0.09	-0.26	Ref.	-0.02	0.04	0.11
Log sSELE	Ref.	-0.36*	-0.20 [†]	-0.08	Ref.	0.23 [‡]	0.04	-0.03	Ref.	0.12	0.18 [†]	0.17 [†]

hs-CRP, high-sensitivity C-reactive protein; sICAM-1, soluble intercellular adhesion molecule 1; sSELE: soluble E-selectin; sVCAM-1, soluble vascular cell adhesion molecule 1. Model 1: Coefficients adjusted for age, sex, current smoking, alcohol drinking, and physical activity.

Model 2: Model 1 + body mass index (BMI).

* $P < 0.0001$.

[†] $P < 0.05$.

[‡] $P < 0.01$.

causality from our results. Second, the relatively small sample size. For this reason, these findings cannot be generalized to the broader community based on this study alone. Third, our factor analysis was limited in terms of subjectivity in determining and labeling DP and the difficulty in extrapolating the findings to other populations. However, the results are the first report in our population about the influence of DP on markers of endothelial function.

In conclusion, the present study supports the hypothesis that detected major DP are related to markers of ED in the studied Argentinian population and findings may be applicable as well to other South Americans, particularly in Uruguay and Chile. Finally, these data lend further support to dietary recommendations to improve diet quality. Further studies are warranted to determine the causal direction of the relationship of DP and ED.

References

- Rubinstein A, Colantonio L, Bardach A, Caporale J, Marti SG, Kopitowski K, et al. Estimation of the burden of cardiovascular disease attributable to modifiable risk factors and cost-effectiveness analysis of preventative interventions to reduce this burden in Argentina. *BMC Public Health* 2010;10:627.
- World Health Organization. Preventing chronic diseases: a vital investment. Available at: http://www.who.int/chp/chronic_disease_report/full_report.pdf. Accessed July 2017.
- World Health Organization. World health statistics 2009. Available at: http://www.who.int/gho/publications/world_health_statistics/EN_WHS09_Full.pdf. Accessed March 2017.
- Gregoski MJ, Barnes VA, Tinggen MS, Dong Y, Zhu H, Treiber FA. Differential impact of stress reduction programs upon ambulatory blood pressure among African American adolescents: influences of endothelin-1 gene and chronic stress exposure. *Int J Hypertens* 2012;2012:510291.
- Mulvihill NT, Foley JB, Crean P, Walsh M. Prediction of cardiovascular risk using soluble cell adhesion molecules. *Eur Heart J* 2002;23:1569–74.
- Ross R. Atherosclerosis—an inflammatory disease. *Am Heart J* 1999;138:S419–20.
- Głowińska-Olszewska B, Tołwińska J, Łuczyński W, Konstantynowicz J, Bosowski A. Cardiovascular risk in nonobese hypertensive adolescents: a study based on plasma biomarkers and ultrasonographic assessment of early atherosclerosis. *J Hum Hypertens* 2013;27:191–6.
- Davignon J, Ganz P. Role of endothelial dysfunction in atherosclerosis. *Circulation* 2004;109(Suppl 1):III27–32.
- Defagó MD, Gu D, Hixson JE, Shimmin LC, Rice TK, Gu CC. Common genetic variants in the endothelial system predict blood pressure response to sodium intake: the GenSalt study. *Am J Hypertens* 2013;26:643–56.
- Oude Griep LM, Wang H, Chan Q. Empirically-derived dietary patterns, diet quality scores, and markers of inflammation and endothelial dysfunction. *Curr Nutr Rep* 2013;2:97–104.
- Defagó MD, Elorriaga N, Irazola VE, Rubinstein AL. Influence of food patterns on endothelial biomarkers: a systematic review. *J Clin Hypertens (Greenwich)* 2014;16:907–13.
- van Bussel BC, Henry RM, Ferreira I, van Greevenbroek MM, van der Kallen CJ, Twisk JW. A healthy diet is associated with less endothelial dysfunction and less low-grade inflammation over a 7-year period in adults at risk of cardiovascular disease. *J Nutr* 2015;145:532–40.
- Rubinstein AL, Irazola VE, Poggio R, Bazzano L, Calandrelli M, Lanús Zanetti FT, et al. Detection and follow-up of cardiovascular disease and risk factors in the Southern Cone of Latin America: the CESCAS I study. *BMJ Open* 2011;1:e000126.
- Elorriaga N, Irazola VE, Defagó MD, Britz M, Martínez-Oakley SP, Witriw AM, et al. Validation of a self-administered FFQ in adults in Argentina, Chile and Uruguay. *Public Health Nutr* 2014;14:1–9.
- Universidad Nacional de Luján. Tabla de Composición de Alimentos. Available at: <http://www.argenfoods.unlu.edu.ar>. Accessed December 2016.
- FAO. Tabla de composición de alimentos de América Latina (2016). Available at: <http://www.rlc.fao.org/es/conozca-fao/que-hace-fao/estadisticas/composicion-alimentos>. Accessed December 2016.
- Ministerio de Salud de la Nación, Argentina. Dirección de Maternidad e Infancia. Available at: <http://www.msal.gov.ar/promin>. Accessed December 2016.
- Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;35:1381–95.
- World Health Organization. GATS Global Adult Tobacco Survey. Available at: <http://www.who.int/tobacco/surveillance/survey/gats/en>. Accessed September 2017.
- The Hispanic Community Health Study of Latinos. Available at: <http://www.csc.unc.edu/hchs>. Accessed December 2016.
- Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: Blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Circulation* 2005;111:697–716.
- Elorriaga N, Defagó D, Gutiérrez L, Desimone H, Poggio R, Irazola V. Dietary patterns in adult population from Argentina. *Ann Nutr Metab* 2013;63(Suppl 1):1461.
- Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol* 2002;13:3–9.
- Demerath E, Towne B, Blangero J, Siervogel RM. The relationship of soluble ICAM-1, VCAM-1, P-selectin and E-selectin to cardiovascular disease risk factors in healthy men and women. *Ann Hum Biol* 2001;28:664–78.
- Blann AD, Amiral J, McCollum CN. Circulating endothelial cell/leucocyte adhesion molecules in ischaemic heart disease. *Br J Haematol* 1996;95:263–5.
- Jilma B, Dirnberger E, Eichler HG, Kapiotis S. Sex differences in circulating P-selectin, E-selectin and thrombomodulin. *Br J Haematol* 1996;95:575–6.
- Friedman EM, Williams DR, Singer BH, Ryff CD. Chronic discrimination predicts higher circulating levels of E-selectin in a national sample: the MIDUS study. *Brain Behav Immun* 2009;23:684–92.
- Guzic-Salobir B, Keber I, Seljeflot I, Arnesen H, Vrabec L. Combined hormone replacement therapy improves endothelial function in healthy postmenopausal women. *J Intern Med* 2001;250:508–15.
- Virdis A, Ghiadoni L, Sudano I, Buralli S, Salvetti G, Taddei S, et al. Endothelial function in hypertension: role of gender. *J Hypertens Suppl* 2002;20:S11–6.
- Din JN, Archer RM, Harding SA, Sarma J, Lyall K, Flapan AD, et al. Effect of ω-3 fatty acid supplementation on endothelial function, endogenous fibrinolysis and platelet activation in male cigarette smokers. *Heart* 2013;99:168–74.
- Beulens JW, Rimm EB, Hu FB, Hendriks HF, Mukamal KJ. Alcohol consumption, mediating biomarkers, and risk of type 2 diabetes among middle-aged women. *Diabetes Care* 2008;31:2050–5.

- [32] Franklin BA. Preventing Exercise-Related Cardiovascular Events: Is a medical examination more urgent for physical activity or inactivity? *Circulation* 2014;129:1081–4.
- [33] Ministerio de Salud de la Nación, Argentina. Tercera Encuesta Nacional de Factores de Riesgo para Enfermedades no Transmisibles, 2013. Available at: http://www.msal.gov.ar/images/stories/bes/graficos/0000000544cnt-2015_09_04_encuesta_nacional_factores_riesgo.pdf. Accessed February 2017.
- [34] Lanas F, Bazzano L, Rubinstein A, Calandrelli M, Chen CS, Elorriaga N, et al. Prevalence, distributions and determinants of obesity and central obesity in the Southern Cone of America. *PLoS One* 2016;11:e0163727.
- [35] Olinto MT, Gigante DP, Horta B, Silveira V, Oliveira I, Willett W. Major dietary patterns and cardiovascular risk factors among young Brazilian adults. *Eur J Nutr* 2012;51:281–91.
- [36] Andreatta MM, Navarro A, Muñoz SE, Aballay L, Eynard AR. Dietary patterns and food groups are linked to the risk of urinary tract tumors in Argentina. *Eur J Cancer Prev* 2010;19:478–84.
- [37] Croveto M, Uauy R. Recommendations for cancer prevention of World Cancer Research Fund (WCRF): situational analysis for Chile. *Rev Med Chil* 2013;141:626–36.
- [38] Ministerio de Salud de la Nación, Argentina. Encuesta Nacional de Nutrición y Salud. Documento de Resultados. Argentina. Available at: <http://msal.gov.ar/hm/Site/ennys/site/default.asp>. Accessed December 2017.
- [39] Tumas N, Niclis C, Aballay LR, Osella AR, Díaz Mdel P. Traditional dietary pattern of South America is linked to breast cancer: an ongoing case-control study in Argentina. *Eur J Nutr* 2014;53:557–66.
- [40] Niclis C, Díaz M, del P, Eynard AR, Román MD, La Vecchia C. Dietary habits and prostate cancer prevention: a review of observational studies by focusing on South America. *Nutr Cancer* 2012;64:23–33.
- [41] Kovalskys I, Indart Rougier P, Amigo MP, De Gregorio MJ, Rausch Herscovici C, Karner M. Food intake and anthropometric evaluation in school-aged children of Buenos Aires. *Arch Argent Pediatr* 2013;111:9–14.
- [42] Monteiro CA, Moubarac JC, Cannon G, Ng SW, Popkin B. Ultra-processed products are becoming dominant in the global food system. *Obes Rev* 2013;14 (Suppl 2):21–8.
- [43] Monteiro CA, Gomes FS, Cannon G. The snack attack. *Am J Public Health* 2010;100:975–81.
- [44] Sun J, Buys N, Shen S. Dietary patterns and cardiovascular disease-related risks in Chinese older adults. *Front Public Health* 2013;1:48.
- [45] Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, et al. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr* 2004;80:1029–35.
- [46] Nanri A, Yoshida D, Yamaji T, Mizoue T, Takayanagi R, Kono S. Dietary patterns and C-reactive protein in Japanese men and women. *Am J Clin Nutr* 2008;87:1488–96.
- [47] Nettleton JA, Steffen LM, Mayer-Davis EJ, Jenny NS, Jiang R, Herrington DM, et al. Dietary patterns are associated with biochemical markers of inflammation and endothelial activation in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr* 2006;83:1369–79.
- [48] Hu FB, Manson JE, Willett WC. Types of dietary fat and risk of coronary heart disease: a critical review. *J Am Coll Nutr* 2001;20:5–19.
- [49] Baker PW, Rye K-A, Gamble JR, Vadas MA, Barter PJ. Phospholipid composition of reconstituted high density lipoproteins influences their ability to inhibit endothelial cell adhesion molecule expression. *J Lipid Res* 2000;41:1261–7.
- [50] Nicholls SJ, Lundman P, Harmer JA, Cutri B, Griffiths KA, Rye KA, et al. Consumption of saturated fat impairs the anti-inflammatory properties of high-density lipoproteins and endothelial function. *J Am Coll Cardiol* 2006;48:715–20.
- [51] De Caterina R, Liao JK, Libby P. Fatty acid modulation of endothelial activation. *Am J Clin Nutr* 2000;7(Suppl 1):213S–23S.
- [52] Fargnoli JL, Fung TT, Olenczuk DM, Chamberland JP, Hu FB, Mantzoros CS. Adherence to healthy eating patterns is associated with higher circulating total and high-molecular-weight adiponectin and lower resistin concentrations in women from the Nurses' Health Study. *Am J Clin Nutr* 2008;88:1213–24.
- [53] Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA* 2001;286:327–34.
- [54] Dain A, Repossi G, Diaz-Gerevini GT, Vanamala J, Das UN, Eynard AR. Long chain polyunsaturated fatty acids (LCPUFAs) and nordihydroguaiaretic acid (NDGA) modulate metabolic and inflammatory markers in a spontaneous type 2 diabetes mellitus model (Stillman Salgado rats). *Lipids Health Dis* 2016;15:205.
- [55] Turhan H, Erbay AR, Yasar AS, Aksoy Y, Bicer A, Yetkin G, et al. Plasma soluble adhesion molecules; intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin levels in patients with isolated coronary artery ectasia. *Coron Artery Dis* 2005;16:45–50.
- [56] Brown AA, Hu FB. Dietary modulation of endothelial function: implications for cardiovascular disease. *Am J Clin Nutr* 2001;73:673–86.
- [57] Jiang Y, Wu SH, Shu XO, Xiang YB, Ji BT, Milne GL, et al. Cruciferous vegetable intake is inversely correlated with circulating levels of proinflammatory markers in women. *J Acad Nutr Diet* 2014;14:700–8.
- [58] Moubarac JC, Martins AP, Claro RM, Levy RB, Cannon G, Monteiro CA. Consumption of ultra-processed foods and likely impact on human health. Evidence from Canada. *Public Health Nutr* 2013;16:2240–8.
- [59] Micha R, Michas G, Lajous M, Mozaffarian D. Processing of meats and cardiovascular risk: time to focus on preservatives. *BMC Med* 2013;11:136.
- [60] Schwingshackl L, Hoffmann G, Lampousi AM, Knüppel S, Iqbal K, Schwedhelm C, et al. Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol* 2017;32:363–75.