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Breakfast association with arterial stiffness and carotid atherosclerotic burden. Insights from the 'Corinthia' study

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Arterial stiffness;
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Dietary habits

Abstract *Background and aims:* The role of dietary patterns, in cardiovascular diseases has been challenged. The role of breakfast as an element of balance energy intake has gained research interest. However, the effects of dietary patterns related to breakfast consumption on vascular function are unknown. We explored the association of breakfast consumption habits with arterial wall elastic properties and carotid atherosclerosis.
Methods and results: In this cross-sectional study we enrolled 2043 inhabitants of the Corinthia region in Greece. Carotid-femoral pulse wave velocity (cf-PWV) was used to assess arterial stiffness. Carotid intima-media thickness (cIMT) was measured and the mean and the maximum cIMT were calculated. According to food frequency questionnaires, breakfast contribution in total daily energy intake (>20%; 5–20% and <5%) was estimated. Subjects were categorized as high-energy breakfast consumers (HeBC), low-energy breakfast consumers (LeBC) and those skipping breakfast (SBf) respectively. From the study population 240 subjects were categorized as HeBC, 897 as LeBC, and 681 as SBf. The mean cf-PWV was significantly higher in subjects SBf compared to LeBC and HeBC (9.35 ± 2.82 m/s vs. 9.09 ± 2.77 m/s vs. 8.76 ± 2.69 m/s, $p = 0.02$). The mean cIMT was significantly higher in subjects SBf compared to LeBC and HeBC (1.04 ± 0.46 mm vs. 0.99 ± 0.43 mm vs. 0.92 ± 0.39 mm, $p = 0.01$). Even after adjustment for potential confounders and cardiovascular risk factors SBf subjects have significantly increased mean cIMT and cf-PWV.
Conclusion: Skipping breakfast has an adverse effect on arterial stiffness and carotid atheromatic burden. Increased breakfast total energy intake may act protectively against atherosclerosis, a finding worth of further pathophysiologic exploration with potential clinical implications.
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Introduction

Several lifestyle factors including diet may influence the risk of cardiovascular diseases either indirectly through modification of established risk factors (i.e. hypertension, hypercholesterolemia, diabetes mellitus, etc.) r through the effects of vitamins, antioxidants and micronutrients on

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the atherosclerosis process [1–3]. Besides the nutritional quality of a diet, acquired eating patterns (i.e. Mediterranean diet) have been recognized as an important determinant of overall and cardiovascular health [4,5]. However, the role of diet and dietary patterns in cardiovascular and total mortality has been challenged and the composition of the so called "healthy diet" has been debated [6].

Recently, the role of breakfast consumption habits on cardiovascular health has attracted research interest. The role of breakfast in daily balanced energy intake is substantial and omitting breakfast may be adversely related to obesity, unfavorable lipid profile and even development of diabetes [7,8]. Skipping breakfast has been additionally associated with risk of coronary heart disease and stroke [9,10]. Recently, Uzhova et al. [11] have documented the protective effects of breakfast consumption in subclinical atherosclerosis.

So far, the effect of dietary breakfast pattern on vascular function is unknown. Therefore, in the context of the Corinthia study [12] we explored the association of breakfast consumption with carotid atherosclerosis and with central aortic stiffness.

Methods

Study design

The Corinthia study was carried out from October 2015 to February 2017. Two thousand forty-three permanent inhabitants of Corinth aged 40 years or older have been voluntarily enrolled in this cross-sectional survey. A multistage sampling method was used to achieve a balance recruitment across different area, census blocks, age categories (per decades) and gender. All participants have been interviewed by the investigator group consisted of physicians, cardiologists, nurses and social scientists.

The Medical Research Ethics Committee of the First Cardiology clinic of Athens Medical School approved the study which was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. An informed consent form was signed by all subjects before participation after detailed information for the purpose, aims and procedure of the study.

Clinical, biochemical and anthropometric characteristics

Standard procedures were used to measure weight and height. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). At the end of the physical examination, an electronic sphygmomanometer was used to measure resting arterial blood pressure with the subject in a sitting position according to the current recommendations. Individuals under anti-hypertensive medication or with blood pressure levels greater or equal to $\geq$140 mmHg for systolic blood pressure (SBP) and/or $\geq$90 mmHg for diastolic blood pressure (DBP) were classified as hypertensive subjects, according to the 2013 ESH/ESC Guidelines for the management of arterial hypertension [13].

Blood samples were collected between 8.00 and 10.00 a.m. after an overnight fast. Serum total cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides were measured using a chromatographic enzymic method in an automatic analyzer (RA-1000). The Friedewald formula: Low-density lipoprotein (LDL) = cholesterol (total cholesterol) − (HDL cholesterol) − 1/5 (triglycerides) was used to calculate LDL cholesterol levels. The intra and inter-assay coefficients of variation of cholesterol levels did not exceed 3%, of triglycerides 4% and of HDL-cholesterol 4%. Individuals under lipid-lowering treatment or with total serum cholesterol levels greater than 200 mg/dl were classified as having hypercholesterolemia.

According to American Diabetes Association diagnostic criteria, the diagnosis of diabetes mellitus type 2 was based on fasting blood glucose levels > 126 mg/dl and or regular use of anti-diabetic medication [14].

As regarding smoking habits, current smokers were defined as those who smoked at least one cigarette per day or had stopped smoking for less than a year, while noncurrent smokers were defined as those who had stopped smoking for at least one year or had never smoked.

Evaluation of arterial stiffness

Arterial stiffness was evaluated in all subjects with pulse wave velocity (cf-PWV) measurements. Carotid-femoral pulse wave velocity (cf-PWV), which is considered as an index of aortic stiffness was calculated from measurements of pulse transit time and the distance traveled between 2 recording sites (cf-PWV = distance in meters divided by transit time in seconds) by using a well validated noninvasive device (SphygmoCor; AtCor Medical) as previously described [15]. Two different pulse waves were obtained at 2 sites (at the base of the neck for the common carotid and over the right femoral artery) with the transducer. Distance was defined as the distance from the suprasternal notch to femoral artery minus the distance from the carotid artery to the suprasternal notch. All measurements were taken between 8.00 and 10.00 a.m. after 10 min rest. Since postprandial measurements of arterial stiffness may be increased [16], all subjects were instructed to be refrained from caffeine, alcohol, smoking and any food for 12 h before each study.

Reference values of PWV for different age group were determined based on the "The Reference Values for Arterial Stiffness' Collaboration" from 16,867 subjects from thirteen different centers across eight European countries [17]. The study population was classified into two groups with respect to PWV values (normal or abnormal). First, we used the 90th percentile cut-of value of PWV for each age group, as determined previously in the reference population [17]. Then, a quadratic equation was fitted ($PWV = a \times age^2 + b \times age + c$) where constants a, b, and c were determined based on the BP category (optimal < 120/80 mmHg; normal ≥ 120/80 mmHg and <130/85 mmHg; high normal ≥ 130/85 mmHg and <140/90 mmHg; grade I hypertension ≥ 140/90 mmHg and

<160/90 mmHg; grade II/III hypertension ≥ 160/100 mmHg). This equation was used to determine the maximum normal values of PWV for each age and blood pressure category, in the reference population. Values of PWV for each age in our population that exceeded the respective maximum reference value for the same age were classified as abnormal and vice versa [17].

Evaluation of carotid intima media thickness (cIMT)

High resolution B-mode images of the right and left common carotid arteries were obtained using a Vivid e ultrasound system (General Electric, Milwaukee, Wisconsin, USA) equipped with a 5.0–13.0 MHz (harmonics) linear array ultrasound.

Carotid IMT was measured at 3 paired segments: in the right and left common carotid artery, the carotid bulb, and the internal carotid artery, as described previously [18]. In each segment, 3 measurements of the cIMT in the far wall were averaged; and the average cIMT was calculated for each of the 2 carotid arteries. The average value of right and left carotid cIMT was defined as mean cIMT. The maximum-cIMT was also studied. Thickness of cIMT > 1.5 mm or protrusion >50% compared to adjacent segments was considered as atherosclerotic plaque. If plaque was present in the distal territory of the examined segment, it was included in the cIMT measurement [19].

Evaluation of dietary habits and breakfast consumption

A validated and reliable weakly food frequency questionnaire, containing nutritional information on 15 food items, was used to assess dietary patterns [20]. Accordingly, consumption of all basic food groups and beverages was assessed in terms of daily, weekly or monthly consumption. Portion size was categorized as small, medium or large. Subjects were specifically asked regarding breakfast consumption and report on frequency and portion of foods that they consumed during breakfast. Accordingly, subjects were categorized as high-energy breakfast consumers (HeBC, breakfast contributing to >20% of total daily energy intake), low-energy breakfast consumers (LeBC, breakfast contributing between 5% and 20% of total daily energy intake) and skipping breakfast (SBf <5% of total daily energy intake).

Statistical analysis

Data are presented as mean ± standard deviation (SD) for continuous variables and as valid percentages for categorical variables. Continuous variables were tested for normality of distribution with Kolmogorov–Smirnov test and by visual inspection of P–P plots. Differences between categories of breakfast consumption were tested with chi square for categorical variables and with analysis of variance for continuous variables (ANOVA) after controlling for equality of variances (homoscedasticity). Differences in values between studied subgroups were tested using post hoc analysis after Scheffe correction. Regression analysis was used to assess the association between breakfast patterns and cf-PWV, mean cIMT and maximum cIMT after adjustment for established risk factors and variables revealed significant by the univariate analysis. All reported p-values were based on two-sided tests. Exact values of $p < 0.05$ were considered statistically significant. Data analysis was performed with SPSS software, version 18.0 (SPSS Inc., Chicago, IL).

Results

Basic characteristics of the participants

From the study participants 70% were characterized as hypertensive, 17% suffer from diabetes mellitus, 47% had hypercholesterolemia, 27% were active smokers and 13% had a history of cardiovascular disease.

According to breakfast consumption the demographic and clinical characteristics of the participants are shown in Table 1. From the study population 13% were categorized as HeBC, 49% as LeBC and the rest as SBf. HeBC had increased prevalence of diabetes mellitus and hypercholesterolemia. However, the rate of current smokers was significantly higher in subjects SBf.

Breakfast consumption and pulse wave velocity

From the study population 11% had increased cf-PWV according to published age and blood pressure reference values. The rate of abnormal cf-PWV was higher in subjects SBf compared to LeBC and HeBC (14.9% vs. 9.4% vs. 8.7%, $p = 0.01$) (Fig. 1, panel A). The mean cf-PWV was significantly higher in subjects SBf compared to LeBC and HeBC (9.35 ± 2.82 m/s vs. 9.09 ± 2.77 m/s vs. 8.76 ± 2.69, $p = 0.02$) (Fig. 1, panel B).

Interestingly regression analysis revealed that even after adjustment for potential confounders LeBC and HeBC were associated with lower values of cf-PWV (Table 2). Specifically, according to these models HeBC subjects are anticipated to have lower cf-PWV compared to subjects SBf by 0.58 m/s independently from the presence or not of other risk factors [$b = -0.588$, 95% CI (−1.011, −0.165), $p = 0.006$].

Breakfast consumption and carotid atherosclerosis

From the study population 26% have atherosclerotic plaques in carotid arteries. The mean cIMT in carotid arteries was significantly higher in subjects SBf compared to LeBC and HeBC (1.04 ± 0.46 mm vs. 0.99 ± 0.43 mm vs. 0.92 ± 0.39, $p = 0.01$) (Fig. 2, panel A). In addition, maximum cIMT in carotid arteries was significantly higher in subjects SBf compared to LeBC and HeBC (1.40 ± 0.91 mm vs. 1.32 ± 0.84 mm vs. 1.19 ± 0.77, $p = 0.03$) (Fig. 2, panel B). Moreover, the frequency of carotid plaque presence was higher in subjects SBf compared to LeBC and HeBC (28% vs. 26% vs. 18%, $p = 0.03$) (Fig. 2, panel C).

Table 1 Characteristic of the study population according to breakfast consumption.

	Subjects skipping breakfast	Low-energy breakfast consumers	High-energy breakfast consumers	*p*-value
Subjects (%)	37	49	13	
Age (%)	63 ± 12	64 ± 12	64 ± 12	0.09
Female gender (%)	59	60	64	0.33
Body mass index (kg/m^2)	28.35 ± 4.39	28.62 ± 4.53	28.63 ± 4.59	0.47
Arterial hypertension (%)	39	41	46	0.21
Anti-hypertensive treatment (%)	33	35	39	0.10
Hypercholesterolemia (%)	42	48	49	0.07
Diabetes mellitus (%)	14	19	19	0.02
Current smokers (%)	43	17	23	<0.001
Cardiovascular disease (%)	14	17	13	0.08
Pulse wave velocity (m/s)	9.35 ± 2.82	9.09 ± 2.77	8.76 ± 2.69*	0.02
Increased PWV	13.9	9.4	8.7	0.01
Mean carotid IMT (mm)	1.03 ± 0.46	0.98 ± 0.42	0.91 ± 0.38	0.01
Maximum carotid IMT (mm)	1.40 ± 0.91	1.32 ± 0.84	1.19 ± 0.77	0.03
Carotid plaque (%)	28	26	18	0.05

*: $p < 0.05$ compared to subjects skipping breakfast.
IMT: intima media thickness.

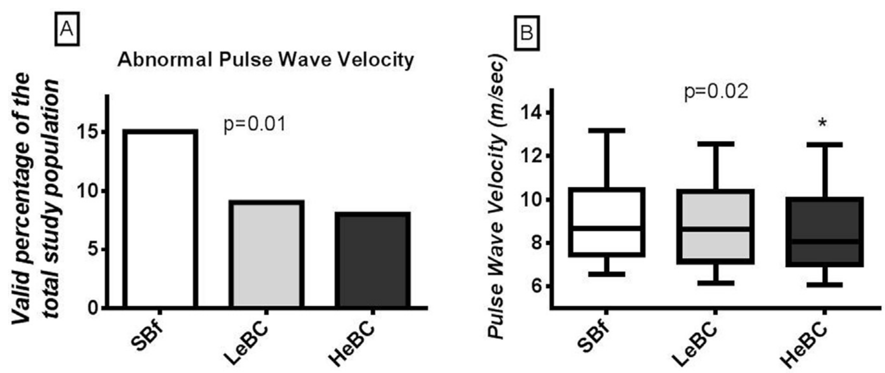

Figure 1 Differences in arterial stiffness according to breakfast consumption patterns. Panel A: bars representing valid percentages of patients with increased pulse wave velocity according to breakfast consumption. Panel B: Box-plots representing pulse wave velocity according to breakfast consumption. SBf: skipping breakfast; LeBC: low energy breakfast consumers; HeBC: high energy breakfast consumers; *: $p < 0.05$ compared to SBf.

Interestingly regression analysis revealed that even after adjustment for potential confounders LeBC and HeBC were associated with decreased mean cIMT and maximum cIMT (Table 3). Specifically, according to these models LeBC are anticipated to have lower mean cIMT compared to subjects SBf by 0.068 mm [$b = -0.068$, 95% CI (−0.128, −0.009), $p = 0.03$]. Moreover, HeBC are anticipated to have lower mean cIMT compared to SBf subjects by 0.111 mm [$b = -0.111$, 95% CI (−0.197, −0.024), $p = 0.01$].

Table 2 Regression analysis of the association of PWV with breakfast consumption and several other confounders.

	b-coefficient	95% Confidence intervals	*p*-value
Age (years)	0.112	0.100, 0.123	<0.001
Male gender	0.418	0.149, 0.687	0.002
Body mass index (kg/m^2)	0.038	0.009, 0.068	0.01
Current smokers	−0.174	−0.483, 0.135	0.27
Arterial hypertension	−0.099	0.384, 0.185	0.49
Diabetes mellitus	0.068	−0.298, 0.434	0.71
Hypercholesterolemia	0.127	−0.147, 0.402	0.36
Cardiovascular disease	−0.004	−0.412, 0.403	0.98
SBf			
LeBC	−0.477	−0.777, −0.177	0.002
HeBC	−0.588	−1.011, −0.165	0.006

SBf: skipping breakfast; LeBC: low energy breakfast consumers; HeBC: high energy breakfast consumers.

Discussion

The present study was conducted in the Mediterranean basin including a wide range of ages (between 40 and 99 years). We investigated the effect of breakfast consumption habits on arterial stiffness and carotid atherosclerotic burden. The main findings of this study are summarized as follows: i) the majority of the participants depicted a moderate energy intake with breakfast (corresponding to 5−20% of the total daily energy intake); ii) low energy intake with breakfast is associated with subclinical atherosclerosis (namely increased central arterial stiffness) and iii) higher carotid atheromatic burden and intima media thickness.

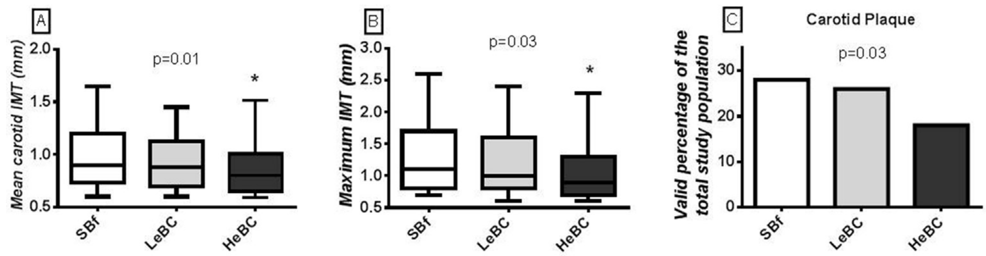

Figure 2 Differences in carotid intima media thickness and carotid plaque according to breakfast consumption patterns. Panel A: Box-plots representing mean intima media thickness according to breakfast consumption. Panel B: Box-plots representing maximum intima media thickness according to breakfast consumption. Panel C: Bars representing valid percentages of patients with carotid plaque according to breakfast consumption, SBf: skipping breakfast; LeBC: low energy breakfast consumers; HeBC: high energy breakfast consumers; IMT: intima media thickness. *: $p < 0.05$ compared to SBf.

Table 3 Regression analysis of the association of mean cIMT and maximum cIMT with breakfast consumption and several other confounders.

	Mean cIMT			Maximum cIMT		
	b coefficient	95% Confidence intervals	*p*-value	*b* coefficient	95% Confidence intervals	*p*-value
Age (years)	−0.002	−0.004, 0.001	0.052	−0.003	−0.007, 0.001	0.115
Male gender	0.007	−0.045, 0.061	0.77	−0.08	−0.113, 0.096	0.87
Body mass index (kg/m^2)	0.003	−0.002, 0.009	0.21	0.006	−0.004, 0.017	0.26
Current smokers	0.046	−0.015, 0.108	0.14	0.092	−0.030, 0.214	0.14
Arterial hypertension	0.155	0.098, 0.213	<0.001	0.234	0.122, 0.347	<0.001
Diabetes mellitus	0.132	0.059, 0.204	<0.001	0.229	0.087, 0.371	0.002
Hypercholesterolemia	0.028	−0.026, 0.084	0.31	0.067	−0.041, 0.176	0.22
Cardiovascular disease	0.301	0.219. 0.384	<0.001	0.573	0.411, 0.736	<0.001
SBf						
LeBC	−0.068	−0.128, −0.009	0.03	−0.128	−0.246, −0.010	0.03
HeBC	−0.111	−0.197, −0.024	0.01	−0.174	−0.344, −0.004	0.04

SBf: skipping breakfast; LeBC: low energy breakfast consumers; HeBC: high energy breakfast consumers; IMT: intima media thickness.

Breakfast patterns and cardiometabolic risk factors

The role of diet in cardiovascular health has been extensively studied and specific dietary patterns such as the Mediterranean or DASH (Dietary Approaches to Stop Hypertension) diet have been proposed for their beneficial cardiovascular effects [4,5,21]. Therefore, a diet pattern rich in natural carbohydrates and low fat content and especially saturated fatty acids was considered protective against cardiovascular disease [1,4]. Several studies have also highlighted the adverse effects of high fat diet and postprandial hyperlipidemia in the progression of vascular endothelial dysfunction in a manner correlated directly to triglycerides levels [22,23].

However, traditional "healthy" dietary patterns are questioned under the light of Prospective Urban Rural Epidemiology (PURE) study [6]. Therefore, it is important to better understand how dietary habits may interact with overall and especially cardiovascular health. Breakfast, as the first meal of the day may have significant contribution to daily energy balance. In our studied population most of the participants has a LeBC while there was no significant association of breakfast energy intake with most of the cardiovascular risk factors. In addition, based on our data SBf subjects have an increased prevalence of cigarette smoking while a reversed pattern was observed concerning diabetes mellitus, with subjects categorized as LeBC and HeBC having the higher prevalence.

Our data concurred with previously reported findings that subjects skipping breakfast tend to adopt additional unhealthy lifestyle patterns such as cigarette smoking [24], while subject's education and training can modify dietary pattern and distribution of daily energy in a favorable way, as it is observed in the diabetes mellitus cohort of our study. Unfortunately, based on our data we cannot conclude which type of breakfast (i.e. high fat or high carbohydrate content) confer the grater cardiovascular benefit. Our findings may however introduce the concept that the type of meal is less important than the total energy intake and the distribution of energy throughout daily meals.

Breakfast patterns and arterial stiffness

One of the main findings of this study was that central aortic stiffness, an established risk factor for cardiovascular disease [25], is improved in patients adherent to a balanced energy distribution dietary pattern including high energy breakfast consumption. Since distinct dietary patterns may be associated with cardiometabolic risk factors, we have proceeded to adjustments for covariates such as age, BMI, arterial hypertension, diabetes mellitus and high cholesterol levels. Interestingly, even after controlling for potential cardiovascular risk factors we confirmed that skipping breakfast was associated with increased arterial stiffness, implying the possibility to consider omitting breakfast as an additional risk factor.

However, high fat diet may also adversely affect postprandial arterial stiffness [16] while low-cholesterol/low saturated fat diet may improve large artery stiffness [26]. Nevertheless, some studies have not confirmed the concept that a low-fat diet can reduce cardiovascular risk [27]. To this direction, the Health Professionals Follow up and the Nurses' Health Study concluded that total fat consumption may be associated with reduced total mortality [28]. The latter findings were confirmed by PURE study in approximately 135,000 subjects from 18 countries concluding that total mortality is lower in subjects consuming increased amount of total fat [6].

The cross-sectional design of our study does not allow causative associations. However, the wide age range of our study population provides insights how breakfast may affect arterial stiffness throughout the life-time spectrum.

Breakfast patterns and carotid atherosclerotic burden

Recently it has been documented that high energy breakfast consumption protects against subclinical atherosclerosis which constitute an early stage in the progression of atheromatic disease [11]. Our data confirm these findings, and they additionally emphasize the spectrum of cardiovascular benefit from arterial wall properties improvement to carotid atheromatic burden when a HeBC is adopted. Omitting breakfast has been associated with cardiometabolic risk factors [29] and diabetes mellitus [30]. Importantly, two large scale prospective studies revealed that breakfast was inversely associated with stroke and coronary artery disease [9,10]. This issue is also pointed out in a recent Scientific Statement from the American Heart Association concluding not only on the beneficial effects of breakfast on glucose/insulin metabolism but also on the promotion of a healthier dietary profile through breakfast adaptation [29]. In addition, breakfast consumption has been associated with a better overall diet quality and control of appetite [31,32] which may attenuate the impact of postprandial lipemia on endothelial dysfunction and on the progress of atheromatosis [22]. There is also evidence that subjects with a higher caloric intake at breakfast compared to dinner have a better and more normalized, serum lipid, glucose and insulin profile [33].

Limitations

Although, this study is based on an adequate sample size and a well-balanced study population is inherent to some limitations. The cross-sectional design of the study does not allow for causative associations and the possible impact of modification of individual breakfast quantitative pattern on subclinical atherosclerosis should be further tested in prospective interventional studies. Moreover, we lack data on qualitative parameters of breakfast consumption which may affect and interact with the results observed in arterial stiffness and atheromatic burden [26]. Another potential limitation of this work concerns the unavailability of data on the level of physical activity. However, we believe that this parameter has not affected our results since this study has been conducted in a rural area with the great majority of the subjects enrolled depicting moderate or high level of physical activity for occupational reasons (employment in the agriculture sector).

Clinical implications

Our data are based on a mixed population consisted of healthy subjects, subjects with cardiovascular risk factors and with established cardiovascular disease. Since the modification of the dietary pattern regarding the breakfast composition could be easily applied at the population level, our findings may be proved of clinical importance for healthy subjects and subjects with identified cardiovascular risk factors. Specifically, modification of breakfast habits could easily substitute more demanding, personalized diet patterns, with a direct and measurable effect in parameters of clinical significance. Moreover, counselling on breakfast consumption may be proved of clinical significance especially in individuals with aortic stiffness associated cardiovascular conditions (i.e. hypertension, left ventricle diastolic dysfunction, renal impairment etc.), in subjects with cardiometabolic risk factors and in those with advanced atheromatosis (i.e. coronary artery disease, peripheral artery disease, stroke).

Conclusions

We found that high energy breakfast consumption is associated with decreased arterial stiffness and carotid atherosclerotic burden in subjects above 40 years of age. Our findings introduce the concept that beyond qualitative composition of meals, balance energy consumption throughout the day may be of significance for the integrity and wellbeing of cardiovascular system. Since the so called “healthy” diet patterns are related to appetite preferences and are sometimes difficult to adopt, a balanced energy intake model with high energy breakfast consumption may be a clinically useful alternative.

Conflicts of interest

The authors declare that they have no conflict of interest.

Ethical standards

The present study has been approved by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All persons gave their informed consent prior to their inclusion in the study.

Disclosures

Nothing to disclose.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2019.04.008.

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