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ORIGINAL INVESTIGATIONS

The Importance of Breakfast in Atherosclerosis Disease

Insights From the PESA Study

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ABSTRACT

BACKGROUND Daily habits, including the number and quality of eating occasions, are potential targets for primary prevention strategies with large health impacts. Skipping breakfast is considered a frequent and unhealthy habit associated with an increased cardiovascular (CV) risk.

OBJECTIVES The study sought to explore the association between different breakfast patterns and CV risk factors and the presence, distribution, and extension of subclinical atherosclerosis.

METHODS Cross-sectional analysis was performed within the PESA (Progression of Early Subclinical Atherosclerosis) study, a prospective cohort of asymptomatic (free of CV events at baseline) adults 40 to 54 years of age. Lifestyle and multivascular imaging data along with clinical covariates were collected from 4,052 participants. Multivariate logistic regression models were used in the analysis.

RESULTS Three patterns of breakfast consumption were studied: high-energy breakfast, when contributing to >20% of total daily energy intake (27% of the population); low-energy breakfast, when contributing between 5% and 20% of total daily energy intake (70% of the population); and skipping breakfast, when consuming <5% of total daily energy (3% of the population). Independent of the presence of traditional and dietary CV risk factors, and compared with high-energy breakfast, habitual skipping breakfast was associated with a higher prevalence of noncoronary (odds ratio: 1.55; 95% confidence interval: 0.97 to 2.46) and generalized (odds ratio: 2.57; 95% confidence interval: 1.54 to 4.31) atherosclerosis.

CONCLUSION Skipping breakfast is associated with an increased odds of prevalent noncoronary and generalized atherosclerosis independently of the presence of conventional CV risk factors. (Progression of Early Subclinical Atherosclerosis [PESA]; NCT01410318) (J Am Coll Cardiol 2017;70:1833–42) © 2017 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CAC = coronary artery calcium

CI = confidence interval

CVD = cardiovascular disease

EI = energy intake

HBF = high-energy breakfast

LBF = low-energy breakfast

MetS = metabolic syndrome

OR = odds ratio

SBF = skipping breakfast

WC = waist circumference

Several conditions associated with the development of cardiovascular disease (CVD) such as diabetes (1), obesity (2), hypertension (3), and dyslipidemia (4) are known to be modifiable by changes in lifestyle. Among lifestyle factors, our diet, including both the nutritional quality and our acquired eating patterns, constitutes a major target of CVD prevention strategies.

Eating patterns are highly dependent on cultural, social and psychological determinants, as people integrate them into their daily life routines. A particular habit that might have a significant effect on CV health is breakfast consumption, as it is associated with factors such as satiety (5), daily energy intake (EI) (6), metabolic efficiency of the diet, and appetite regulation (7). A number of studies have reported associations between the habit of omitting breakfast and increased cardiometabolic health markers (8), including obesity (9), diabetes (10), and unfavorable lipid profile (11). Although there are some studies linking skipping breakfast with coronary heart disease risk (12,13), to the best of our knowledge, no studies have investigated the association with this dietary habit on the presence of subclinical atherosclerosis. The aim of our study was to characterize the association between different breakfast patterns and CVD risk factors, and in particular, whether regularly skipping breakfast is associated with subclinical atherosclerosis, by investigating the presence of atherosclerotic plaques in the carotid arteries, aorta, and iliofemoral arteries or coronary artery calcium, in a population with no previous history of CVD.

SEE PAGE 1843

METHODS

STUDY OVERVIEW. The PESA (Progression of Early Subclinical Atherosclerosis) study is an ongoing observational prospective cohort of 4,082 employees of the Bank Santander Headquarters in Madrid, Spain, aiming to discover the factors related to the development and progression of atherosclerosis. A detailed description of the study design and procedures of data collection has been reported elsewhere (14). The study protocol was approved by the Ethic committee of Instituto de Salud Carlos III (Madrid, Spain). All participants provided written informed consent (14).

STUDY PARTICIPANTS. Male and female volunteers 40 to 54 years of age were included in the study if at baseline they were free of any CV or chronic kidney disease, were not under active treatment for cancer, did not have previous transplant, did not exceed body mass index (BMI) of 40 kg/m^2, and did not have any disease that might affect life expectancy and decrease it to <6 years. Of the initial participants, 26 having missing values in some of the variables of interest, and 4 reporting extreme values for daily EI (<800 or >4,200 kcal for men, and <500 or >3,500 kcal for women) (15) were excluded from the analyses. The final sample consisted therefore of 4,052 participants.

DIETARY ASSESSMENT. To estimate usual diet of PESA study participants we used a computerized questionnaire (dietary history of the ENRICA [Estudio de Nutrición y Riesgo Cardiovascular] study) developed and validated for the Spanish population within the ENRICA study (16) containing nutritional information on 861 food items (including 184 typically consumed Spanish meals and dishes). Briefly, subjects were asked to report foods consumed in the past 15 days, taking into consideration eating occasions (waking up, breakfast, midmorning, lunch, midafternoon, and dinner). Once a food item was consumed at least once, it was considered "usually consumed." Conversion factors were used to calculate the annual frequency of consumption (16). Based on these data, the variable "energy consumed during breakfast" was computed and the breakfast patterns in our study was based on the percentage of the daily total EI consumed at breakfast. As a first step, our definition of breakfast was based on quantitative description provided by Timlin and Pereira (7), where it is defined as "the first meal of the day that breaks the fast after the longest period of sleep, eaten before or at the start of daily activities (e.g., errands, travel, work), within 2 h of waking, typically no later than 10:00 in the morning, and of an energy level between 20 and 35% of total daily energy need." Based on this definition, we identified foods consumed before 10:00 AM in the PESA study database and those participants whose energy intake at breakfast exceeded 20% of total energy intake, were considered breakfast consumers (high-energy breakfast [HBF]). As a second step, we applied the qualitative definition of breakfast provided by O'Neil et al. (17), where

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breakfast is defined as "a food or beverage from at least one food group, and may be consumed at any location. Coffee, water and nonalcoholic beverages are not included in a food group." Therefore, taking into account only coffee, and nonalcoholic beverages, we estimated that 300 ml of orange juice (typically consumed for breakfast in Spain) would contain 123 kcal, 100 ml of coffee with milk would contain 38 kcal, and 100 ml of coffee with milk and 20 g of added sugar would contain 119 kcal according to Spanish food composition database (18). The mean energy intake in the PESA study population is 2,314 kcal/day, and 123 kcal/day would represent 5% of the total intake. Therefore, we hypothesized that if participants' morning energy intake would not exceed 123 kcal (5% of total daily energy intake), that could be approximated as skipping breakfast (SBF) as no other food was consumed. Following this rationale, 3 major groups were identified: those having <5% of total EI in the morning as a proxy for having only coffee or coffee with milk, juice, or other nonalcoholic beverages (SBF); those having >20% of total EI in the morning as breakfast consumers (HBF); and those participants in between 5% and 20% were called low-energy breakfast (LBF) consumers. Overall dietary quality was assessed by participants' adherence to a posteriori defined dietary patterns (Mediterranean, Western, and Social-business), which are described in detail in our previous work (19).

TABLE 1 Demographics and Lifestyle Characteristics

	HBF (n = 1,122)	LBF (n = 2,812)	SBF (n = 118)
Demographics			
Age, yrs	45.41 ± 4.23*†	45.95 ± 4.27‡	46.53 ± 4.27‡
Female	503 (44.8)*†	951 (33.8)‡	34 (28.8)‡
Education			
High school or lower	238 (21.4)*	741 (26.5)‡	34 (28.8)
College degree	160 (14.4)	423 (15.2)	21 (17.8)
University degree or higher	714 (64.2)*	1628 (58.3)‡	63 (53.4)
Marital status			
Married	851 (83.4)	2,139 (83.8)	91 (82.0)
Single	73 (7.2)	219 (8.6)	14 (12.6)
Divorced	90 (8.80)	185 (7.20)	6 (5.40)
Widow	6 (0.60)	11 (0.40)	0 (0.00)
Lifestyle			
Physical activity level (total physical activity counts/day)	3,604 ± 6,071	3,537 ± 5,179	3,668 ± 5,223
Smoking status			
Current smoker	196 (17.5)*†	588 (20.9)†‡	49 (41.5)*‡
Social smoker	103 (9.2)	226 (8.0)	11 (9.3)
Ex-smoker	344 (30.7)	928 (33.0)	33 (28.0)
Nonsmoker	479 (42.7)*†	1070 (38.1)†‡	25 (21.2)*‡
Dieting to lose weight	89 (7.9)*†	367 (13.1)‡	21 (17.8)‡
Time spent on breakfast, min	11.00 ± 5.81*†	8.40 ± 5.84†‡	4.93 ± 7.16*‡
% of daily EI at lunch	38.63 ± 6.25*†	41.97 ± 6.55†‡	47.53 ± 9.25*‡

Values are mean ± SD or n (%). Bonferroni correction was applied for categorical variables ($p < 0.017$). *$p < 0.05$ vs. LBF. †$p < 0.05$ vs. SBF. ‡$p < 0.05$ vs. HBF.

EI = energy intake; HBF = high-energy breakfast; LBF = low-energy breakfast; PA = physical activity; SBF = skipping breakfast; WC = waist circumference.

ANTHROPOMETRIC AND CLINICAL MEASUREMENTS. Anthropometric (height, weight, and waist circumference [WC]) and clinical measurements were collected as previously reported and through standardized procedures according to the PESA study protocol (14). Using this information, CVD risk factors were defined as follows: obesity if BMI was ≥30 kg/m^2; hypercholesterolemia if total cholesterol was ≥240 mg/dl or low-density lipoprotein cholesterol was ≥160 mg/dl or high-density lipoprotein cholesterol was <40 mg/dl, or use of lipid-lowering mediation (20); hypertension if average blood pressure was >140/90 mm Hg or use of antihypertensive mediation (21); diabetes if fasting plasma glucose levels were >126 mg/dl or glycosylated hemoglobin was >6.5 or use of insulin or hypoglycemic medication (22). Metabolic syndrome (MetS) was defined as presenting at least 3 of the following criteria: WC >88 cm for women and WC >102 cm for men, fasting plasma glucose >100 mg/dl or medication treatment, triglycerides >150 mg/dl or medication treatment, high-density lipoprotein cholesterol <40 mg/dl or medication treatment, and blood pressure >140/90 mm Hg or medication treatment (20). The European Society of Cardiology cardiovascular disease risk assessment tool, the Systematic Coronary Risk Evaluation, was used to assess the fatal cardiovascular risk (23).

OTHER VARIABLES. Other variables including age (years), sex (male or female), marital status (single, married, divorced, widow), highest educational level achieved (high school, college degree, or university and higher), smoking status (current smoker, nonsmoker, social smoker, or ex-smoker), and dieting to lose weight (yes/no) were self-reported. Physical activity was assessed by a triaxial accelerometer placed on the waist for a period of 7 days, providing activity counts per day (Acti Trainer, Actigraph, Pensacola, Florida).

ASSESSMENT OF ATHEROSCLEROSIS. The assessment of atherosclerotic plaques in multiple vascular territories; bilateral carotid, infrarenal abdominal aorta and iliofemoral arteries was performed by 2-dimensional ultrasound (Philips iU22 ultrasound, Philips Healthcare, Bothell, Washington) in the PESA study examination center as previously described (14). The presence of atherosclerotic plaques was

JACC VOL. 70, NO. 15, 2017
OCTOBER 10, 2017:1833–42

TABLE 2 Overall Dietary Profile of PESA Study Participants According to Breakfast Pattern

	HBF (n = 1,122)	LBF (n = 2,812)	SBF (n = 118)
Macronutrients, g/day or mg/day			
Energy intake, kcal	2,234 ± 450*†	2,345 ± 467‡	2,358 ± 562‡
Total protein	94.3 ± 18.0*†	102.4 ± 20.0‡	105.7 ± 24.0‡
Animal protein	64.8 ± 15.0*†	72.1 ± 17.1†‡	76.6 ± 20.7*‡
Vegetable protein	29.08 ± 8.23*	29.84 ± 8.39‡	28.69 ± 9.83
Total fat	103.1 ± 22.9*†	108.3 ± 24.2‡	113.6 ± 30.6‡
Cholesterol	334.4 ± 98.2*†	361.6 ± 94.8†‡	385.7 ± 111.0*‡
MUFA	47.0 ± 11.6*†	49.3 ± 11.5†‡	52.4 ± 13.8*‡
PUFA	16.62 ± 5.09*†	17.81 ± 5.48†‡	19.05 ± 7.06*‡
SFA	29.98 ± 8.62*†	32.05 ± 9.00‡	32.84 ± 10.90‡
Carbohydrates	218.5 ± 58.1†	220.0 ± 58.8†	197.0 ± 63.8*‡
Sugar	94.0 ± 31.8*†	90.9 ± 30.6†‡	75.5 ± 34.4*‡
Polysaccharides	119.7 ± 40.6*	125.7 ± 43.2‡	119.2 ± 46.0
Fiber	21.08 ± 6.48†	20.90 ± 5.99†	18.99 ± 6.19*‡
Food group, g/day			
Fruits and vegetables	474 ± 210*†	435 ± 202†‡	369 ± 182*‡
Dried fruits	7.30 ± 10.76	7.94 ± 12.26	9.65 ± 16.64
Legumes	25.2 ± 21.2	26.0 ± 22.9	27.4 ± 23.3
Potatoes	20.0 ± 17.1	21.1 ± 17.7	19.3 ± 16.7
Refined grains	216.0 ± 92.8*	234.0 ± 98.7‡	231.0 ± 101.5
Whole grains	14.3 ± 31.9*†	9.1 ± 21.6†‡	2.5 ± 10.6*‡
Nuts	5.03 ± 5.92	5.41 ± 5.68	5.16 ± 4.91
Olives	4.05 ± 6.30*†	4.65 ± 6.52†‡	7.26 ± 15.13*‡
Red meat	93.0 ± 42.2*†	112.9 ± 50.1†‡	145.1 ± 68.6*‡
Lean meat	63.3 ± 30.7*	66.9 ± 33.5‡	67.7 ± 32.6
Seafood (fish, shellfish)	75.8 ± 36.2*	79.1 ± 38.9‡	78.1 ± 39.9
Dairy	207 ± 151†	196 ± 137†	141 ± 116*‡
Low-fat dairy	88.3 ± 125.8	90.0 ± 121.8†	61.4 ± 112.7*
Vegetable oil and fat	5.02 ± 5.92	5.40 ± 5.68	5.15 ± 4.91
Butter	5.89 ± 6.72*†	4.26 ± 4.39†‡	2.30 ± 2.03*‡
Olive oil	31.7 ± 14.1*	29.9 ± 12.2‡	31.0 ± 11.8
Precooked meals, fast food	55.6 ± 34.0*†	66.9 ± 42.1‡	68.6 ± 35.6‡
Chips and snacks	5.02 ± 7.06*†	6.49 ± 9.12†‡	8.69 ± 11.73*‡
Commercial bakery	71.4 ± 50.0†	69.6 ± 47.8†	54.3 ± 47.5*‡
Alcohol (distilled spirits, wine, beer)	122 ± 144*†	190 ± 227†‡	299 ± 328*‡
SSB	132 ± 184*†	157 ± 204†‡	256 ± 439*‡
Tea, coffee	167 ± 131†	174 ± 128	202 ± 193‡
Dietary quality			
Mediterranean cluster	533 (47.5)*†	1,052 (37.4)†‡	30 (25.4)*‡
Western cluster	485 (43.2)†	1,148 (40.8)†	35 (29.7)*‡
Social business cluster	104 (9.3)*†	612 (21.8)†‡	53 (44.9)*‡

Values are mean ± SD or n (%). Bonferroni correction was applied for categorical variables ($p < 0.017$). *$p < 0.05$ vs. LBF. †$p < 0.05$ vs. SBF. ‡$p < 0.05$ vs. HBF.

MUFA = monounsaturated fatty acids; PESA = Progression of Early Subclinical Atherosclerosis; PUFA = polyunsaturated fatty acids; SFA = saturated fatty acids; SSB = sugar-sweetened beverages; other abbreviations as in Table 1.

assessed by cross-sectional sweep of above mentioned territories. Plaque was defined as a focal protrusion into the arterial lumen of thickness >0.5 mm or >50% of the surrounding intima-media thickness or a diffuse thickness >1.5 mm measured between the media-adventitia and intima-lumen interfaces (24). Coronary artery calcium (CAC) was assessed by noncontrast electrocardiography-gated prospective acquisition with a 16-slice computed tomography scanner (Philips Brilliance CT, Philips Healthcare, Andover, Massachusetts) and CAC score was calculated using an Agatston equation (25). Subclinical atherosclerosis was defined as the presence of plaque in the right carotid, left carotid, aorta, right iliofemoral, or left iliofemoral or as the presence of calcium (CAC score >0) in the coronary arteries; noncoronary atherosclerosis was defined as presence of plaque in the previously mentioned territories and excluding CAC. Depending on the number of sites affected with atherosclerosis (a maximum of 6), if 4 to 6 sites were affected, it was defined as generalized atherosclerosis (26).

STATISTICAL ANALYSIS. Baseline characteristics are presented as count and percentage for categorical variables, and as mean ± SD for continuous variables. Analysis of variance for continuous variables and chi-square for categorical variables were used to compare the data between categories with Bonferroni correction for multiple comparisons. Multivariate logistic regression models were used to assess the association between breakfast patterns: 1) main outcomes: subclinical, noncoronary and generalized atherosclerosis, presence of atherosclerotic plaques in the aorta, carotid and iliofemoral arteries, CAC score >0; and 2) secondary outcomes: obesity (BMI $\geq$30 kg/m^2), abdominal obesity, MetS, low high-density lipoprotein cholesterol, and hypertension. We followed a 2-step approach for the inclusion of covariates in the models. First, sociodemographic, clinical, and lifestyle variables were compared among the 3 breakfast groups. Those variables that significantly differed between breakfast groups were included in the model. Second, the remaining variables were introduced sequentially in the model and kept if the beta coefficient varied more than 10% (27). All statistical analyses were performed with IBM SPSS Statistics for Windows, version 24 (IBM Corporation, Armonk, New York).

RESULTS

Of 4,052 participants, 2.9%, 69.4%, and 27.7% fell into SBF, LBF, and HBF categories, respectively. Compared with HBF and LBF, the SBF group consisted of mostly men, who were currently smokers, reported having changed their diet in the past year to lose weight, and consumed the highest percentage of energy at lunch. Compared with HBF, LBF participants were more likely to be a man with a lower education level, a current smoker, and also consume a greater proportion of calories at lunch (Table 1). In terms of nutritional quality, SBF participants were more likely to consume more energy, protein (particularly from animal sources), and dietary cholesterol; have the lowest fiber and carbohydrate intakes; and tended to consume more alcoholic and sugar-sweetened beverages, as well as red meat. Compared with HBF, participants in the LBF group had greater daily EI, animal protein intake, and dietary cholesterol intake, and lower intakes of sugar and polysaccharides. This group also had lower intakes of fruits and vegetables, whole grains, and olive oil, and higher intakes of refined grains, red meat, fast food, and precooked meals as well as lean meat and seafood (Table 2). Participants in the HBF group presented significantly greater intakes of carbohydrates and dietary fiber, and tended to consume greater amounts of fruits and vegetables, whole grains, high-fat dairy, and sweets (Table 2).

Morning dietary habits differed significantly across breakfast groups. On average, SBF participants spent no more than 5 min on breakfast, and consumed mostly coffee or orange juice. The most frequent choices among the HBF group were coffee, orange juice, bread toasts with olive oil, tomato, ham, fresh fruit, breakfast cereal, whole grain cookie, or pastries and jam. Regarding LBF participants, they were more likely to have coffee, orange juice, as well as fresh fruit, toast, cookies, or pastries (Online Table 1).

Lunch and dinner intakes also differed significantly between the breakfast patterns groups (Online Tables 2 and 3). Across all the groups SBF participants had the highest intakes of red and processed meat, appetizers, sugar-sweetened beverages, and alcohol at lunch and dinner, as well as the lowest consumption of fruits during lunch. The LBF group compared with HBF had similar intakes of fruits, and higher consumption of appetizers at lunchtime, and also higher intakes of vegetables, lean meat, seafood, and eggs, as well as potatoes, pasta, commercial bakery goods, red and processed meat, sugar-sweetened beverages, and alcohol at dinner.

Compared with the HBF group, cardiometabolic risk markers were more prevalent in the LBF group and even more so in the SBF group, showing the greatest WC and BMI, blood pressure, blood lipids, and fasting glucose levels (Table 3). SBF participants were also more likely to score the highest on the European Society of Cardiology Systematic Coronary Risk Evaluation risk scale (Table 3). The probabilities of presenting obesity, abdominal obesity, MetS, low high-density lipoprotein cholesterol, and hypertension were significantly higher for participants in the SBF group compared with HBF (Figure 1, Online Table 4). Taking

TABLE 3 Distribution of CVD Risk Factors of PESA Study Participants According to Breakfast Pattern

CVD Risk Factors	HBF (n = 1,122)	LBF (n = 2,812)	SBF (n = 118)
Central obesity	136 (12.1)*†	680 (24.2)†‡	45 (38.1)*‡
Weight, kg	72.5 ± 13.8*†	78.1 ± 14.9†‡	83.3 ± 17.6*‡
BMI, kg/m^2	25.01 ± 3.39*†	26.55 ± 3.85†‡	28.04 ± 4.66*‡
Waist circumference, cm	85.6 ± 11.0*†	90.7 ± 12.0†‡	95.5 ± 14.5*‡
Hypertension, mm Hg	97 (8.6)*†	356 (12.7)†‡	27 (22.9)*‡
SBP	114.3 ± 12.1*†	117.0 ± 12.6‡	119.0 ± 13.6‡
DBP	70.75 ± 8.88*†	73.12 ± 9.52†‡	75.36 ± 10.20*‡
Dyslipidemia, mg/dl	374 (33.3)*†	1241 (44.1)†‡	66 (55.9)*‡
Total cholesterol	196.4 ± 31.4*†	202.0 ± 33.8‡	205.8 ± 35.5‡
LDL-c	128.5 ± 28.0*†	133.7 ± 30.2‡	136.0 ± 30.9‡
HDL-c	50.8 ± 12.1*†	48.4 ± 12.1‡	46.8 ± 13.2‡
Triglycerides	84.5 ± 45.4*†	98.3 ± 59.9†‡	114.0 ± 74.5*‡
Diabetes	8 (0.7)*†	65 (2.3)‡	6 (5.1)‡
Fasting glucose, mg/dl	87.9 ± 8.8*†	91.4 ± 15.0†‡	94.7 ± 15.9*‡
CVD risk scores			
SCORE, %	0.40 ± 0.53*†	0.60 ± 0.61†‡	0.85 ± 0.85*‡
Number of CVD risk factors			
0	594 (52.9)*†	1,158 (41.2)†‡	32 (27.1)*‡
1	395 (35.2)*	1,135 (40.4)‡	39 (33.1)
2	120 (10.7)*†	445 (15.8)†‡	35 (29.7)*‡
>2	13 (1.2)*†	74 (2.6)†‡	12 (10.2)*‡

Values are mean ± SD or n (%). *$p < 0.05$ vs. LBF. †$p < 0.05$ vs. SBF. ‡$p < 0.05$ vs. HBF.
BMI = body mass index; CVD = cardiovascular disease; DBP = diastolic blood pressure; HDL-c = high-density lipoprotein cholesterol; LDL-c = low density lipoprotein cholesterol; SBP = systolic blood pressure; SCORE = European Society of Cardiology Systematic Coronary Risk Evaluation; other abbreviations as in Tables 1 and 2.

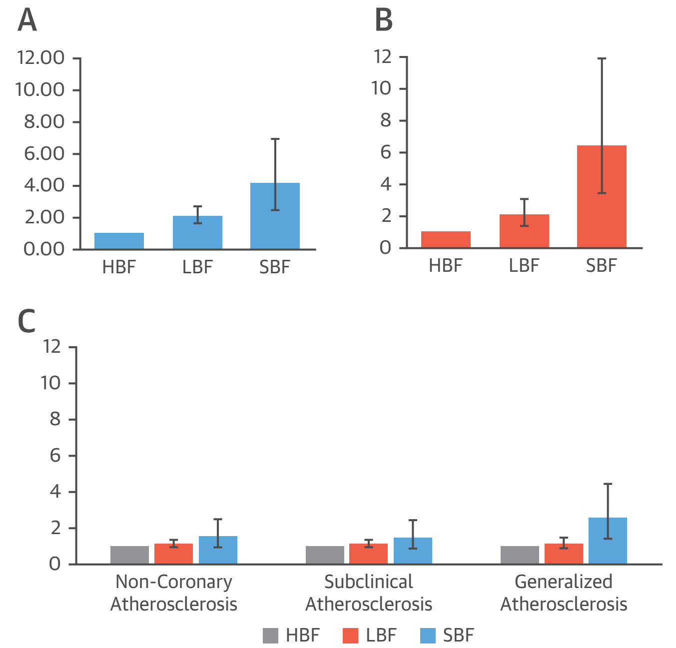
into consideration the higher proportion of participants reporting to be on a diet to lose weight among SBF participants, the model for the association with obesity (BMI >30 kg/m^2) was additionally adjusted for dieting in a sensitivity analysis, resulting in a 4.7% decrease in the association (data not shown).

The prevalence of subclinical, noncoronary and generalized atherosclerosis for PESA participants included in the final analysis were 62.5%, 60.3%, and 13.4%, respectively (Central Illustration). Highest prevalence of atherosclerotic plaques was found in iliofemoral (44.2%) and carotid arteries (31.5%), with the lowest prevalence observed in the aorta (24.6%). CAC score >0 was detected among 18.1% of the total PESA study population.

Subclinical atherosclerosis was observed more frequently among the SBF group (Central Illustration); with higher odds of having plaques in abdominal aorta (odds ratio [OR]: 1.79; 95% confidence interval [CI]: 1.16 to 2.77), carotid atherosclerotic plaques (OR: 1.76; 95% CI: 1.17 to 2.65), and iliofemoral plaques (OR: 1.72; 95% CI: 1.11 to 2.64) (Tables 4 and 5). Regarding the presence of noncoronary and generalized atherosclerosis, the odds were significantly higher for SBF participants, compared with HBF

JACC VOL. 70, NO. 15, 2017
OCTOBER 10, 2017:1833–42

FIGURE 1 **Association Between Breakfast Patterns and Obesity, MetS, and Atherosclerosis**



(A) Adjusted odds ratios for obesity by breakfast pattern (odds ratio [OR] and 95% confidence interval [CI]). Model adjusted for age (years), sex (male/female), energy intake (kcal/day), smoking (yes/no), daily alcohol consumption (g/day), hypertension (yes/no), diabetes (yes/no), dyslipidemia (yes/no), and dieting (yes/no). Obesity defined as body mass index $\geq$30 kg/m^2. **(B)** Adjusted ORs for metabolic syndrome (MetS) by breakfast pattern (OR and 95% CI). Model adjusted for age (years), sex (male/female), energy intake (kcal/day), smoking (yes/no), daily alcohol consumption (g/day), and family history of cardiovascular disease (yes/no). **(C)** Adjusted odds ratios for atherosclerosis by breakfast pattern (OR and 95% CI). Model adjusted for age (years), sex (male/female), smoking (yes/no), hypertension (yes/no), diabetes (yes/no), dyslipidemia (yes/no), waist circumference (cm), and daily intakes of red meat, alcohol, and salt (g). HBF = high-energy breakfast; LBF = low-energy breakfast; SBF = skipping breakfast.

(OR: 1.55; 95% CI: 0.97 to 2.46; OR: 2.57; 95% CI: 1.54 to 4.31) (**Figure 1**). Participants in the LBF group had higher risk of presenting carotid or iliofemoral atherosclerotic plaques (OR: 1.21; 95% CI: 1.03 to 1.43; OR: 1.17; 95% CI: 1.00 to 1.37) (**Tables 4 and 5**).

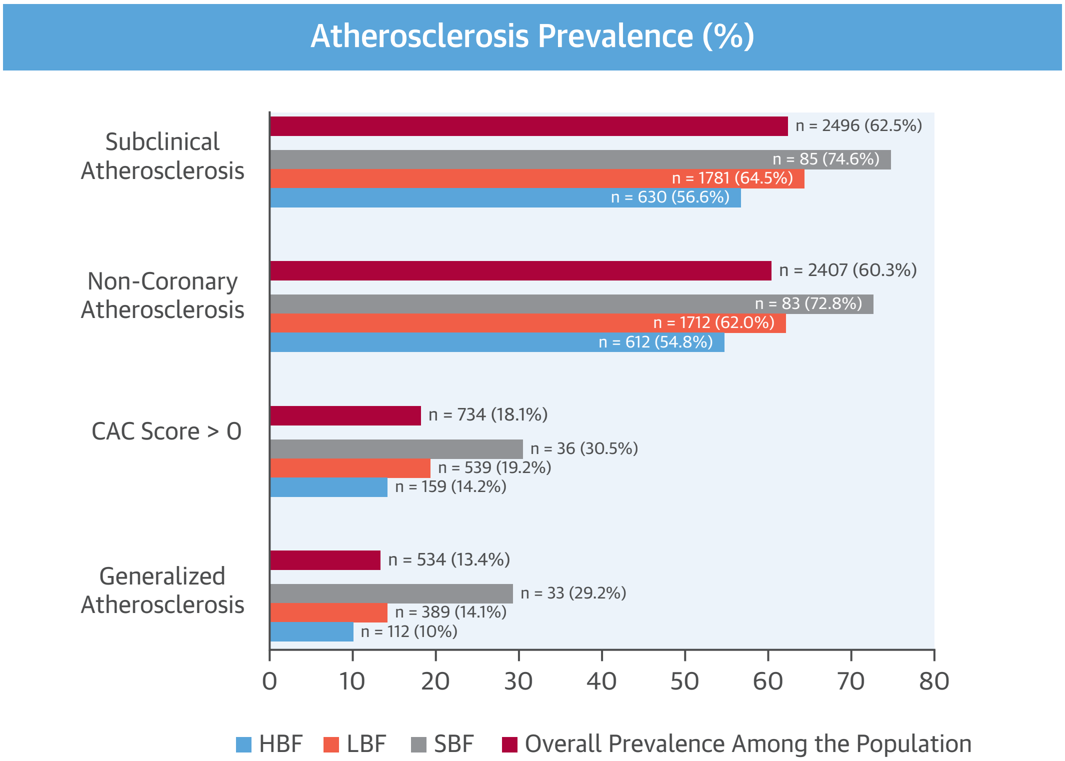
DISCUSSION

We report here, for the first time, evidence of the association between different breakfast patterns such as SBF as well as LBF and HBF consumption with the risk of atherosclerosis. In our study, regular skipping breakfast was associated with a 1.55- and 2.57-fold higher odds for noncoronary and generalized atherosclerosis, respectively, independently of the presence of conventional CVD risk factors and considering overall diet quality. A modest 3% of the participants were classified as not consuming breakfast (<5% of total daily EI consumed up to 10:00 AM), and were further characterized by following an overall unhealthy lifestyle, including poor overall diet, frequent alcohol consumption, and smoking. These findings are in agreement with previous reports where skipping breakfast was associated with smoking (28), increased EI (9), and noncompliance with Healthy Eating recommendations (29). The results from our most adjusted models suggest a possible at least partial association between skipping breakfast and prevalence of subclinical atherosclerosis independent of the overall unhealthy lifestyle of these participants in the SBF group. Also, participants in the LBF group, who consumed mostly toasts or pastries and coffee in the morning, had an increased risk of having carotid and iliofemoral atherosclerotic plaques compared with participants in the HBF group.

To date there are only 2 studies evaluating the habit of regularly skipping breakfast in relation to CVD. Results from a cohort study showed a 14%, 18%, and 36% greater risks for total CVD, total stroke, and hemorrhage, respectively, among those skipping breakfast (13). In a second study, participants who reported skipping breakfast had on average 27% higher risk of coronary heart disease; however, the risk was mediated by BMI and health conditions (12). To investigate whether the observed association in our study could be simply explained by the higher prevalence of CVD risk factors among SBF participants, we performed a multivariable analysis controlling for waist circumference, hypertension, diabetes, dyslipidemia, and smoking. After adjusting for these conditions, as well as the exclusion of obese participants in a sensitivity analysis (data not shown), the risk estimates decreased but remained significant, suggesting that indeed skipping breakfast could be 1 of the risk factors clustering around the early onset and development of atherosclerosis.

The overall dietary pattern followed by SBF participants falls predominantly into our previously defined "social-business eating pattern" (19), with 45% of participants following this specific behavior. It is characterized by overall unhealthy food choices, frequent eating out, and busy schedules, which might shed light not only on the factors affecting the association between skipping breakfast and disease outcomes, but on the underlying reasons for this habit. In line with this cluster of behaviors, we hypothesize that aside from a direct association with CV risk factors, and atherosclerosis that deserves further research, SBF might serve as a marker for a general unhealthy diet or lifestyle, which in turn is associated with the development and progression of atherosclerosis.

CENTRAL ILLUSTRATION Overall Prevalence of an Atherosclerosis Among PESA Study Participants and According to the Type of Breakfast Consumed



Uzhova, I. et al. J Am Coll Cardiol. 2017;70(15):1833–42.

The prevalence of an atherosclerosis is presented for total population, as well as by breakfast habits categories. The SBF group presents the highest proportion of individuals with subclinical, noncoronary, generalized atherosclerosis and increased coronary artery calcium score. CACs = coronary artery calcium score; HBF = high-energy breakfast; LBF = low-energy breakfast; PESA = Progression of Early Subclinical Atherosclerosis; SBF = skipping breakfast.

In line with the previously mentioned observation regarding overall unhealthy dietary choice, by examining specifically dietary intakes at lunch and dinner, we showed that SBF participants had the highest intakes of red and processed meat, appetizers, SSB and alcohol during the rest of the day. The LBF group compared with HBF was higher in intakes of commercial bakery goods, red and processed meat, sugar-sweetened beverages, and alcohol. However, they still consumed similar or for some food groups higher amounts of cardioprotective food items including fruits, vegetables, lean meat, seafood, and eggs, which might explain the lack of an association observed between LBF and atherosclerosis.

It is worth mentioning that the percentage of participants in our study who were overweight or obese was significantly higher among SBF compared with LBF or HBF participants. In has been shown that adipose tissue not only serves as body energy storage but also plays an important role in CV inflammation processes. Obesity is a major source of inflammatory factors such as C-reactive protein, interleukin-6, P-selectin, vascular cell adhesion protein-1, fibrinogen, and others, and it is directly related to systemic inflammation and atherosclerosis (30). The results of the association of SBF with obesity seen in our study are in line with the observations of a large prospective cohort of men (9), although in this study the investigators reported that their findings could be partially explained by the higher proportion of sedentary individuals among the SBF group. In our study, SBF participants were not less physically active, and the observed association between breakfast and obesity was not mediated by the level of physical activity. In addition to the higher prevalence of obese individuals among the SBF group, this group was also more likely to engage in dieting, probably in an attempt

TABLE 4 Association Between Breakfast Pattern and Coronary Artery Calcification

	HBF (n = 1,122)	LBF (n = 2,812)	SBF (n = 118)
CAC score >0			
Cases/noncases	159/963	539/2,273	36/82
Model 1	1.00 (reference)	1.19 (0.97–1.47)	2.07 (1.29–3.30)*
Model 2	1.00 (reference)	1.08 (0.87–1.34)	1.62 (1.00–2.63)†
Model 3	1.00 (reference)	1.04 (0.84–1.29)	1.43 (0.87–2.36)
CAC score >100			
Cases/noncases	23/1,099	112/2,700	7/111
Model 1	1.00 (reference)	1.63 (1.02–2.59)†	2.10 (0.85–5.13)
Model 2	1.00 (reference)	1.44 (0.90–2.31)	1.52 (0.60–3.84)
Model 3	1.00 (reference)	1.37 (0.85–2.22)	1.31 (0.51–3.41)
CAC score >300			
Cases/noncases	12/1,122	34/2,778	2/116
CAC score >400			
Cases/noncases	7/1,115	21/2,791	1/117

Values are n/N or odds ratio (95% confidence interval). Model 1: age, sex; Model 2: Model 1 plus waist circumference, hypertension, dyslipidemia, diabetes, and smoking. Model 3: Model 2 plus red meat, alcohol, and salt. Regression for coronary calcium (CAC) score >300 and >400 was not performed due to small number of cases. *p < 0.01. †p < 0.05.

Abbreviations as in Table 1.

to lose weight. Once dieting was included in the model, the risk slightly decreased by 4.7%, modifying the degree of the relationship between SBF and obesity (data not shown).

A recent report from American Heart Association discussed the time of eating occasions with relation to cardiometabolic risk, suggesting that a greater percentage of energy consumed earlier in a day may beneficially impact risk factors for heart disease and diabetes (8). Clinical studies report that consuming a high-calorie meal in the morning would result in a significant decrease in fasting glucose and insulin (31), as well as reduced plasma ghrelin concentrations, a hormone associated with food perception, leading toward lower energy foods preference (32). Moreover, studies linking breakfast consumption with overall diet quality and regulation of appetite (33,34), reported that not only micronutrient-rich breakfast but the morning meals in general were potentially satiating and had a beneficial effect on appetite regulation, which would help to balance the EI throughout the day and prevent overeating and subsequent obesity.

Considering the importance of regular breakfast consumption for primary CVD prevention, our findings are important for health professionals and might be used as an important key, and simple message for lifestyle-based interventions and public health strategies, as well as informing dietary recommendations and guidelines.

STUDY STRENGTHS AND LIMITATIONS. Our study has some limitations worth considering. Due to the cross-sectional nature of this study we are not able to address a temporal association between breakfast skipping and atherosclerosis. For obesity, reverse causation could not be ruled out and the observed results might be explained by obese participants skipping breakfast to lose weight, rather than skipping breakfast directly influencing the obesity and CVD risk factors associated with this condition. The fact that those participants who skip breakfast were more likely to report having been dieting, we could assume that they might have weight instability (so-called weight fluctuation), which has been reported to be associated with a higher risk of coronary and CVD events (35), and therefore might have served as a mediator between skipping breakfast and atherosclerosis presence in our study. However, taking into account that the nature of our analysis is cross-sectional and there are no available follow-up data, we were unable to address this issue. Additionally, even though our study comprised a large sample size, the participants of the PESA study have a characteristic occupation and lifestyle that might not be representative of the general population. Also, the duration of the overnight fasting was not available in our data and that variable could not be factored into the models; participants who regularly skip breakfast could have a late dinner, and therefore the duration of overnight fasting in this group would have been

TABLE 5 Association Between Breakfast Patterns and Presence of Atherosclerotic Plaques in Several Territories According to Breakfast Habits Categories Among PESA Study Participants

	HBF (n = 1,122)	LBF (n = 2,812)	SBF (n = 118)
Plaque in abdominal aorta			
Case number	244/876	707/2,091	41/75
Model 1	1.00 (reference)	1.14 (0.96–1.35)	1.75 (1.15–2.66)*
Model 2	1.00 (reference)	1.19 (1.01–1.42)†	1.92 (1.25–2.94)*
Model 3	1.00 (reference)	1.17 (0.98–1.40)	1.79 (1.16–2.77)*
Plaque in carotid artery			
Case number	297/825	926/1,884	53/65
Model 1	1.00 (reference)	1.25 (1/06–1.46)*	1.96 (1.32–2.93)*
Model 2	1.00 (reference)	1.23 (1.05–1.45)*	1.86 (1.24–2.79)*
Model 3	1.00 (reference)	1.21 (1.03–1.43)†	1.76 (1.17–2.65)*
Plaque in iliofemoral artery			
Case number	417/702	1,294/1,501	71/64
Model 1	1.00 (reference)	1.27 (1.09–1.48)*	2.17 (1.43–3.30)‡
Model 2	1.00 (reference)	1.23 (1.05–1.43)*	1.95 (1.28–2.99)*
Model 3	1.00 (reference)	1.17 (1.00–1.37)†	1.72 (1.11–2.64)*

Values are n/N or odds ratio (95% confidence interval). Model 1: age, sex; Model 2: Model 1 plus waist circumference, hypertension, dyslipidemia, diabetes, and smoking. Model 3: Model 2 plus red meat, alcohol, and salt. *p < 0.01. †p < 0.05. ‡p < 0.0001.

Abbreviations as in Tables 1 and 2.

equal to the one of the group who consumed breakfast in the morning and had earlier dinner, resulting in a somehow similar metabolic profile. Another limitation of our study is the sample size of the SBF group: only 3% of the population was considered to skip breakfast. However, this rather extreme definition was chosen to allow the comparison with previous studies on skipping breakfast (7,17). It might be interesting for future studies to validate our definition of breakfast and replicate the findings in a different population, as well as to study the association between fasting time and atherosclerosis disease development and progression. Despite the previously mentioned limitations, key advantages of our study are its large sample size, well-characterized diet and lifestyle data, atherosclerosis assessment measured by direct indicators of disease such as presence of plaques, and the possibility to study the association on middle-aged asymptomatic individuals, who would be the ideal candidates for primary prevention.

CONCLUSIONS

Skipping breakfast could serve as a marker of unhealthy dietary and lifestyle behavior and is associated with the presence of noncoronary and generalized atherosclerosis independent of conventional CVD risk factors in a sample of middle-aged asymptomatic individuals. Our findings highlight the message of the importance of healthy eating, including an energetic breakfast.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Regular breakfast skipping in a middle-aged asymptomatic population without previously diagnosed CVD is associated with increased odds of atherosclerosis independent of the presence of CVD risk factors.

TRANSLATIONAL OUTLOOK: Highlighting the importance of observing a quality breakfast in our daily routines is a simple but important message to be used by health professionals to prevent atherosclerosis disease at its earliest stages.

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KEY WORDS atherosclerosis, atherosclerotic plaque, coronary artery calcification, lifestyle, skipping breakfast

APPENDIX For supplemental tables, please see the online version of this article.