JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 70, NO. 20, 2017

ISSN 0735-1097
https://doi.org/10.1016/j.jacc.2017.09.032

ORIGINAL INVESTIGATIONS

Predicting Subclinical Atherosclerosis in Low-Risk Individuals

Ideal Cardiovascular Health Score and Fuster-BEWAT Score

Juan Miguel Fernández-Alvira, PhD,[a] Valentín Fuster, MD, PhD,[a,b] Stuart Pocock, PhD,[a,c] Javier Sanz, MD,[a,b] Leticia Fernández-Friera, MD, PhD,[a,d,e] Martín Laclaustra, MD, PhD,[a,f] Rodrigo Fernández-Jiménez, MD,[a,b,e] José Mendiguren, MD,[g] Antonio Fernández-Ortiz, MD, PhD,[a,h,k] Borja Ibáñez, MD, PhD,[a,e,j] Héctor Bueno, MD, PhD[a,i,k]

JACC JOURNAL CME/MOC

This article has been selected as the month's *JACC* Journal CME/MOC activity, available online at http://www.acc.org/jacc-journals-cme by selecting the *JACC* Journals CME/MOC tab.

Accreditation and Designation Statement

The American College of Cardiology Foundation (ACCF) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The ACCF designates this Journal-based CME/MOC activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Method of Participation and Receipt of CME/MOC Certificate

To obtain credit for *JACC* CME/MOC, you must:

1. Be an ACC member or *JACC* subscriber.
2. Carefully read the CME/MOC-designated article available online and in this issue of the journal.
3. Answer the post-test questions. At least 2 out of the 3 questions provided must be answered correctly to obtain CME/MOC credit.
4. Complete a brief evaluation.
5. Claim your CME/MOC credit and receive your certificate electronically by following the instructions given at the conclusion of the activity.

CME/MOC Objective for This Article: Upon completion of this activity, the learner should be able to: 1) compare the differences between the Ideal Cardiovascular Health Score (ICHS) and the Fuster-BEWAT score (FBS), including benefits and limitations for predicting the presence of subclinical atherosclerosis and cardiovascular events; 2) review the key components of the definition of an ideal cardiovascular health; 3) evaluate the impact of an optimal CV health on the risk of subclinical atherosclerosis; and 4) identify settings or situations where the use of the FBS show advantages compared with the ICHS.

CME/MOC Editor Disclosure: *JACC* CME/MOC Editor Ragavendra R. Baliga, MD, FACC, has reported that he has no financial relationships or interests to disclose.

Author Disclosures: The PESA study was co-funded by Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) and Banco Santander. Funding was also provided by Institute of Health Carlos III (PI15/02019) and European Regional Development Fund. CNIC is supported by the Ministry of Economy, Industry and Competitiveness and by Pro CNIC Foundation and is a Severo Ochoa Center of Excellence (SEV-2015-0505). This work is part of a project that received funding from the European Union Horizon 2020 research and innovation program under Marie Skłodowska-Curie grant 707642 and from American Heart Association grant 14SFRN20490315. Dr. Bueno has received research funding from Instituto de Salud Carlos III (PIE16/00021), AstraZeneca, Bristol-Myers Squibb, Janssen, and Novartis; is a consultant for Abbott, AstraZeneca, Bayer, Bristol-Myers Squibb-Pfizer, and Novartis; and has received speakers fees and travel and attendance support from AstraZeneca, Bayer, Bristol-Myers Squibb-Pfizer, Ferrer, Novartis, Servier, and Medscape. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Medium of Participation: Print (article only); online (article and quiz).

CME/MOC Term of Approval

Issue Date: November 14/21, 2017
Expiration Date: November 20, 2018

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain; [b]Icahn School of Medicine at Mount Sinai, New York, New York; [c]London School of Hygiene and Tropical Medicine, London, United Kingdom; [d]Departamento de Cardiología, Hospital Universitario HM Montepríncipe, Centro Integral de Enfermedades Cardiovasculares (CIEC), Madrid, Spain; [e]Centro de Investigación Biomédica en Red (CIBER) de Enfermedades Cardiovasculares, Spain; [f]Aragon Institute for

JACC VOL. 70, NO. 20, 2017
NOVEMBER 14/21, 2017:2463–73

Predicting Subclinical Atherosclerosis in Low-Risk Individuals

Ideal Cardiovascular Health Score and Fuster-BEWAT Score

Juan Miguel Fernández-Alvira, PhD,[a] Valentín Fuster, MD, PhD,[a,b] Stuart Pocock, PhD,[a,c] Javier Sanz, MD,[a,b] Leticia Fernández-Friera, MD, PhD,[a,d,e] Martín Laclaustra, MD, PhD,[a,f] Rodrigo Fernández-Jiménez, MD,[a,b,e] José Mendiguren, MD,[g] Antonio Fernández-Ortiz, MD, PhD,[a,h,k] Borja Ibáñez, MD, PhD,[a,e,j] Héctor Bueno, MD, PhD[a,i,k]

ABSTRACT

BACKGROUND The ideal cardiovascular health score (ICHS) is recommended for use in primary prevention. Simpler tools not requiring laboratory tests, such as the Fuster-BEWAT (blood pressure [B], exercise [E], weight [W], alimentation [A], and tobacco [T]) score (FBS), are also available.

OBJECTIVES The purpose of this study was to compare the effectiveness of ICHS and FBS in predicting the presence and extent of subclinical atherosclerosis.

METHODS A total of 3,983 participants 40 to 54 years of age were enrolled in the PESA (Progression of Early Subclinical Atherosclerosis) cohort. Subclinical atherosclerosis was measured in right and left carotids, abdominal aorta, right and left iliofemoral arteries, and coronary arteries. Subjects were classified as having poor, intermediate, or ideal cardiovascular health based on the number of favorable ICHS or FBS.

RESULTS With poor ICHS and FBS as references, individuals with ideal ICHS and FBS showed lower adjusted odds of having atherosclerotic plaques (ICHS odds ratio [OR]: 0.41; 95% confidence interval [CI]: 0.31 to 0.55 vs. FBS OR: 0.49; 95% CI: 0.36 to 0.66), coronary artery calcium (CACS) ≥1 (CACS OR: 0.41; 95% CI: 0.28 to 0.60 vs. CACS OR: 0.53; 95% CI: 0.38 to 0.74), higher number of affected territories (OR: 0.32; 95% CI: 0.26 to 0.41 vs. OR: 0.39; 95% CI: 0.31 to 0.50), and higher CACS level (OR: 0.40; 95% CI: 0.28 to 0.58 vs. OR: 0.52; 95% CI: 0.38 to 0.72). Similar levels of significantly discriminating accuracy were found for ICHS and FBS with respect to the presence of plaques (C-statistic: 0.694; 95% CI: 0.678 to 0.711 vs. 0.692; 95% CI: 0.676 to 0.709, respectively) and for CACS ≥1 (C-statistic: 0.782; 95% CI: 0.765 to 0.800 vs. 0.780; 95% CI: 0.762 to 0.798, respectively).

CONCLUSIONS Both scores predict the presence and extent of subclinical atherosclerosis with similar accuracy, highlighting the value of the FBS as a simpler and more affordable score for evaluating the risk of subclinical disease.

Health Research, Translational Research Unit, Hospital Universitario Miguel Servet, Zaragoza, Spain; [g]Banco de Santander, Madrid, Spain; [h]Departamento de Cardiología, Hospital Clínico San Carlos, Madrid, Spain; [i]Instituto de Investigación i+12, Cardiology Department, Hospital Universitario 12 de Octubre, Madrid, Spain; [j]Departamento de Cardiología, Instituto de Investigación Sanitaria (IIS)-Fundación Jiménez Díaz Hospital, Madrid, Spain; and the [k]Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain. The PESA study was co-funded by Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) and Banco Santander. Funding was also provided by Institute of Health Carlos III (PI15/02019) and European Regional Development Fund. CNIC is supported by the Ministry of Economy, Industry and Competitiveness and Pro CNIC Foundation; and is a Severo Ochoa Center of Excellence (SEV-2015-0505). This work is part of a project that received funding from the European Union Horizon 2020 research and innovation program under Marie Skłodowska-Curie grant 707642 and American Heart Association grant 14SFRN20490315. Dr. Bueno has received research funding from Instituto de Salud Carlos III (PIE16/00021), AstraZeneca, Bristol-Myers Squibb, Janssen, and Novartis; is a consultant for Abbott, AstraZeneca, Bayer, Bristol-Myers Squibb-Pfizer, and Novartis; and has received speakers fees and travel and attendance support from AstraZeneca, Bayer, Bristol-Myers Squibb-Pfizer, Ferrer, Novartis, Servier, and Medscape. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Matthew Budoff, MD, served as Guest Editor for this paper.

Manuscript received July 17, 2017; revised manuscript received September 8, 2017, accepted September 11, 2017.

Cardiovascular disease (CVD) remains the first cause of mortality and morbidity worldwide (1,2). In 2010, the American Heart Association proposed a new paradigm by shifting the classic focus on reducing the prevalence of CVD to a national goal of improving CV health in the population by measuring the ideal cardiovascular health score (ICHS) (3). The ICHS metrics focus on a number of lifestyle factors (smoking, body weight, physical activity, and diet) and 3 established risk factors (blood cholesterol, blood glucose, and blood pressure). Since 2010, extensive research has explored the prevalence of ideal CV health in different populations showing very low prevalence of ideal ICHS metrics overall (4) and its association with lower CVD and all-cause mortality (5).

SEE PAGE 2474

The association between ICHS metrics and subclinical disease is a key area of interest to explore the pathways underlying the associations between ICHS and CV risk (6). Among several markers of subclinical CVD, the coronary artery calcification score (CACS) has been identified as one of the most robust markers of subclinical disease and predictor of future CVD events (7). Higher ICHS metrics are associated with lower CACS (8-11). The association among ICHS and other markers of subclinical disease, such as the carotid intima-media thickness (12,13), carotid plaque area (13), and pulse wave velocity as a measurement of arterial stiffness (14,15) has been investigated, but their predictive value is limited (16,17). To the best of our knowledge, the association between ICHS metrics and extensive subclinical atherosclerosis measured by the presence of atherosclerotic plaques in several arterial regions has not been studied yet.

In addition to ICHS, other screening tools, such as the Fuster-BEWAT (blood pressure [B], exercise [E], weight [W], alimentation [A], and tobacco [T]) score (FBS) (18) have been recently developed for use in lifestyle-based CVD prevention. FBS collects clinical information on lifestyle and risk factors including smoking, physical activity, diet (fruit and vegetable consumption), body weight, and blood pressure, but contrary to ICHS, it does not require laboratory results, making it easier and more suitable for use. Nevertheless, whether FBS is useful for predicting subclinical atherosclerosis and whether its discriminating accuracy is similar to ICHS are unknown.

This study, first, explored the association between ICHS and FBS metrics and the presence and extent of subclinical atherosclerosis measured by 2-dimensional (2D)-carotid, aortic, and iliofemoral vascular ultrasonography and CACS by computed tomography (CT) and, second, compared the accuracy of both scores for predicting subclinical atherosclerosis.

ABBREVIATIONS AND ACRONYMS

CACS = coronary artery calcium score

CT = computed tomography

CV = cardiovascular

CVD = cardiovascular disease

FBS = Fuster-BEWAT (blood pressure [B], exercise [E], weight [W], alimentation [A], and tobacco [T]) score

ICH = ideal cardiovascular health

METHODS

STUDY DESIGN AND POPULATION. The PESA (Progression of Early Subclinical Atherosclerosis) study rationale and design have been described elsewhere (19). Briefly, PESA is a prospective cohort study of 4,184 asymptomatic employees of Banco Santander in Madrid (Spain), 40 to 54 years of age, and free of CVD; the study was designed to assess the prevalence and determinants of subclinical atherosclerosis. Participants underwent a complete clinical evaluation, blood and urine analysis, lifestyle questionnaire analysis, accelerometry assessment of physical activity, electrocardiography, and assessment of subclinical atherosclerosis by noninvasive vascular imaging tests, including 2D vascular ultrasonography and CT for CACS measurement. Complete data for the actual analysis were available for 3,983 participants (95.2%). The Ethics Committee of Instituto de Salud Carlos III in Madrid, Spain, approved the study protocol, and written informed consent was obtained from each participant prior to enrollment.

ASSESSMENT OF PARTICIPANTS' CHARACTERISTICS: LIFESTYLE AND CVD RISK FACTORS. Conventional risk factors, such as smoking habits, and a diagnosis of hypertension, diabetes, or dyslipidemia, or family history of CVD were previously defined (20) and were collected as part of each participant's medical history. Blood pressure was measured at rest by using an automatic oscillometric sphygmomanometer (Omron Hem-907, Omron Healthcare, Kyoto, Japan). Anthropometric measurements were obtained following a standardized procedure. Body mass index was calculated as body mass in divided by the participant's height squared (kg/m^2). Blood and urine samples were collected after >8 h of fasting. Dietary intake was assessed by using a computerized questionnaire (Dietary History-Enrica) (21), previously validated (22), conducted by trained dieticians, designed to record habitual food intake over the previous year. Physical activity was assessed by triaxial accelerometry (ActiTrainer accelerometers; Actigraph, Pensacola, Florida) during 7 consecutive days, including sleeping time. Moderate and vigorous levels of physical activity were defined according to Troiano cutoff points (23).

JACC VOL. 70, NO. 20, 2017
NOVEMBER 14/21, 2017:2463–73

TABLE 1 Distribution of ICHS Components in PESA

ICHS Metrics	Total Sample (N = 3,983)	Men (n = 2,501)	Women (n = 1,482)	p Value*
Blood pressure				
Poor (SBP ≥140 or DBP ≥90 mm Hg)	245 (6.2)	207 (8.3)	38 (2.6)	<0.001
Intermediate (SBP 120-139 or DBP 80-89 mm Hg or treated to goal)	1,359 (34.1)	1,134 (45.3)	225 (15.2)	
Ideal (<120/<80 mm Hg)	2,379 (59.7)	1,160 (46.4)	1,219 (82.3)	
Physical activity				
Poor (No moderate and vigorous activity)	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
Intermediate (1–74 min/week vigorous, 1–149 min/week moderate, or equivalent combination)	280 (7.0)	120 (4.8)	160 (10.8)	
Ideal (≥75 min/week vigorous, ≥150 min/week moderate, or equivalent combination)	3,703 (93.0)	2,381 (95.2)	1,322 (89.2)	
Body mass index				
Poor (≥30 kg/m^2)	558 (14.0)	458 (18.3)	100 (6.7)	<0.001
Intermediate (25 to <30 kg/m^2)	1,773 (44.5)	1,399 (55.9)	374 (25.2)	
Ideal (<25 kg/m^2)	1,652 (41.5)	644 (25.7)	1,008 (68.0)	
Diet†				
Poor (0–1 components)	557 (14.0)	395 (15.8)	162 (10.9)	<0.001
Intermediate (2–3 components)	2,649 (66.5)	1,741 (69.6)	908 (61.3)	
Ideal (4–5 components)	777 (18.8)	365 (14.6)	412 (27.8)	
Smoking				
Poor (current)	1,122 (28.2)	681 (27.2)	441 (29.8)	0.219
Intermediate (quit <1 yr)	117 (2.9)	76 (3.0)	41 (2.8)	
Ideal (never or quit >1 yr)	2744 (68.9)	1,744 (69.7)	1,000 (67.5)	
Total cholesterol				
Poor (≥240 mg/dl)	457 (11.5)	329 (13.2)	128 (8.6)	<0.001
Intermediate (200-239 mg/dl or treated to goal)	1,653 (41.5)	1,118 (44.7)	535 (36.1)	
Ideal (<200 mg/dl)	1,873 (47.0)	1,054 (42.1)	819 (55.3)	
Plasma glucose				
Poor (≥126 mg/dl)	45 (1.1)	41 (1.6)	4 (0.3)	<0.001
Intermediate (100-125 mg/dl or treated to goal)	480 (12.1)	427 (17.1)	53 (3.6)	
Ideal (<100 mg/dl)	3,458 (86.8)	2,033 (81.3)	1,425 (96.2)	
Number of ideal metrics				
0	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
1	92 (2.6)	80 (3.2)	12 (0.8)	
2	370 (9.3)	326 (13.0)	44 (3.0)	
3	843 (21.2)	689 (27.5)	154 (10.4)	
4	1,000 (25.1)	692 (27.7)	308 (20.8)	
5	970 (24.4)	493 (19.7)	477 (32.2)	
6	581 (14.6)	198 (7.9)	383 (25.8)	
7	127 (3.2)	23 (0.9)	104 (7.0)	

Values are n (%). *p Values were compared between men and women using a test for trend for each ICHS metric. †Dietary components (ideal values): fruits and vegetables (≥400 g/day), fish (≥200 g/week), fiber (≥1.1 g per 10 g of carbohydrates), sodium (<1,500 mg/day), and soft drinks (<450 kcal/week). Intake goals expressed for a 2,000-kcal diet.

DBP = diastolic blood pressure; ICHS = ideal cardiovascular health score; PESA = Progression of Early Subclinical Atherosclerosis; SBP = systolic blood pressure.

VASCULAR ULTRASONOGRAPHY. Imaging studies included 2D vascular ultrasonography of carotid arteries, infrarenal aortas, and iliofemoral arteries and CACS by CT scan. Vascular ultrasonography was performed using an iU22 ultrasound station (Philips Healthcare, Bothell, Washington), with adapted scanning protocols (20). Plaques were defined as any focal protrusion of more than 0.5 mm or more than 50% thicker than the surrounding intima-media (24). CACS were estimated by using the Agatston method by noncontrast electrocardiography-gated prospective acquisition, using a 16-slice Brilliance CT scanner (Philips Healthcare, Andover, Massachusetts) (20) and graded as <1, 1 to <100, 100 to <400, or ≥400 (25). The PESA Core Imaging Laboratory at the Centro Nacional de Investigaciones Cardiovasculares Carlos III analyzed all imaging recordings.

DEFINITION OF SUBCLINICAL ATHEROSCLEROSIS. Subclinical atherosclerosis at each vascular site was defined as the presence of any atherosclerotic plaque in the carotid, aortic, or iliofemoral territory or having

TABLE 2 Distribution of FBS Components in the PESA Study

FBS Metrics	Total Sample (N = 3,983)	Men (n = 2,501)	Women (n = 1,482)	p Value*
Blood pressure				
0 (SBP ≥140 and/or DBP ≥90 mm Hg)	245 (6.2)	207 (8.3)	38 (2.6)	<0.001
1 (SBP 130–139 and/or DBP 85–89 mm Hg)	396 (9.9)	335 (13.4)	61 (4.1)	
2 (SBP 120–129 and/or DBP 80–84 mm Hg)	894 (22.4)	745 (29.8)	149 (10.1)	
3 (SBP <120 and DBP <80 mm Hg)	2,448 (61.5)	1,214 (48.5)	1,234 (83.3)	
Exercise				
0 (<10 moderate to vigorous activity min/week)	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
1 (<75 moderate to vigorous activity min/week)	10 (0.3)	4 (0.2)	6 (0.4)	
2 (75–149 moderate to vigorous activity min/week)	252 (6.3)	106 (4.2)	146 (9.9)	
3 (≥150 moderate to vigorous activity min/week)	3,721 (93.4)	2,391 (95.6)	1,330 (89.7)	
Weight				
0 (≥30 kg/m^2)	558 (14.0)	458 (18.3)	100 (6.7)	<0.001
1 (25 to <30 kg/m^2)	1,773 (44.5)	1,399 (55.9)	374 (25.2)	
3 (<25 kg/m^2)	1652 (41.5)	644 (25.7)	1,008 (68.0)	
Alimentation				
0 (<1 fruit/vegetable servings daily)	179 (4.5)	107 (4.3)	72 (4.9)	0.073
1 (1–2 fruit/vegetable servings daily)	1,838 (46.1)	1,117 (44.7)	721 (48.7)	
2 (3–4 fruit/vegetable servings daily)	949 (23.8)	607 (24.3)	342 (23.1)	
3 (>4 fruit/vegetable servings daily)	1017 (25.5)	670 (26.8)	347 (23.4)	
Tobacco				
0 (>1 pack of tobacco per day)	184 (4.6)	128 (5.1)	56 (3.8)	0.002
1 (<1 pack of tobacco per day)	933 (23.4)	549 (22.0)	384 (25.9)	
3 (Nonsmoker)	2,866 (72.0)	1,824 (72.9)	1,042 (70.3)	
Number of ideal metrics				
0	21 (0.5)	14 (0.6)	7 (0.5)	<0.001
1	286 (7.2)	236 (9.4)	50 (3.4)	
2	1,121 (28.1)	873 (34.9)	248 (16.7)	
3	1,320 (33.1)	851 (34.0)	469 (31.6)	
4	975 (24.5)	433 (17.3)	542 (36.6)	
5	260 (6.5)	94 (3.8)	166 (11.2)	

Values are n (%). *The p values were compared between men and women using a test for trend for each FBS metric.
BEWAT = blood pressure (B), exercise (E), weight (W), alimentation (A), and tobacco (T); FBS = Fuster-BEWAT score; other abbreviations as in Table 1.

CACS of ≥1. The number of vascular sites affected (right carotid, left carotid, abdominal aorta, right iliofemoral artery, left iliofemoral and coronary arteries) was used for defining the multiterritorial extent of subclinical atherosclerosis and classified as disease free (no vascular sites affected) or as having focal (1 site), intermediate (2 to 3 sites), or generalized (4 to 6 sites) atherosclerosis (20).

CARDIOVASCULAR HEALTH METRICS. The 7 ICHS behaviors and risk factors (exercise, body mass index, diet, smoking status, blood pressure, serum cholesterol, and fasting glucose) were classified according to American Heart Association definitions (3) as poor, intermediate, or ideal (Table 1). Each component was then dichotomized as being ideal versus nonideal, and subjects were classified as having poor, intermediate, or ideal CV health based on the total number of ideal metrics (0 to 2 poor, 3 to 5 intermediate, 6 to 7 ideal) (2).

The 5 FBS components, blood pressure (B), exercise (E), weight (W), alimentation (A), and tobacco (T), were divided into 4 categories ranging from 0 to 3 according to the previously published description (Table 2) (18). Each component was dichotomized as ideal (3) or nonideal (0 to 2), and subjects were classified as having poor, intermediate, or ideal CV health based on the total number of ideal components (0 to 1 poor, 2 to 3 intermediate, 4 to 5 ideal).

STATISTICAL ANALYSIS. All statistical analyses were performed using SPSS software version 20.0 (IBM, Armonk, New York). Subclinical atherosclerosis was dichotomized as presence of plaque versus no plaque. CACS was dichotomized as <1 and ≥1 Agatston unit. Distribution of each individual ICHS (classified as poor, intermediate, ideal) and FBS (classified as 0, 1, 2, 3) metrics are presented for the total sample and stratified by sex, as well as by distribution of the number of ideal metrics for each score.

TABLE 3 Association Between ICHS and FBS and Subclinical Atherosclerosis Measured as Plaque Presence at Any Site and CACS of ≥1

	n	OR	95% CI	p Value
Presence of atherosclerotic plaque*				
ICHS				
Poor	462	ref		
Intermediate	2,813	0.61	0.48–078	<0.001
Ideal	708	0.41	0.31–0.55	<0.001
C-statistic (95% CI)		0.694 (0.678–0.711)		
FBS				
Poor	307	ref		
Intermediate	2,441	0.62	0.46–0.82	0.001
Ideal	1,235	0.49	0.36–0.66	<0.001
C-statistic (95% CI)		0.692 (0.676–0.709)		
CACS ≥1†				
ICHS				
Poor	462	ref		
Intermediate	2,813	0.58	0.46–0.73	<0.001
Ideal	708	0.41	0.28–0.60	<0.001
C-statistic (95% CI)		0.782 (0.765–0.800)		
FBS				
Poor	307	ref		
Intermediate	2,441	0.70	0.53–0.93	0.014
Ideal	1,235	0.53	0.38–0.74	<0.001
C-statistic (95% CI)		0.780 (0.762–0.798)		

Logistic regression models were adjusted for age, sex, education level, and family cardiovascular disease history. ICHS categories were based on the number of ideal factors (0 to 2 poor, 3 to 5 intermediate, 6 to 7 ideal). FBS categories were based on the number of ideal factors (0 to 1 poor, 2 to 3 intermediate, 4 to 5 ideal). *Reference category, that is, no plaque. †Reference category was CACS of <1.

CI = confidence interval; OR = odds ratio; CACS = coronary artery calcium; other abbreviations as in Tables 1 and 2.

Associations between individual metrics in the ICHS and FBS and the presence of subclinical atherosclerosis defined as having plaque or CACS ≥1 were examined by use of logistic regression models. The associations between the ICHS and FBS categorized as poor, intermediate, and ideal and the presence of subclinical atherosclerosis were also examined by logistic regression models. Ordinal regression models were fitted to explore the association between ICHS and FBS and the multiterritorial extent of subclinical atherosclerosis and the amount of CACS (divided into <1, 1 to <100, 100 to <400, and ≥400 Agatston units). All regression models were adjusted for age, sex, family CVD history, and educational level. The C-statistic or area under the receiver operating characteristic (ROC) curve (AUC) and 95% confidence interval (CI) were calculated for each model as a measure of the discriminatory power of each score.

RESULTS

The mean age of the 3,983 participants was 45.8 ± 4.3 years (62.8% men). The 10-year Framingham risk score was 5.8 ± 4.3 for the total sample (men: 7.7 ± 4.3; women: 2.8 ± 2.0), and the 30-year Framingham risk score was 17.7 ± 11.7 overall (men: 22.8 ± 11.3; women: 9.1 ± 6.0).

Overall, only 3.2% of subjects met all 7 ideal ICHS metrics, whereas 6.5% of subjects met all 5 ideal FBS metrics (Tables 1 and 2). Most of the sample (71.7%) met between 3 and 5 ideal ICHS metrics (intermediate CV health). Likewise, 61.2% of the sample met between 2 and 3 ideal FBS components (intermediate CV health). The overall prevalence of a favorable ICHS (at least 6 ideal metrics) or favorable FBS (at least 4 ideal metrics) was 17.8% and 31.0%, respectively. Women presented a significantly higher number of ideal metrics in both scores and significantly higher proportion of ideal levels in all metrics, except for fruit and vegetable consumption and smoking status.

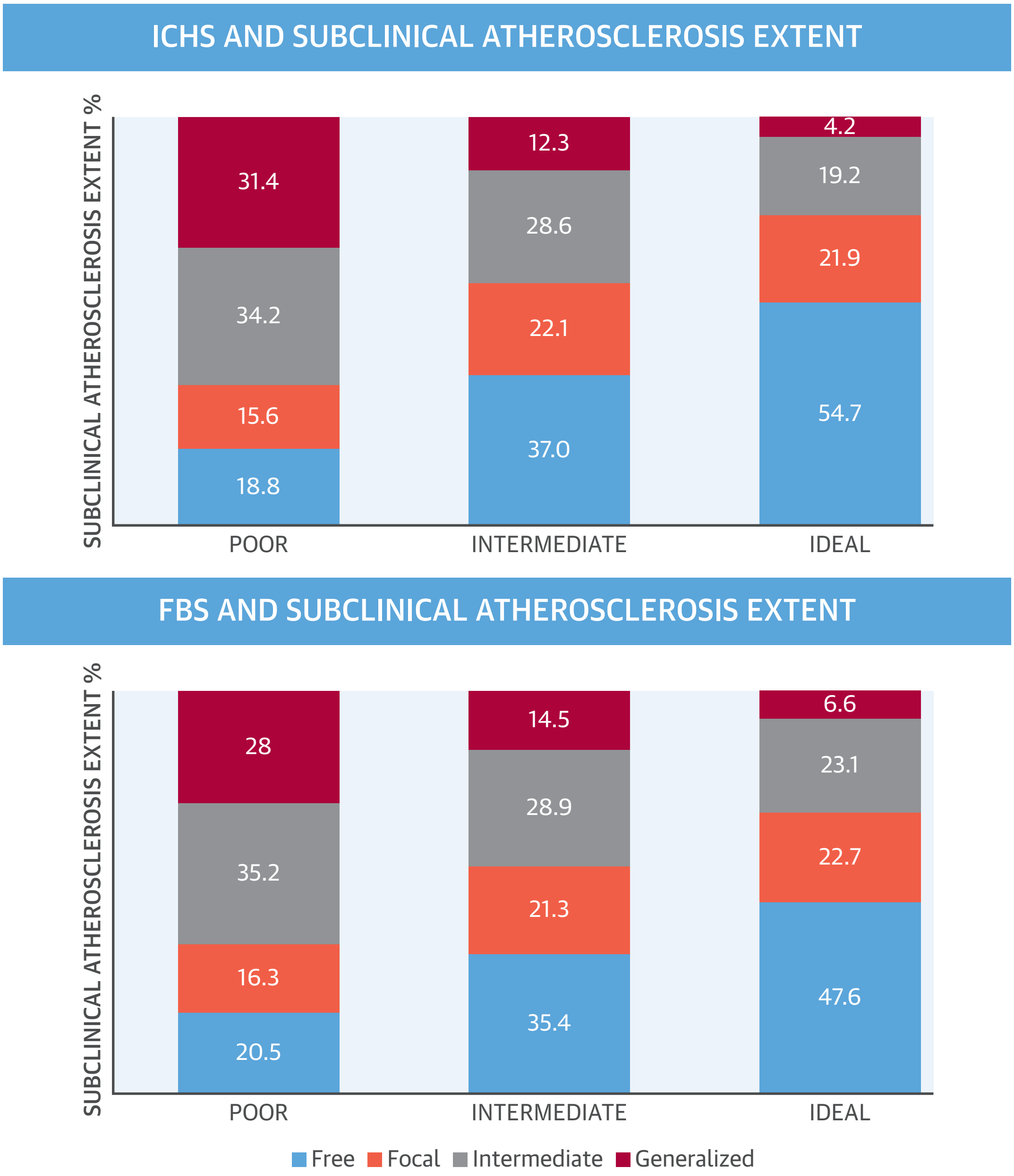
Among health behaviors, ideal dietary metrics had the lowest prevalence (18.8% for ICHS and 25.5% for FBS), whereas ideal physical activity levels were highly prevalent (93.0% for ICHS and 93.4% for FBS). The prevalence of ideal blood pressure was 59.7% for ICHS and 61.5% for FBS, and ideal body mass index prevalence was 41.5% for both scores. The prevalence of ideal total cholesterol and plasma glucose, assessed only for ICHS, was 47.0% and 86.8%, respectively. Nonsmokers represented 68.9% and 72.0% of the total sample according to the ICHS and FBS, respectively.

SUBCLINICAL ATHEROSCLEROSIS AND ASSOCIATION WITH ICHS AND FBS RESULTS. The presence of at least 1 atherosclerotic plaque could be identified in 2,377 subjects (59.7%), more frequently in men than in women, and more often in the iliofemoral bed than in other arterial beds (Online Table 1). Although involvement of multiple territories was found in 1,619 individuals (40.7%), calcium calcification with Agatston score ≥1 was observed in 700 participants (17.6%).

Overall, there was a strong inverse association between ICHS and FBS and subclinical atherosclerosis. Compared with participants categorized as having poor ICHS (0 to 2 ideal factors) or poor FBS (0 to 1 ideal factor), adjusted odds ratios (ORs) for plaque presence and for CACS ≥1 were significantly lower among subjects classified as having intermediate and ideal scores (Table 3). The association between the individual components of both scores and subclinical atherosclerosis is shown in Online Table 2. Both scores were also associated with the extent of subclinical atherosclerosis and with the degree of coronary calcification (Central Illustration, Table 4, Online Figure 1).

The AUC analysis showed similar levels of discriminating accuracy of ICHS (C-statistic: 0.694;

CENTRAL ILLUSTRATION ICHS and FBS Distribution According to the Multiterritorial Extent of Subclinical Atherosclerosis



Fernández-Alvira, J.M. et al. J Am Coll Cardiol. 2017;70(20):2463–73.

Distribution of subclinical atherosclerosis categorized as free, focal, intermediate, and generalized according to ICH and FBS levels, categorized into poor, intermediate, and ideal. BEWAT = blood pressure (B), exercise (E), weight (W), alimentation (A), and tobacco (T); FBS = Fuster-BEWAT score; ICHS = ideal cardiovascular health score.

95% confidence interval [CI]: 0.678 to 0.711) and FBS (C-statistic: 0.692; 95% CI: 0.676 to 0.709) in identifying the presence of plaques as well as for identifying CACS ≥1 (C-statistic: 0.782; 95% CI: 0.765 to 0.800, vs. C-statistic: 0.780; 95% CI: 0.762 to 0.798, respectively) (**Table 3, Figure 1**). By using ordinal regression models, the ORs for a greater extent of subclinical atherosclerosis, measured by the number

TABLE 4 Association Between ICHS and FBS and Multiterritorial Extent of Subclinical Atherosclerosis and CACS Level

	n	OR	95% CI	p Value
Multiterritorial extent of subclinical atherosclerosis*				
ICHS				
Poor	462	ref		
Intermediate	2,813	0.48	0.40–0.58	<0.001
Ideal	708	0.32	0.26–0.41	<0.001
C-statistic (95% CI)		0.779 (0.759–0.795)		
FBS				
Poor	307	ref		
Intermediate	2,441	0.52	0.42–0.65	<0.001
Ideal	1,235	0.39	0.31–0.50	<0.001
C-statistic (95% CI)		0.773 (0.752–0.795)		
Level of CACS†				
ICHS				
Poor	462	ref		
Intermediate	2,813	0.56	0.45–0.69	<0.001
Ideal	708	0.40	0.28–0.58	<0.001
C-statistic (95% CI)		0.881 (0.836–0.925)		
FBS				
Poor	307	ref		
Intermediate	2,441	0.69	0.53–0.91	0.009
Ideal	1,235	0.52	0.38–0.72	<0.001
C-statistic (95% CI)		0.861 (0.816–0.907)		

*Defined according to the number of vascular sites affected, divided into 4 categories: disease free (0 vascular sites affected) or as having focal (1 site), intermediate (2 to 3 sites), or generalized (4 to 6 sites) atherosclerosis. †Categorical variables were as follows: <1, ≥1, and <100; ≥100 and <400; or ≥400 Agatston units. Ordinal regression models were adjusted for age, sex, education level, and family history of cardiovascular disease. ICHS categories were based on the number of ideal factors (0 to 2 poor, 3 to 5 intermediate, 6 to 7 ideal). FBS categories were based on the number of ideal factors (0 to 1 poor, 2 to 3 intermediate, 4 to 5 ideal). Odds ratios express the probability of being in a higher level of atherosclerosis extent or being in a higher CACS category.

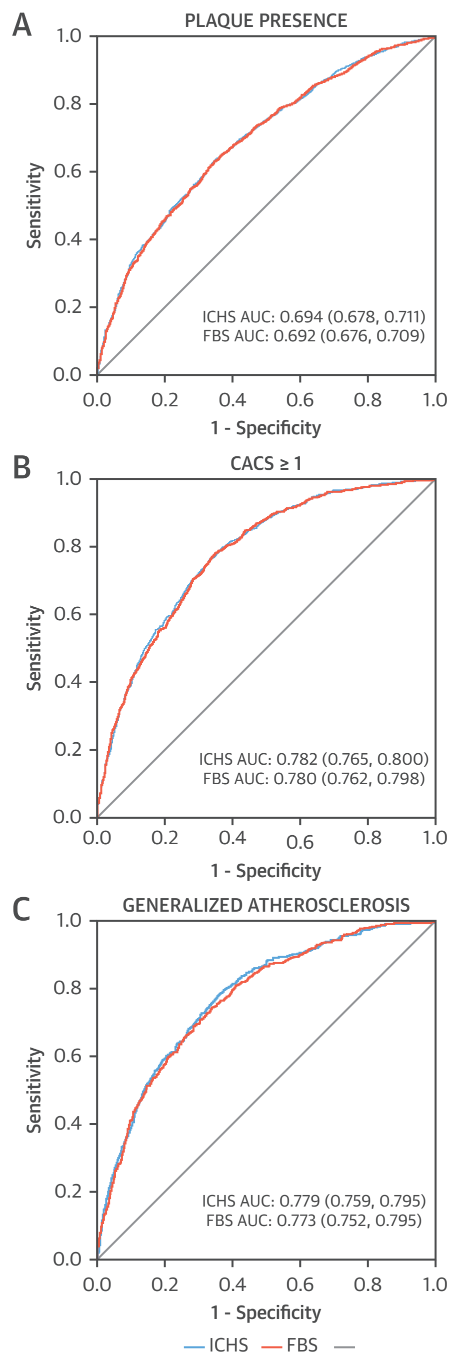
Abbreviations as in Tables 1 to 3.

of diseased vascular sites (none, focal, intermediate, or generalized) and CACS level (<1, 1 to <100, 100 to <400, or ≥400) were significantly lower among subjects with ideal ICHS or ideal FBS, taking the poorest score as a reference ($p < 0.001$ for all comparisons). The AUC analysis showed equivalent discriminating accuracy levels for both models in predicting generalized subclinical atherosclerosis: ICHS C-statistic of 0.779 (95% CI: 0.759 to 0.795); a FBS C-statistic of 0.773 (95% CI: 0.752 to 0.795); and very similar values in predicting CACS ≥400 level, with ICHS C-statistic of 0.881 (95% CI: 0.836 to 0.925) and an FBS C-statistic of 0.861 (95% CI: 0.816 to 0.907) (Table 4, Online Figure 1).

DISCUSSION

Better profiles of CV health behaviors and risk factors, reflected by higher ICHS and FBS metrics, are strongly associated with a lower prevalence and a lower extent of subclinical atherosclerosis in healthy individuals.

FIGURE 1 Prediction of Plaque Presence, CACS ≥1, and Generalized Atherosclerosis by ICHS and FBS Levels



The ROC curves reflect the prediction accuracy of ICHS and FBS for generalized atherosclerosis, plaque presence, and CACS ≥1 detection. AUC = area under the curve; BEWAT = blood pressure (B), exercise (E), weight (W), alimentation (A), and tobacco (T); CACS = coronary artery calcium; FBS = Fuster-BEWAT score; ICHS = ideal cardiovascular health score; ROC = receiver operating characteristic.

This is good evidence of the impact of lifestyle and risk factors on the early phase of the disease. Both scores showed good and comparable predictive values for all outcomes measured in the PESA cohort, including the presence of any atherosclerotic plaque, presence and amount of calcium in coronary arteries, and number of affected arterial sites.

Our study shows an inverse relationship between ideal CV risk score metrics and the presence of subclinical atherosclerosis, evaluated by 2 different indices. To our knowledge, this is the first study to show this relationship with multiterritorial disease in a large cohort of healthy individuals. Previous studies evaluating ICHS metrics and subclinical atherosclerosis used coronary calcium as the marker. Robbins et al. (9) and Bensenor et al. (11) showed a strong inverse relationship between ICHS metrics and prevalence of coronary artery calcium in adults. Saleem et al. (10) also found that middle-aged men and women with a favorable ICHS have a lower prevalence and severity of subclinical atherosclerosis as estimated by CACS. Ahmed et al. (26) found that regular exercise, adherence to a Mediterranean-style diet, smoking avoidance, and maintenance of normal weight were associated with lower CAC incidence and progression, and significantly lower all-cause mortality over 7.6 years in participants 44 to 84 years of age from the MESA (Multi-Ethnic Study of Atherosclerosis) study. It has been shown, however, that the absence of coronary artery calcium does not necessarily mean that individuals are disease free (20). The high prevalence of atherosclerotic plaques (59.7%) compared with the prevalence of CACS ≥1 (17.6%) in our study suggests that coronary artery calcium represents a more advanced stage of disease. Other studies also concluded that exploring several territories allows overcoming the potential problem of not detecting lesions when only a single territory is taken into account (27). In fact, the overall prevalence of subclinical atherosclerosis found in our cohort is high.

The majority of participants (approximately 80%) with poor ICHS and FBS in our study presented at least 1 affected site. However, subclinical atherosclerosis was also present in approximately one-half of the population with ideal ICHS and FBS metrics. The follow-up data in the PESA cohort will allow investigating whether participants showing ideal ICHS and FBS metrics have less progression of subclinical atherosclerosis and/or lower incidence of clinical events over time and whether remaining in ICHS and FBS categories (ideal, intermediate, poor) leads to different rates of worsening subclinical atherosclerosis and transition to clinical atherosclerosis, including CV events and mortality.

Although the ICHS and the FBS share 5 metrics (blood pressure, physical activity, dietary metric, body weight, and tobacco consumption), the ICHS also includes cholesterol and fasting glucose levels. Because the FBS does not require laboratory analyses to be derived and given the comparable predictive value of both scores, the FBS may be considered a practical and affordable option with which to foster primary CV prevention in settings where easy laboratory data are not available. This may not be considered an advantage in high-resource environments, where routine screening for risk factors by laboratory analysis are recommended (28,29) but may be particularly relevant in low resource areas, such as in developing countries, where the burden of CVD is growing faster. It also may be used for educational purposes in nonmedical environments (i.e., schools) and for personal self-monitoring as a tool to improve self-CV care.

STUDY LIMITATIONS. It must be acknowledged that the benefit of predicting subclinical atherosclerosis is still not well defined. Although subclinical atherosclerosis precedes clinical cardiovascular disease, it needs be proven that if, for a given level of cardiovascular risk, people with subclinical noncoronary atherosclerosis are at higher risk of later clinical atherosclerosis than people without subclinical atherosclerosis and whether they may benefit from more intensive primary prevention strategies at an earlier stage.

A number of other limitations should be considered when interpreting this study. First, the results are based on cross-sectional data from the PESA cohort at baseline and therefore cannot establish causality. However, the ongoing PESA follow-up will study the association between CV health and the progression of subclinical atherosclerosis and subsequent CV events. Second, the PESA cohort consists of middle-aged participants, predominantly middle- to high-income Caucasian workers not randomly selected from the general population, and therefore, the generalizability of the results is limited. In comparison with previous reports of the distribution of ICHS metrics, our sample presents a higher prevalence of good ICHS metrics (28,29). Despite these limitations, the use of contemporary imaging technology, the systematic and extensive collection of behavioral and risk factors, and the overall high-quality data profile obtained from a relatively young cohort may help provide useful insights into the early stages of subclinical atherosclerosis and its association with risk and its association with CV risk and behavioral patterns and will help understanding their influence on monitoring atherosclerosis progression.

CONCLUSIONS

The use of scores assessing CV health behaviors and risk factors is useful for predicting the presence of subclinical atherosclerosis in healthy adults at low short-term CV risk. Although the ICHS and the FBS showed similar predictive values for detecting subclinical disease, the FBS is simpler and does not need laboratory results. Therefore, it may be considered the first option in settings where access to laboratory analysis is limited.

ADDRESS FOR CORRESPONDENCE: Dr. Valentín Fuster, Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Melchor Fernández Almagro, 3, 28029-Madrid, Spain. E-mail: vfuster@cnic.es. OR Dr. Héctor Bueno, Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Melchor Fernández Almagro, 3, 28029-Madrid, Spain. E-mail: hector.bueno@cnic.es.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: The ICHS, which incorporates 7 metrics (exercise, body mass index, diet, smoking status, blood pressure, and blood cholesterol and fasting glucose levels), has validated predictive value for cardiovascular events. The Fuster-BEWAT score uses 5 metrics (blood pressure [B], exercise [E], weight [W], alimentation [A], and tobacco [T]) and does not require laboratory tests. Both scores exhibit comparable predictive values for detection of subclinical atherosclerosis in ostensibly healthy individuals.

TRANSLATIONAL OUTLOOK: The FBS is an easy, painless, inexpensive tool that could be implemented in resource-constrained health care settings to identify individuals with a high likelihood of subclinical atherosclerosis at whom preventive management strategies can be directed.

REFERENCES

1. Roth GA, Forouzanfar MH, Moran AE, et al. Demographic and epidemiologic drivers of global cardiovascular mortality. N Engl J Med 2015;372:1333–41.

2. Writing Group M, Mozaffarian D, Benjamin EJ, et al. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. Circulation 2016;133:e38–360.

3. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic impact goal through 2020 and beyond. Circulation 2010;121:586–613.

4. Maclagan LC, Tu JV. Using the concept of ideal cardiovascular health to measure population health: a review. Curr Opin Cardiol 2015;30:518–24.

5. Fang N, Jiang M, Fan Y. Ideal cardiovascular health metrics and risk of cardiovascular disease or mortality: a meta-analysis. Int J Cardiol 2016;214:279–83.

6. Nasir K, Blankstein R. Disparities between ideal cardiovascular health metrics and subclinical atherosclerotic burden: more than meets the eye. Circ Cardiovasc Imaging 2015;8:e002761.

7. McClelland RL, Jorgensen NW, Budoff M, et al. 10-year coronary heart disease risk prediction using coronary artery calcium and traditional risk factors: derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) with validation in the HNR (Heinz Nixdorf Recall) study and the DHS (Dallas Heart Study). J Am Coll Cardiol 2015;66:1643–53.

8. Alman AC, Maahs DM, Rewers MJ, Snell-Bergeon JK. Ideal cardiovascular health and the prevalence and progression of coronary artery calcification in adults with and without type 1 diabetes. Diabetes Care 2014;37:521–8.

9. Robbins JM, Petrone AB, Carr JJ, et al. Association of ideal cardiovascular health and calcified atherosclerotic plaque in the coronary arteries: the National Heart, Lung, and Blood Institute Family Heart Study. Am Heart J 2015;169:371–8.

10. Saleem Y, DeFina LF, Radford NB, et al. Association of a favorable cardiovascular health profile with the presence of coronary artery calcification. Circ Cardiovasc Imaging 2015;8.

11. Bensenor IM, Goulart AC, Santos IS, et al. Association between a healthy cardiovascular risk factor profile and coronary artery calcium score: results from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). Am Heart J 2016;174:51–9.

12. Kulshreshtha A, Goyal A, Veledar E, et al. Association between ideal cardiovascular health and carotid intima-media thickness: a twin study. J Am Heart Assoc 2014;3:e000282.

13. Sturlaugsdottir R, Aspelund T, Bjornsdottir G, et al. Carotid atherosclerosis and cardiovascular health metrics in old subjects from the AGES-Reykjavik study. Atherosclerosis 2015;242:65–70.

14. Aatola H, Hutri-Kahonen N, Juonala M, et al. Prospective relationship of change in ideal cardiovascular health status and arterial stiffness: the Cardiovascular Risk in Young Finns Study. J Am Heart Assoc 2014;3:e000532.

15. Crichton GE, Elias MF, Robbins MA. Cardiovascular health and arterial stiffness: the Maine-Syracuse longitudinal study. J Hum Hypertens 2014;28:444–9.

16. Kavousi M, Elias-Smale S, Rutten JH, et al. Evaluation of newer risk markers for coronary heart disease risk classification: a cohort study. Ann Intern Med 2012;156:438–44.

17. Yeboah J, McClelland RL, Polonsky TS, et al. Comparison of novel risk markers for improvement in cardiovascular risk assessment in intermediate-risk individuals. JAMA 2012;308:788–95.

18. Gomez-Pardo E, Fernandez-Alvira JM, Vilanova M, et al. A comprehensive lifestyle peer group-based intervention on cardiovascular risk factors: the randomized controlled fifty-fifty program. J Am Coll Cardiol 2016;67:476–85.

19. Fernandez-Ortiz A, Jimenez-Borreguero LJ, Penalvo JL, et al. The Progression and Early detection of Subclinical Atherosclerosis (PESA) study: rationale and design. Am Heart J 2013;166:990–8.

20. Fernandez-Friera L, Penalvo JL, Fernandez-Ortiz A, et al. Prevalence, vascular distribution, and multiterritorial extent of subclinical atherosclerosis in a middle-aged cohort: the PESA (Progression of Early Subclinical Atherosclerosis) study. Circulation 2015;131:2104–13.

21. Rodriguez-Artalejo F, Graciani A, Guallar-Castillon P, et al. [Rationale and methods of the study on nutrition and cardiovascular risk in Spain (ENRICA)]. Rev Esp Cardiol 2011;64:876–82.

22. Guallar-Castillon P, Rodriguez-Artalejo F, Tormo MJ, et al. Major dietary patterns and risk of coronary heart disease in middle-aged persons from a Mediterranean country: the EPIC-Spain cohort study. Nutr Metab Cardiovasc Dis 2012; 22:192–9.

23. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. Med Sci Sports Exerc 2008;40:181–8.

24. Stein JH, Korcarz CE, Hurst RT, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. J Am Soc Echocardiogr 2008;21:93–111; quiz 189–90.

25. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15: 827–32.

26. Ahmed HM, Blaha MJ, Nasir K, et al. Low-risk lifestyle, coronary calcium, cardiovascular events, and mortality: results from MESA. Am J Epidemiol 2013;178:12–21.

27. Belcaro G, Nicolaides AN, Ramaswami G, et al. Carotid and femoral ultrasound morphology screening and cardiovascular events in low risk subjects: a 10-year follow-up study (the CAFES-CAVE study[1]). Atherosclerosis 2001; 156:379–87.

28. Bambs C, Kip KE, Dinga A, Mulukutla SR, Aiyer AN, Reis SE. Low prevalence of “ideal cardiovascular health” in a community-based population: the heart strategies concentrating on risk evaluation (Heart SCORE) study. Circulation 2011;123:850–7.

29. Yancy CW. Is ideal cardiovascular health attainable? Circulation 2011;123:835–7.

KEY WORDS cardiovascular risk, Fuster-BEWAT score, ideal cardiovascular health, predictive tools, subclinical atherosclerosis

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

Go to http://www.acc.org/jacc-journals-cme to take the CME/MOC quiz for this article.