Subclinical Coronary Atherosclerosis in Asymptomatic Filipino and White Women

Maria Rosario G. Araneta, PhD; Elizabeth Barrett-Connor, MD

Background—Coronary heart disease (CHD) is the leading cause of morbidity and mortality in persons with type 2 diabetes mellitus (T2DM). Electron-beam computed tomography (EBCT) detects coronary artery calcium (CAC), a marker of atherosclerotic plaque. Few studies have described EBCT-defined CHD among ethnic minorities with elevated T2DM prevalence. The objective of this study was to compare EBCT-defined CAC in Filipino and white women without known cardiovascular disease.

Methods and Results—Subjects were participants aged 55 to 78 years in the Rancho Bernardo Study (n = 1100) and the University of California at San Diego’s Filipino Women’s Health Study (n = 100). Glucose, blood pressure, lipids, anthropometric measurements, and lifestyle factors were measured from 1995 to 1999. EBCT-defined CAC scores, visceral and subcutaneous fat, and statin use were assessed in 2001 to 2002. Compared with whites, Filipinas had a significantly higher prevalence of T2DM (32.6% versus 6.1%, \( P < 0.001 \)) and the metabolic syndrome (32.6% versus 13.8, \( P < 0.001 \)). Filipinas were younger (64.4 versus 66.7 years), had higher triglyceride levels (155 versus 135 mg/dL), had a higher ratio of total cholesterol to HDL cholesterol (4.3 versus 3.5), more frequently used statins (31% versus 19%), and had more visceral fat (69.4 versus 62.1 cm\(^3\)) and lower HDL cholesterol levels (54 versus 66 mg/dL) than whites. Exercise frequency, body mass index, and waist girth did not differ by ethnicity. Nevertheless, extensive (CAC score \( \geq 400 \); 9% versus 9%) and moderate (CAC score 150 to 399; 13% versus 11%) atherosclerotic plaque did not differ by ethnicity, even after adjustment for age, T2DM, hypertension, estrogen use, statin use, smoking, lipids, and visceral fat.

Conclusions—Filipinas had no excess of subclinical atherosclerosis despite their significantly higher prevalence of T2DM, the metabolic syndrome, hypertension, and visceral adiposity. (Circulation. 2004;110:2817-2823.)

Key Words: coronary disease ■ diabetes mellitus ■ plaque ■ tomography

Coronary heart disease (CHD) is the leading cause of morbidity and mortality in postmenopausal women. Coronary artery plaque is predictive of subsequent cardiovascular events and is a marker of subclinical atherosclerosis. Ultrafast high-intensity electron-beam computed tomography (EBCT) is a noninvasive method to measure coronary artery plaque. The EBCT-generated coronary artery calcium (CAC) score correlates with coronary artery plaque burden as assessed by pathology\(^1\) and is predictive of subsequent cardiac events in symptomatic and asymptomatic adults.\(^1\)\(^-\)\(^3\)

Few studies of EBCT-defined subclinical atherosclerosis have been performed among women and ethnic minorities. Cardiovascular disease (CVD) and CHD are elevated among individuals with type 2 diabetes (T2DM) and the metabolic syndrome,\(^4\) and T2DM prevalence is elevated among ethnic minorities. However, some studies have suggested ethnic differences in CVD prevalence. In 2 multiethnic populations with uniform health coverage, Asian-Americans with T2DM had fewer CVD complications than whites, Latinos, and blacks with T2DM.\(^5\)\(^-\)\(^6\) Pima Indians and Naurus have elevated T2DM prevalence but lower CHD rates than whites.\(^7\)\(^-\)\(^9\) It remains unclear whether ethnic disparities in the prevalence of CVD, CHD, or subclinical atherosclerosis are due to differences in lifestyle, access to health care, or other factors.

The second-largest immigrant population in the United States (second only to Mexicans\(^10\)) is from the Philippines, but clinical studies of Filipino-Americans are scarce. The few published studies have reported a 16% to 36% T2DM prevalence, despite the absence of obesity by Western standards.\(^11\)\(^-\)\(^13\) A population-based study of Filipino-Americans in North Kohala, Hawaii, showed a 24% prevalence of T2DM (Andrew Grandinetti, PhD, unpublished data, 2003), similar to the 22% T2DM prevalence measured among Filipino-Americans in Oahu, Hawaii, 40 years earlier.\(^11\) The University of California San Diego (UCSD) Filipino Women’s Health Study showed that 50- to 69-year-old Filipina women had more than 3 times the prevalence of T2DM and the metabolic syndrome than white women of similar age, body size, and percent body fat.\(^13\) Studies in California have shown

Received February 26, 2004; de novo received May 28, 2004; accepted July 7, 2004.
From the Department of Family and Preventive Medicine, University of California San Diego, La Jolla, Calif.
Correspondence to Maria Rosario G. Araneta, PhD, Department of Family and Preventive Medicine, University of California San Diego, 9500 Gilman Dr, 0607, La Jolla, CA 92037. E-mail haraneta@ucsd.edu
© 2004 American Heart Association, Inc.
Circulation is available at http://www.circulationaha.org DOI: 10.1161/01.CIR.0000146377.15057.CC

2817
a higher prevalence of hypertension among Filipino women than among other Asian or black women.14,15

Subclinical atherosclerosis may be undiagnosed among individuals without known cardiovascular disease. EBCT measurements of coronary artery plaque can offer valuable estimates of subclinical atherosclerosis in asymptomatic individuals. The objectives of the present study were (1) to compare EBCT-defined CAC scores among postmenopausal 55- to 80-year-old community-dwelling Filipina and white women without known cardiovascular disease and (2) to determine whether ethnic differences in EBCT-defined subclinical atherosclerosis were explained by ethnic differences in the prevalence of T2DM, the metabolic syndrome, hypertension, visceral fat, or other common cardiovascular risk factors.

Methods

Study Population

Filipino women were recruited between 1995 and 1999 to a cross-sectional study designed to estimate the prevalence of several chronic conditions, including osteoporosis, CVD, hypertension, and T2DM.13 Population-based sampling was not possible because Filipinos were not identified separately in the 1990 census; consequently, a convenience sample was recruited from San Diego, Calif. Volunteer participants were recruited with the help of Filipino community leaders and organizations, local Filipino media, and brochures posted in stores, medical clinics, and social services centers that serve Filipino populations. Research staff included bilingual Filipino women who recruited study participants at churches and during Filipino social functions and festivals. Recruitment materials emphasized general health and included tests for osteoporosis and other diseases, in addition to diabetes, to reduce self-selection bias for participants with known diabetes. All recruitments were based on logarithmic data. Univariate analysis was conducted to identify putative predictor variables associated with subclinical atherosclerosis. Multiple logistic regression analyses were used to assess the association of ethnicity with subclinical atherosclerosis; age, diabetes status, hypertension, statin use, estrogen use, and visceral fat were evaluated as covariates. Statistical significance was designated at P<0.05 or odds ratios (ORs) that excluded 1.

Data Collection and Clinical Evaluation

Clinical evaluations for both Filipina and white women took place at the UCSD Rancho Bernardo Research Clinic with the same protocol, clinic facility, and clinic staff. All participants gave written informed consent. The data instruments and EBCT consent form were not translated into Tagalog but were administered by a Philippine-born native Tagalog speaker and translated when necessary. All participants spoke functional English.

Demographic characteristics, years postmenopause, lifestyle behaviors (including cigarette smoking, alcohol use, and physical activity), physician-diagnosed diseases, hospitalizations, and surgeries were determined with structured questionnaires.13 Participants who were using prescription or nonprescription medications in the month before the clinic visit brought pills and prescriptions to the clinic to be verified and recorded by a nurse.

Two morning blood pressure readings were recorded in seated subjects using a mercury sphygmomanometer and the Hypertension Detection and Follow-up Program protocol.11 Pulse pressure was calculated as the difference between systolic and diastolic pressure. Height and weight were measured with participants wearing light-weight clothing without shoes. Body mass index (BMI; kg/m²) was computed as an estimate of obesity. Waist circumference was measured at the bending point (the natural indentation when bending sideways) and the narrowest circumference; these measurements correlated by 98%, and the bending point measurement was used for the analysis.

A 75-g oral glucose tolerance test was administered in the morning after a minimum 8-hour fast; blood samples were obtained by venipuncture at 0 and 2 hours. Plasma glucose was measured by the glucose-oxidase method, and insulin was determined by radioimmunoassay in a diabetes research laboratory. Proinsulin and C-peptide were measured in the research laboratory of S. Edwin Fineberg (Indiana University). Proinsulin was measured by radioimmunoassay based on a method by Bowsher et al.18 C-peptide was measured by radioimmunoassay (Linco Research, Inc). Fasting plasma lipids and lipoproteins, total cholesterol, HDL cholesterol, and triglyceride levels were measured by enzymatic methods.19 LDL cholesterol was calculated with the Friedewald formula.20 The total cholesterol and HDL cholesterol ratio was computed as a marker of the atherogenic dyslipidemic state. Insulin resistance was estimated with the homeostasis model assessment (HOMA-IR).21

T2DM was defined by the 1999 World Health Organization criteria: fasting plasma glucose level ≥126 mg/dL, or 2-hour postchallenge glucose level ≥200 mg/dL, or a history of T2DM diagnosed by a physician, or treatment with an oral hypoglycemic agent or insulin.21 Impaired fasting glucose was defined as those without T2DM but who had fasting plasma glucose of 100 to 125 mg/dL, and impaired glucose tolerance was defined as 2-hour postchallenge glucose of 140 to 199 mg/dL.21

The metabolic syndrome was defined as the presence of at least 3 of the following risk determinants: (1) waist circumference >88 cm; (2) triglycerides ≥150 mg/dL; (3) HDL cholesterol <50 mg/dL; (4) systolic blood pressure ≥130 mm Hg or diastolic pressure ≥85 mm Hg or use of antihypertensive medication; or (5) fasting glucose ≥110 mg/dL.24 CAC was determined with an Imatron C-150 ultrafast CT scanner, a stationary source-detector combination, and a rotating electron beam that produces serial contiguous thin-section (100-ms) scans. Scans were obtained at end diastole, usually during a single breath hold, and calcium was measured at the following 4 coronary arteries: left descending, left circumflex, left main, and right coronary. The total CAC score, the sum of all 4 vessels, was quantified by the Agatston method; this is the product of the area of calcification per coronary tomographic segment and a factor rated 1 though 4 depending on the maximal calcium x-ray density in that segment. CAC scores were classified as follows: minimal atherosclerotic plaque, CAC scores ≤10; mild, 11 to 149; moderate, 150 to 399; and extensive atherosclerotic plaque, ≥ 400. For the present analysis, subclinical atherosclerosis was defined as having a CAC score ≥150. Use of lipid-lowering medication was ascertained at the EBCT visit. A single-slice CT scan of the abdomen (between L4 and L5) was obtained to measure visceral and subcutaneous fat in cubic centimeters.

Statistical Analysis

Data were analyzed with Statistical Analysis Systems (SAS version 8.2). Student t tests, general linear models, and χ² analysis were used for descriptive statistics. Age-adjusted rates were calculated by the direct method. Because triglycerides, HDL and LDL cholesterol, and pulse pressure showed slightly skewed distributions, analyses were performed by means of log-transformed data. Mean values were presented for untransformed data; however, all probability values were based on logarithmic data. Univariate analysis was conducted to identify putative predictor variables associated with subclinical atherosclerosis. Multiple logistic regression analyses were used to assess the association of ethnicity with subclinical atherosclerosis; age, diabetes status, hypertension, statin use, estrogen use, and visceral fat were evaluated as covariates. Statistical significance was designated at P<0.05 or odds ratios (ORs) that excluded 1.

<table>
<thead>
<tr>
<th></th>
<th>Filipina (n=181)</th>
<th>White (n=196)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64.4 (6.0)</td>
<td>66.7 (6.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>College graduate, %</td>
<td>52</td>
<td>36</td>
<td>0.017</td>
</tr>
<tr>
<td>Smoker (ever), %</td>
<td>13</td>
<td>50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol ≥3 drinks/wk, %</td>
<td>1</td>
<td>55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exercise ≥3× per week, %</td>
<td>70</td>
<td>72</td>
<td>0.624</td>
</tr>
<tr>
<td>Estrogen use, %</td>
<td>23</td>
<td>61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statin use, %</td>
<td>31</td>
<td>19</td>
<td>0.005</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.6 (3.4)</td>
<td>26.0 (4.7)</td>
<td>0.343</td>
</tr>
<tr>
<td>Waist girth, cm</td>
<td>82.0 (9.4)</td>
<td>80.6 (12.3)</td>
<td>0.213</td>
</tr>
<tr>
<td>Visceral fat, cm³</td>
<td>69.1 (29.1)</td>
<td>62.3 (34.4)</td>
<td>0.037</td>
</tr>
<tr>
<td>Subcutaneous fat, cm³</td>
<td>155.8 (55.8)</td>
<td>158.4 (72.2)</td>
<td>0.707</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>218.9 (39.3)</td>
<td>216.2 (32.9)</td>
<td>0.482</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>133.1 (34.7)</td>
<td>128.2 (69.3)</td>
<td>0.105</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>53.6 (12.5)</td>
<td>65.8 (16.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>155.3 (89.3)</td>
<td>134.0 (67.3)</td>
<td>0.010</td>
</tr>
<tr>
<td>Total/HDL cholesterol</td>
<td>4.3 (1.3)</td>
<td>3.5 (0.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>135 (20.1)</td>
<td>128 (19.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>79 (9.4)</td>
<td>75 (7.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>56 (15.4)</td>
<td>52 (15.7)</td>
<td>0.022</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>108.2 (37.9)</td>
<td>101.5 (27.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Postchallenge glucose, mg/dL</td>
<td>186.5 (89.3)</td>
<td>119.8 (51.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting insulin, mg/dL</td>
<td>0.45 (0.37)</td>
<td>0.48 (0.59)</td>
<td>0.576</td>
</tr>
<tr>
<td>Postchallenge insulin, mg/dL</td>
<td>3.15 (2.1)</td>
<td>2.24 (2.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.10 (3.4)</td>
<td>3.03 (3.9)</td>
<td>0.861</td>
</tr>
<tr>
<td>Proinsulin, pmol/L</td>
<td>13.9 (9.2)</td>
<td>10.5 (9.9)</td>
<td>0.003</td>
</tr>
<tr>
<td>C-peptide, ng/mL</td>
<td>1.22 (0.62)</td>
<td>1.54 (1.00)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BP indicates blood pressure.
Values in parentheses are SDs.
*1999 World Health Organization criteria.
†2001 National Cholesterol Education Program criteria.

Results

A total of 181 Filipino women and 196 white women aged 55 to 78 years completed the clinical evaluation between 1995 and 1999 and had an EBCT scan in 2001 to 2002. As shown in Table 1, Filipinas differed significantly from whites for nearly all characteristics. The mean interval between clinical evaluation and the EBCT scan was 2.0 years for whites and Filipinas, respectively.

Filipinas had significantly higher age-adjusted levels of fasting plasma glucose and 2-hour postchallenge glucose and insulin levels (Table 1). Fasting insulin and HOMA-IR values did not vary by ethnicity. Fasting proinsulin concentration was available for 56% of participating Filipinas and 91% of whites, whereas C-peptide was measured in 96% of Filipinas and all whites. Filipinas had significantly higher proinsulin levels and significantly lower levels of C-peptide (Table 1).

Filipinas had a significantly higher prevalence of T2DM (32.6% versus 6.1%), impaired glucose tolerance (32.6% versus 19.9%), and the metabolic syndrome (32.6% versus 13.8%). Prevalence of impaired fasting glucose was significantly higher among whites (27.0%) than Filipinas (16.0%). Three components of the metabolic syndrome were significantly higher for Filipinas, including hypertension, hypertriglyceridemia, and low HDL cholesterol levels. Waist girth (≥88 cm) and fasting glucose (≥110 mg/dL) were the only components of the metabolic syndrome that did not differ by ethnicity. Half of Filipinas and more than one third of whites with T2DM also had the metabolic syndrome; however, when the analysis was restricted to nondiabetics, the prevalence of the metabolic syndrome remained significantly higher for Filipinas (24.6% versus 9.2%, P=0.0003).

As shown in Table 2, no ethnic differences were observed in any of the 4 CAC score categories (minimal, mild, moderate, or extensive) for atherosclerotic plaque. Despite the ethnic similarities in CAC, Filipinas had significantly higher T2DM prevalence at every CAC score category (Figure). Almost half (44%) of Filipinas and 52% of whites had no or minimal atherosclerotic plaque; however, T2DM prevalence was 24.2% among Filipinas compared with just 0.7% among whites in the minimal
plaque category. Although an equal proportion (9%) of Filipinas and whites had extensive atherosclerotic plaque, in this group, T2DM prevalence was 59.4% among Filipinas compared with 7% in whites.

Similarly, among women without T2DM, no ethnic differences were observed in CAC despite the higher prevalence of the metabolic syndrome among Filipinas.

Among women without T2DM, 14.7% of Filipinas and 19.5% of whites ($P = 0.279$) had subclinical atherosclerosis despite a nearly 3-fold higher prevalence of the metabolic syndrome among nondiabetic Filipino women.

Lipid-lowering drugs can reduce coronary artery plaque. Filipinas were more likely to use statins, which might account for their lower-than-expected CAC scores. However, no ethnic differences were observed in analysis limited to those who did not use statins (moderate CAC: Filipinas 10% versus whites 11%; extensive CAC: Filipinas 5% versus whites 9%) despite a higher prevalence of T2DM (23% versus 3%) among non–statin-using Filipinas.

Whites were more likely to smoke cigarettes and to use hormone replacement therapy. In analysis limited to never-smokers, no ethnic differences were observed among women with either moderate (Filipinas 14% versus whites 9%) or extensive (Filipinas 9% versus whites 6%) plaque, despite elevated T2DM prevalence among Filippina non-smokers (Filipinas 34% versus whites 7%, $P<0.001$). Similarly, among nonusers of hormone replacement therapy, no ethnic differences were observed among women with either moderate (Filipinas 12% versus whites 11%) or extensive (Filipinas 11% versus whites 16%) atherosclerotic plaque, despite higher T2DM prevalence (Filipinas 35% versus whites 12%, $P<0.001$) among Filipinas who did not use hormone replacement therapy.

Logistic regression models were constructed to identify putative factors associated with subclinical atherosclerosis. A regression model that included age and ethnicity showed that Filipino ethnicity (adjusted OR 1.44, 95% CI 0.85 to 5.93) was not associated with subclinical atherosclerosis. When T2DM was included in the model, older age (adjusted OR 1.76, 95% CI 1.40 to 2.21) and the presence of T2DM (adjusted OR 3.11, 95% CI 1.63 to 5.93) were associated with subclinical atherosclerosis, but ethnicity was not. A regression model that included age, ethnicity, and smoking (ever) also showed no association between ethnicity and subclinical atherosclerosis.

In multivariable analysis, compared with white women, Filipino ethnicity was not associated with subclinical atherosclerosis (adjusted OR 1.01, 95% CI 0.51 to 1.97). Among Filipinas, T2DM and hypertension were independently associated with subclinical atherosclerosis, after adjustment for age, estrogen use, smoking history, education, visceral fat, total:HDL cholesterol ratio, and statin use (Table 3). In contrast, older age, history of cigarette smoking, and elevated total:HDL cholesterol ratio were independently associated with subclinical atherosclerosis among whites. Multivariable analyses was performed separately for 3 age categories (59, 60 to 69, and ≥70 years); ethnicity was not associated with the risk of subclinical atherosclerosis in any age group, despite the significantly higher prevalence of T2DM among Filipinas in every age category. Because few whites had T2DM, combining those with abnormal glucose tolerance (either T2DM, impaired fasting glucose, or impaired glucose tolerance) provided a larger sample for comparison; how-

| TABLE 3. Multivariable Analysis: Covariates Associated With Subclinical Atherosclerosis* Among Filipino and White Women |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Filipina (n=181) | White (n=196)   | Filipina (n=122) | White (n=196)   |
| **Covariate**   | **OR**          | **95% CI**      | **OR**          | **95% CI**      |
| Age (5 years)   | 1.33            | 0.95–1.88       | 2.36            | 1.48–3.75       |
| T2DM            | 2.39            | 1.04–5.49       | 1.06            | 0.16–7.17       |
| Hypertension    | 2.98            | 1.02–8.72       | 0.61            | 0.24–1.56       |
| Estrogen use    | 0.88            | 0.32–2.42       | 1.13            | 0.46–2.77       |
| Smoke (ever)    | 0.80            | 0.23–2.81       | 2.96            | 1.24–7.05       |
| College graduate| 1.03            | 0.45–2.34       | 0.90            | 0.36–2.29       |
| Visceral fat (5 cm³) | 0.98        | 0.91–1.05       | 0.99            | 0.93–1.06       |
| Total:HDL cholesterol | 1.01       | 0.74–1.38       | 1.75            | 1.06–2.89       |
| Statin use      | 2.16            | 0.91–5.11       | 0.52            | 0.14–1.91       |

*CAC score ≥150.
ever, no ethnic differences were observed in subclinical atherosclerosis after adjustment for abnormal glucose tolerance, statin use, and history of cigarette smoking (data not shown).

Multivariable analysis was performed among nondiabetic women because nondiabetic Filipinas had a 3-fold higher prevalence of the metabolic syndrome (24.6%) compared with nondiabetic white women (9.2%). However, compared with white women, Filipino ethnicity was not associated with subclinical atherosclerosis (adjusted OR 0.81, 95% CI 0.36 to 1.81) among nondiabetic women. Older age and elevated total: HDL cholesterol ratio were independently associated with subclinical atherosclerosis among white women without T2DM (Table 3). However, we were unable to identify covariates associated with subclinical atherosclerosis among Filipinas, including components of the metabolic syndrome such as hypertension and visceral adiposity. Multivariable models that included the metabolic syndrome as a covariate showed it was not a significant predictor of subclinical atherosclerosis in nondiabetic Filipino or white women after adjustment for age, smoking history, statin use, estrogen use, visceral fat, and education (data not shown).

**Discussion**

Atherosclerosis is hypothesized to develop as a consequence of chronic exposure to hyperglycemia and associated atherogenic abnormalities, and the risk is increased among cigarette smokers and individuals with T2DM.27 We therefore expected that Filipinas would have an excess of moderate and extensive atherosclerotic plaque given their higher prevalence of T2DM, the metabolic syndrome, hypertension, dyslipidemia, and visceral fat. Cardioprotective factors more common in Filipinas included infrequency of cigarette smoking and more frequent statin use; however, stratification for covariates did not explain the ethnic similarities in subclinical atherosclerosis.

These results are similar to studies of black women who had similar coronary calcium scores as white women despite higher prevalence of diabetes, hypertension, and other CVD risk factors.28 Healthy Latino men had reduced CAC compared with age-matched white men despite higher levels of C-reactive protein and insulin resistance.29 Lower coronary calcium was observed among Asians than among whites when multiple Asian nationalities were reported collectively.30 The mechanism for reduced arterial calcification among blacks, Latinos, and Filipinos despite elevated prevalence of T2DM, hypertension, and other CVD factors remains unknown. We did not measure C-reactive protein, fibrinogen, plasminogen activator inhibitor-1, or other markers that might play a role in atherogenesis; however, these factors did not explain the reduced CAC risk among Latinos.29

Despite the rapid growth of the Filipino population in California, epidemiological studies of CVD risk among Filipinos are limited to 1 hospital-based study in San Francisco.31 In that study of patients treated for coronary artery disease, Filipino-Americans had a significantly higher incidence of diabetes and hypertension and less general obesity and smoking than white patients.31 Filipino-Americans appear to have different CVD risks from other Asian nationalities, as evidenced by their higher prevalence of hypertension and T2DM.11,14,15 Genetic susceptibility may play a role in the etiology of T2DM complications among Filipinos, including CHD. Filipinos have different genetic admixture from Chinese, Japanese, and Koreans; are anthropologically classified as Polynesian; and have Austronesian, Malay, Indonesian, Arabic, Indian, Spanish, and Chinese admixture.32 Lipid profiles among adolescent Filipinos in the Philippines were elevated compared with other populations in the Asia Pacific Region despite low dietary fat intake and a near absence of obesity.33 Filipinos in Saudi Arabia showed a high frequency of an allele at the A-UC-III gene cluster that is associated with CHD in European populations.34 Some epidemiological studies have suggested that proinsulin and C-peptide are associated with atherosclerosis and CVD.35,36 Fasting proinsulin concentration was significantly higher among Filipinas, whereas C-peptide was significantly higher among white women. However, neither proinsulin nor C-peptide was an independent predictor of subclinical atherosclerosis in the combined cohort or within each ethnic group. Our observations are similar to a study of Japanese-Americans, in which proinsulin was not related to CHD.37

This is the first study to measure EBCT-defined subclinical atherosclerosis among Filipino-Americans; however, some study limitations require acknowledgment. Filipina participants were obtained from a convenience sample of volunteers, whereas white participants were derived from a population-based sample. The 181 Filipina EBCT participants were generally representative of the 453 participants of the UCSD Filipina Women’s Health Study with regard to diabetes and the metabolic syndrome and other CVD factors. In this cohort, 52% of Filipinas were college graduates, compared with 45% among all participants of the UCSD Filipina Women’s Health Study and 42% of all Filipino women (aged =25 years) in the United States.38 A sizable portion of these college-educated Filipina participants were registered nurses, and as such, they may have engaged in healthy behaviors to reduce CVD risks. However, exercise and smoking behavior did not differ by college attainment among Filipino women.

Duration of diabetes is an important factor in the pathogenesis of complications. We did not measure oral glucose tolerance temporarily and could not ascertain the duration of T2DM. Forty-one percent of Filipino women with T2DM had this diagnosis before the 1995 to 1999 clinical evaluation; the remaining 59% of diabetics were so diagnosed at the 1995 to 1999 clinical evaluation; however, subclinical atherosclerosis did not differ among Filipina participants with known versus newly diagnosed T2DM. Among the few whites with T2DM, the majority (83%) were diagnosed recently, between 1997 and 1999. The smaller proportion of whites with previously diagnosed T2DM might suggest that more whites were ex-
cluded from the EBCT study if they had had more symptomatic CHD. However, the proportion of women who were excluded from participating because of previously diagnosed CVD did not differ by ethnicity (Filipinas 21%, whites 23%). Therefore, participation bias resulting from differential diagnosis of prior CHD by ethnicity was unlikely.

Diabetes status and risk factors for CHD could have changed between the clinical evaluation and the EBCT scan. Although the proportion of women with prediabetes (impaired fasting glucose or impaired glucose tolerance) was similar by ethnicity, T2DM prevalence could have increased substantially for Filipino women after 4.9 years and might have increased just slightly for white women after a 2-year follow-up period. Risk behavior was not assessed during the EBCT visit and could have changed temporally, specifically with regard to cigarette smoking, alcohol intake, and physical activity; however, data from the UCSD Rancho Bernardo Study showed no temporal change in BMI or physical activity between 1986 and 1999.

High-fat diets have been associated with increased risk of CVD, and diet may contribute to ethnic disparities in CVD. A 24-hour food-recall questionnaire was administered during the initial clinical visit, and results were analyzed at the Harvard Willett laboratory. Dietary information was available for 84% of white women and 39% of Filipino women; however, intake of animal fat, vegetable fat, saturated fat, monounsaturated fat, polyunsaturated fat, and cholesterol did not differ by ethnicity.

Our findings among Filipinas support other observations of a higher risk of CAC among individuals with T2DM. Such was not the case among white women, which likely was due to the small number of white women with T2DM in the present cohort. However, our findings are inconsistent with observations of elevated risk of CAC among nondiabetics with the metabolic syndrome. In summary, T2DM and hypertension are significant health problems in the growing Filipino-American community and are independent risk factors for subclinical atherosclerosis. Despite elevated prevalence of T2DM, hypertension, and the metabolic syndrome among Filipino-American women, subclinical atherosclerosis was similar to white women. Future studies should consider the role of inflammatory markers and adipocytokines and their etiologic role in CHD in populations with elevated T2DM prevalence. Such studies may provide useful information to explain ethnic differences in macrovascular complications of T2DM.

Acknowledgment
This study was funded by the American Heart Association (0070088Y) and NIH/NIDDK R03 DK60575.

References


Subclinical Coronary Atherosclerosis in Asymptomatic Filipino and White Women
Maria Rosario G. Araneta and Elizabeth Barrett-Connor

Circulation. 2004;110:2817-2823; originally published online October 25, 2004;
doi: 10.1161/01.CIR.0000146377.15057.CC
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/110/18/2817

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located,
click Request Permissions in the middle column of the Web page under Services. Further information about
this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/