The puzzle of high-density lipoprotein in cardiovascular prevention
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Value of the apolipoprotein B/A-I ratio in cardiovascular risk assessment: A case–control analysis in the EPIC-Norfolk study

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ABSTRACT

Background – An elevated apolipoprotein B to A-I ratio (apolipoprotein B/A-I) ratio is a risk factor for future coronary artery disease (CAD). It is not known whether this ratio is better for risk assessment and prediction than are traditional lipid values, and whether it adds predictive value to the Framingham Risk Score.

Objective – To evaluate whether the apolipoprotein B/A-I ratio is associated with future CAD events independent of traditional lipid measurements and the Framingham Risk Score, and to evaluate the ability of this ratio to predict occurrence of future CAD.

Design – Prospective nested case-control study.

Setting – Norfolk, United Kingdom.

Participants – Apparently healthy men and women (45 to 79 years of age) who were participating in the European Prospective Investigation into Cancer and Nutrition-Norfolk study. Cases (n = 869) were persons who developed fatal or nonfatal CAD. Controls (n = 1511) were persons without CAD who were matched for age, sex, and enrollment period.

Measurements – Total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, apolipoproteins, and C-reactive protein were measured directly. Low-density lipoprotein (LDL) cholesterol values were calculated by using the Friedewald formula.

Results – The apolipoprotein B/A-I ratio was associated with future CAD events, independent of traditional lipid values (adjusted odds ratio, 1.85 [95% CI, 1.15 to 2.98]), including the total cholesterol–HDL cholesterol ratio, and independent of the Framingham Risk Score (adjusted odds ratio, 1.77 [CI, 1.31 to 2.39]). However, it did no better than lipid values at predicting future CAD events (area under the receiver-operating characteristic curve, 0.670 for total cholesterol/HDL cholesterol ratio vs. 0.673 for apolipoprotein B/A-I ratio [P = 0.38]) and did not add further to the predictive value of the Framingham risk score (area under the receiver-operating characteristic curve, 0.594 for Framingham risk score alone versus 0.617 for Framingham risk score plus apolipoprotein B/A-I ratio [P < 0.001]).

Limitations – No participant was taking lipid-lowering medication, and diabetes was uncommon.

Conclusions – The apolipoprotein B/A-I ratio is independently associated with, but adds little to, existing measures for CAD risk assessment and prediction in the general population. Other characteristics of the test, such as the ability to perform it on nonfasting samples, may still make it useful in some settings.
INTRODUCTION

Low-density lipoprotein (LDL) cholesterol is a primary treatment target in coronary artery disease (CAD) prevention guidelines (1), but it is a poor predictor of future cardiovascular events (2). Similarly, the ratio of total cholesterol to high-density lipoprotein (HDL) cholesterol is a potent risk factor for CAD (3, 4), but it improves CAD risk prediction only modestly (5).

Apolipoprotein B and apolipoprotein A-I are the main structural proteins of atherogenic lipoproteins and HDL particles, respectively. In theory, the ratio of apolipoprotein B to apolipoprotein A-I (apolipoprotein B/A-I ratio) could improve lipoprotein-related cardiovascular risk prediction. Apolipoprotein B levels reflect the entire spectrum of pro-atherogenic particles, including very-low-density, intermediate-density, and low-density lipoproteins, whereas LDL cholesterol levels do not (6). Apolipoprotein B levels also provide a good measure of the number of LDL particles, which reflects the atherogenicity of LDL (7, 8). In addition, apolipoprotein A-I is more important than the HDL cholesterol content for biochemical pathways that make HDL antiatherogenic, including adenosine triphosphate binding cassette A-1–mediated cellular cholesterol efflux (9), lecithin-cholesteryl acyltransferase–mediated maturation of HDL particles (10), and several antioxidative processes (11). Besides these physiologic considerations, apolipoprotein assessment does not require fasting blood samples (6), which greatly facilitates logistics at outpatient clinics. Collectively, these considerations have led to recommendations to implement the apolipoprotein B/A-I ratio in routine clinical care (12).

Studies before 1993 focusing on the relationship between apolipoprotein levels and CAD incidence have reported inconsistent results (13-17). These discrepancies are largely attributable to the lack of standardization of the laboratory tests at that time. Since the introduction of standardized reference materials by the International Federation of Clinical Chemistry (18, 19), large studies, such as the AMORIS (Apolipoprotein-related Mortality RISK) (20) and INTERHEART (21), have unambiguously demonstrated that the apolipoprotein B/A-I ratio is a robust risk factor for future CAD events. However, these studies did not address the crucial question of whether the apolipoprotein B/A-I ratio predicts those events better than traditional lipid values do.

We sought to evaluate whether the apolipoprotein B/A-I ratio is associated with future CAD events, independent of traditional lipid-based variables and of the Framingham risk score (22), and to evaluate the ability of the ratio to predict CAD events.

MATERIALS AND METHODS

Design

We performed a nested case-control study among participants of the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk study. The EPIC-Norfolk study was
a prospective population study of 25,663 men and women 45 to 79 years of age residing in Norfolk, United Kingdom, who completed a baseline questionnaire survey and attended a clinic visit (23). Participants were recruited from age and sex registers of general practices in Norfolk as part of the 10-country collaborative EPIC study, which was designed to investigate dietary and other determinants of cancer. Additional data were obtained in EPIC-Norfolk so that determinants of other diseases could also be assessed.

The design and methods of EPIC-Norfolk are described in detail elsewhere (23). In short, eligible participants were recruited by mail. At the baseline survey between 1993 and 1997, participants completed a detailed health and lifestyle questionnaire. Nonfasting blood samples were obtained by vein puncture into plain and citrate bottles. Blood samples were processed for assay at the Department of Clinical Biochemistry, University of Cambridge, or stored at –80°C. All participants were flagged for death certification at the United Kingdom Office of National Statistics, and vital status was ascertained for the entire cohort. In addition, participants admitted to hospital were identified by using their unique National Health Service number through data linkage with the East Norfolk Health Authority database, which identifies all hospital contacts throughout England and Wales for residents of Norfolk. Coronary artery disease was defined as codes 410 through 414 of the International Classification of Diseases, 9th Revision. Participants were identified as having CAD during follow-up if they had a hospital admission or died with CAD as underlying cause. Previous validation studies in our cohort indicate high specificity for such case ascertainment (24). The study was approved by the Norwich District Health Authority Ethics Committee, and all participants gave signed informed consent.

Participants

We describe elsewhere a similarly designed nested case–control study (24-26). Extension of follow-up has resulted in the identification of more CAD cases, allowing the current study to be considerably larger. We excluded all persons who reported a history of heart attack or stroke or use of lipid-lowering drugs at the baseline clinic visit. Cases were persons who developed fatal or nonfatal CAD during follow-up until November 2003 (mean follow-up, 6 years). Controls were study participants who remained free of any cardiovascular disease during follow-up. We matched 2 controls to each case by age (within 5 years), sex, and time of enrollment (within 3 months).

Biochemical analyses

Serum total cholesterol, HDL cholesterol, and triglycerides were measured in fresh samples by using the RA-1000 analyzer (Bayer Diagnostics, Basingstoke, United Kingdom). Low-density lipoprotein cholesterol levels were calculated by using the Friedewald formula (27) to closely approach current clinical procedures. Non-HDL cholesterol was calculated as total cholesterol minus HDL cholesterol. Serum apolipoprotein A-I and apolipoprotein B were measured by using rate immunonephelometry (Behring Nephelometer BNII, Marburg, Germany) with calibration
traceable to the International Federation of Clinical Chemistry primary standards (28). The interassay coefficients of variation were 5% for apolipoprotein A-I and 3% for apolipoprotein B. Plasma C-reactive protein was measured by using a sandwich-type enzyme-linked immunosorbent assay, as described elsewhere (29). Samples were analyzed in random order to avoid systematic bias. Researchers and laboratory personnel were blinded to identifiable information and could identify samples by number only.

**STATISTICAL ANALYSIS**

Statistical analyses were performed by using SPSS software, version 12.0.1 (SPSS, Inc., Chicago, Illinois). A P value less than 0.05 was considered statistically significant. Before being used as continuous variables in the analyses, triglycerides were log-transformed to approach a normal distribution more closely. Baseline characteristics were compared between cases and controls, taking into account the matching. A mixed-effects model was used for continuous variables, and conditional logistic regression was used for categorical variables.

To evaluate the association between a risk factor and occurrence of CAD, odds ratios and corresponding 95% CIs were calculated by using conditional logistic regression analysis, taking into account matching for sex, age, and time of enrolment (30). Odds ratios were calculated per quartile of each risk factor, on the basis of the distribution among controls. The first quartile was used as the reference group (odds ratio, 1.00). P values represent significance for linearity across the odds ratios connected to the 4 quartiles of each risk factor. First, we calculated odds ratios per quartile of total cholesterol, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol levels and the total cholesterol/HDL cholesterol and apolipoprotein B/A-I ratios (model 1). We selected the 2 variables with the highest odds ratios in the fourth quartile (the apolipoprotein B/A-I ratio and total cholesterol/HDL cholesterol ratio), then fit a model for each ratio that adjusted for diabetes (yes or no), body mass index, smoking (yes or no), systolic blood pressure, and C-reactive protein level (model 2). We then added variables for LDL cholesterol and HDL cholesterol (model 3a) and for triglycerides (model 3b). We then entered apolipoprotein B/A-I and total cholesterol/HDL cholesterol ratios simultaneously into a new model that adjusted for all major cardiovascular risk factors. Finally, to assess the association of the apolipoprotein B/A-I ratio with CAD independent of the Framingham Risk Score, we categorized all participants into 3 risk groups (low [<10%], intermediate [10% to 20%], or high [>20%]) based on the Framingham Risk Score algorithm (22, 31) and calculated odds ratios for future CAD by quartile of the apolipoprotein B/A-I ratio, with adjustment for the Framingham Risk Score category.

To evaluate the ability of the apolipoprotein B/A-I ratio to predict the occurrence of CAD (that is, to discriminate between patients who will and will not develop a future CAD event) we constructed receiver-operating characteristic (ROC) curves (32, 33) and calculated the areas under the curves (AUCs) from regression models that included apolipoprotein B/A-I or total...
cholesterol/HDL cholesterol ratio, plus diabetes mellitus (yes or no), body mass index, smoking (yes or no), systolic blood pressure, and C-reactive protein level. We used bootstrapping of the ROC curves to calculate the statistical significance of the differences in AUCs (34, 35). Similarly, we evaluated differences in AUCs when the apolipoprotein B/A-I ratio was added to a model including the Framingham Risk Score (on a continuous scale).

To provide a clinical view of the value of the apolipoprotein B/A-I ratio for risk prediction, we used logistic regression analysis to calculate the predicted probability of being a case or control in the study sample, comparing prediction models with the apolipoprotein B/A-I ratio or total cholesterol/HDL cholesterol ratio and adjusting for diabetes mellitus (yes or no), body mass index, smoking (yes or no), systolic blood pressure, and C-reactive protein level. We categorized the predicted probability values into 4 subgroups (0 to 0.25, 0.25 to 0.50, 0.50 to 0.75, and 0.75 to 1.00) to assess the number of participants reclassified by apolipoprotein B/A-I ratio into a different category of probability.

Role of the funding sources
The EPIC-Norfolk study is supported by program grants from the Medical Research Council United Kingdom and Cancer Research United Kingdom and receives additional support from the European Union, Stroke Association, British Heart Foundation, United Kingdom Department of Health, Food Standards Agency, and the Wellcome Trust. Some of the lipid and apolipoprotein measurements described in this article were funded by an educational grant from the Future Forum. The funding sources had no role in study design, conduct, analysis, or decision to submit the manuscript for publication.

RESULTS

Baseline characteristics
We identified 869 persons who did not report a history of cardiovascular disease at the baseline visit but developed CAD during follow-up. Of these, 611 persons (70.3%) had nonfatal events and 258 (29.7%) had fatal events. We were able to match 642 cases to 2 controls and 227 cases to 1 control; thus, the control group comprised 1511 people. Because of matching, sex distribution and age were similar between cases and controls (Table 1). As expected, cases were more likely than controls to smoke and have diabetes (Table 1). Body mass index; systolic and diastolic blood pressure; and total cholesterol, LDL cholesterol, non-HDL cholesterol, triglycerides, apolipoprotein B, and C-reactive protein values were also statistically significantly higher in cases than controls, whereas HDL cholesterol and apolipoprotein A-I values were statistically significantly lower (Table 1). The apolipoprotein B/A-I ratio was statistically significantly higher in cases. The patterns for these differences were similar when cases were divided into fatal and nonfatal events and when men and women were analyzed separately (data not shown).
Analysis of association

In unadjusted analyses (Table 2), the odds ratio for future CAD increased per quartile of total cholesterol level, LDL cholesterol level, non-HDL cholesterol level, total cholesterol/HDL cholesterol ratio, and apolipoprotein B/A-I ratio and decreased per quartile of HDL cholesterol level (P < 0.001 for all). Similar patterns were observed when men and women were analyzed separately. Estimates of risk were highest for the total cholesterol/HDL cholesterol ratio (odds ratio for highest versus lowest quartile, 2.57 [95% CI, 1.98 to 3.33]; P < 0.001 for linearity) and apolipoprotein B/A-I ratio (odds ratio, 2.64 [CI, 2.04 to 3.42]; P < 0.001 for linearity). Adjustment for major cardiovascular risk factors (model 2 in Table 3) had little effect on the apolipoprotein B/A-I ratio estimate, whereas adjustment for LDL and HDL cholesterol levels (model 3a in Table 3) and triglyceride level (model 3b in Table 3) reduced it slightly (odds ratio for apolipoprotein B/A-I ratio and CAD, 1.85 [CI, 1.15 to 2.98]; P = 0.01 for linearity [model 3b]). Separate analyses for men and women yielded similar patterns. In a multivariable analysis that adjusted for total cholesterol/HDL cholesterol ratio and apolipoprotein B/A-I ratios simultaneously, the total cholesterol/HDL cholesterol ratio lost statistical significance (Table 4) but the apolipoprotein B/A-I ratio remained statistically significant (odds ratio for highest versus lowest quartile, 2.03 [CI,
1.23 to 3.36); $P = 0.006$ for linearity) (Table 4). The ratio also remained significant in an analysis that adjusted for the Framingham Risk Score (odds ratio, 1.77 [CI, 1.31 to 2.39]; $P < 0.001$ for linearity).

### Analysis of discriminative ability

Areas under the ROC curves derived from models that adjusted for total cholesterol/HDL cholesterol ratio or apolipoprotein B/A-I ratio plus several major cardiovascular risk factors (diabetes, body mass index, smoking, systolic blood pressure, and C-reactive protein level) did not statistically significantly differ (0.670 for total cholesterol/HDL cholesterol ratio versus 0.673 for apolipoprotein B/A-I ratio; $P = 0.38$). Areas under the ROC curves derived from adjustment...
for the Framingham risk score without and with the apolipoprotein B/A-I ratio differed significantly in statistical but not clinical terms (0.594 for Framingham risk score alone vs. 0.613 for Framingham risk score plus apolipoprotein B/A-I ratio; P < 0.001).

The models using apolipoprotein B/A-I ratio or total cholesterol/HDL cholesterol ratio to predict the probability of being a case or control in the study sample categorized 749 of 834 cases (89.8%) and 1336 of 1469 controls (90.9%) similarly (Table 5). Eighty-five cases and 133 controls were reclassified by the apolipoprotein B/A-I ratio. Of the 85 cases, 35 (41.1%) were reclassified into lower categories of probability. Of the 133 controls, 67 (50.4%) were reclassified into higher categories of probability.

**DISCUSSION**

Recent studies have convincingly shown that the apolipoprotein B/A-I ratio is strongly associated with future CAD (20, 21). This association, and the ability to perform apolipoprotein measurements on nonfasting blood samples, have led to recommendations that the apolipoprotein
B/A-I ratio be used in routine clinical care (12). The recommendation cannot be fully justified, however, until the apolipoprotein B/A-I ratio is shown to be associated with CAD independent of traditional lipid variables and to be better at predicting future CAD events.

The 2 largest studies in this field, AMORIS (20) and INTERHEART (21), did not report whether the association between the apolipoprotein B/A-I ratio and CAD was independent of traditional lipid variables. In the AMORIS study, LDL cholesterol and HDL cholesterol were indirectly estimated from total cholesterol, triglyceride, and apolipoprotein A-I values, which precluded simultaneous use of these variables in 1 statistical model. In INTERHEART, LDL cholesterol and HDL cholesterol were measured directly, but these values were not incorporated in the statistical analyses. Earlier data from the Québec Cardiovascular Study showed that apolipoprotein B level was associated with CAD independent of LDL cholesterol level, but apolipoprotein A-I level was not associated with CAD independent of HDL cholesterol level (7). The Prospective Epidemiological Study of Myocardial Infarction (PRIME) reported that apolipoprotein A-I level was associated with CAD independent of HDL cholesterol level (36). Data from the Atherosclerosis Risk in Communities study suggested that apolipoprotein A-I and B levels no longer contributed to CAD risk prediction when considered together with traditional lipid values (37);
<table>
<thead>
<tr>
<th>Model</th>
<th>Men and Women</th>
<th>Men Only</th>
<th>Women Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quartile 1</td>
<td>Quartile 2</td>
<td>Quartile 3</td>
</tr>
<tr>
<td>Model 2†</td>
<td>1.34</td>
<td>1.88</td>
<td>2.55</td>
</tr>
<tr>
<td>TC/HDL-C</td>
<td>1.00</td>
<td>(0.99–1.80)</td>
<td>(1.41–2.52)</td>
</tr>
<tr>
<td>ApoB/A-I</td>
<td>1.00</td>
<td>(1.04–1.93)</td>
<td>(1.33–2.40)</td>
</tr>
<tr>
<td>Model 3a</td>
<td>1.27</td>
<td>1.49</td>
<td>2.08</td>
</tr>
<tr>
<td>ApoB/A-I‡</td>
<td>1.00</td>
<td>(0.90–1.79)</td>
<td>(1.01–2.19)</td>
</tr>
<tr>
<td>Model 3b</td>
<td>1.23</td>
<td>1.40</td>
<td>1.85</td>
</tr>
<tr>
<td>ApoB/A-I§</td>
<td>1.00</td>
<td>(0.87–1.74)</td>
<td>(0.95–2.07)</td>
</tr>
</tbody>
</table>

*Odds ratios were calculated by using conditional logistic regression that took into account matching for sex, age, and time to enrollment. TC/HDL-C = total to HDL cholesterol ratio; apoB/A-I = apolipoprotein B to A-I ratio.
†Adjusted for age, sex, time to enrollment, diabetes (yes or no), body mass index, smoking status (yes or no), systolic blood pressure, and C-reactive protein level.
‡Adjusted for all variables in model 2, low-density lipoprotein cholesterol level, and HDL cholesterol level.
§Adjusted for all variables in models 2 and 3a and log-transformed triglyceride values.
however, the apolipoproteins were quantified by using radial immunodiffusion, a technique that has known problems with linearity and reproducibility. The Caerphilly study (38) corroborated the lack of a lipid-independent association between apolipoprotein levels and CAD. Collectively, these studies provide conflicting results that may be attributable to differences in samples; limited statistical power; and, in at least one instance, poorly standardized methods for apolipoprotein measurement.

We have overcome most of these potential problems in the current study by evaluating a large number of cases and by using carefully standardized methods for measurement of apolipoproteins and lipids. We show that the apolipoprotein B/A-I ratio is associated with future CAD events independent of standard cardiovascular risk factors (diabetes, body mass index, smoking, systolic blood pressure, and C-reactive protein level) and lipid values (LDL, HDL, and triglyceride levels and, in a separate model, total cholesterol/HDL cholesterol ratio). This may be because the apolipoprotein B level reflects the presence of small LDL particles, which may be more atherogenic, more accurately than do cholesterol values (7, 8). The adjusted odds ratio of 1.85 (CI, 1.15 to 2.98) for the highest quartile of apolipoprotein B/A-I ratio (model 3b in table 3) approximates that of the classic (39, 40) and some of the newer risk factors (such as C-reactive protein level (21, 41)). In addition, inclusion of the apolipoprotein B/A-I ratio and total cholesterol/HDL cholesterol ratio in a single multivariable model suggested that the apolipoprotein B/A-I ratio retains CAD risk information, whereas the total cholesterol/HDL cholesterol ratio does not (Table 4). Moreover, the apolipoprotein B/A-I ratio remained a significant risk factor independent of the Framingham Risk Score. These findings suggest that the apolipoprotein B/A-I ratio may be a valuable alternative to traditional lipid-based variables for assessing future risk for CAD. However, when we used ROC analysis to evaluate whether and to what extent this apparent advantage of the apolipoprotein B/A-I ratio translates into improved CAD risk prediction (33), we found that the apolipoprotein B/A-I ratio did not contribute to the total cholesterol/HDL cholesterol ratio, and added only marginally to the Framingham Risk Score. These findings suggest that the apolipoprotein B/A-I ratio is no better than the total cholesterol/HDL cholesterol ratio at discriminating individual risk. This conclusion was strengthened by the model suggesting that many cases and controls were incorrectly reclassified, and that the net proportion of cases who were correctly reclassified is modest and not clinically relevant (Table 5).

Our study has several limitations. First, case ascertainment is an issue in the design of every prospective study. However, a validation study indicated that case ascertainment in our study was at least equivalent to that of other large prospective cohort studies (24). Second, our conclusions apply only to apparently healthy people who are not receiving lipid-lowering medication. Lipid-based variables have been shown to lose their association with future CAD in persons receiving lipid-lowering therapy with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) (42, 43). The relationship between apolipoprotein B level, apolipoprotein A-I level, or apolipoprotein B/A-I ratio and future CAD in this subgroup could differ. In addition,
Apolipoprotein values are of particular relevance in detecting atherogenic dyslipidemias in persons who have low or normal LDL cholesterol levels but increased LDL particle number (44-46). These persons, comprising those with diabetes or the metabolic syndrome, are at very high risk for CAD. Our cohort contained only few diabetic participants, and information was insufficient to determine the presence of the metabolic syndrome. Therefore, our findings do not apply to these patients.

### Table 4 Odd Ratios for Future Coronary Artery Disease, by Quartile of Total Cholesterol/HDL Cholesterol and Apolipoprotein B/Apolipoprotein A-I Ratio*

<table>
<thead>
<tr>
<th>Ratio</th>
<th>Predicted Probability Based on ApoB/A-I</th>
<th>Predicted Probability Based on TC/HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>ApoB/A-I</td>
<td>0–0.25</td>
<td>0.25–0.50</td>
</tr>
<tr>
<td></td>
<td>1.28</td>
<td>1.44</td>
</tr>
<tr>
<td>TC/HDL-C</td>
<td>1.00</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td>(0.75–1.56)</td>
<td>(0.78–1.93)</td>
</tr>
</tbody>
</table>

*Odds ratios were calculated by using conditional logistic regression that took into account matching for sex, age, and time to enrollment and was adjusted for diabetes (yes or no), body mass index, smoking status (yes or no), systolic blood pressure, C-reactive protein level, and log-transformed triglyceride level. apo B/apo A-I = apolipoprotein B/apolipoprotein A-I; HDL = high-density lipoprotein.

†For linear trend.

### Table 5 Observed Number of Patients in Each Group of Predicted Probability of Coronary Artery Disease, by Total Cholesterol/HDL Cholesterol Ratio or Apolipoprotein B/Apolipoprotein A-I Ratio*

<table>
<thead>
<tr>
<th>Predicted Probability Based on ApoB/A-I</th>
<th>Predicted Probability Based on TC/HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–0.25</td>
<td>77/374</td>
</tr>
<tr>
<td>0.25–0.50</td>
<td>16/32</td>
</tr>
<tr>
<td>0.50–0.75</td>
<td>0/0</td>
</tr>
<tr>
<td>0.75–1.00</td>
<td>0/0</td>
</tr>
<tr>
<td>0–0.25</td>
<td>10/54</td>
</tr>
<tr>
<td>0.25–0.50</td>
<td>502/848</td>
</tr>
<tr>
<td>0.50–0.75</td>
<td>142/110</td>
</tr>
<tr>
<td>0.75–1.00</td>
<td>28/4</td>
</tr>
</tbody>
</table>

*Probability of being considered a case or control (n/n) in the study sample. Values were calculated by using a logistic regression model that included total cholesterol/HDL cholesterol ratio or apolipoprotein B/apolipoprotein A-I ratio plus diabetes (yes or no), body mass index, smoking status (yes or no), systolic blood pressure, C-reactive protein level.

### CONCLUSION

In conclusion, in a case–control cohort of apparently healthy persons not receiving lipid-lowering therapy, we showed that the apolipoprotein B/A-I ratio was more closely associated with future CAD events than was the total cholesterol/HDL cholesterol ratio, but that the 2 measures were equivalent in their ability to discriminate between persons with and those without cardiovascular events. Thus, our data suggest that replacement of traditional lipid values with the apolipoprotein B/A-I ratio adds little to CAD risk assessment in the general population.
However, other characteristics of the test, such as the ability to perform it on nonfasting samples, may make it useful in some settings.

ACKNOWLEDGMENTS

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