Appendix 1 (as supplied by the authors): Supplementary material

Methods

Study participants

The case-control study participants consisted of apparently healthy men and women who participated in the EPIC-Norfolk cohort and developed fatal or nonfatal coronary heart disease during follow-up. Controls were apparently healthy study participants who remained free of coronary heart disease during follow-up. Controls were matched to cases by sex, age and enrolment time. The nested case-control set of participants (drawn from the entire cohort) for whom additional data were available for C-reactive protein, apolipoprotein A-I, apolipoprotein B levels as well as low-density lipoprotein size and glycated hemoglobin (HbA1c) comprised a subsample of 1798 men and 1058 women.

Biochemical analyses

Nonfasting serum levels of total cholesterol, high-density lipoprotein cholesterol, and triglycerides were measured on fresh samples with the RA 1000 (Bayer Diagnostics, Basingstoke, UK), and low-density lipoprotein cholesterol levels were calculated with the Friedewald formula [1]. Serum levels of apolipoprotein B were measured by rate immunonephelometry (Behring Nephelometer BNII, Marburg, Germany) with calibration traceable to the International Federation of Clinical Chemistry primary standards [2]. C-reactive protein levels were measured with a sandwich-type enzyme-linked immunosorbent assay, as previously described [3]. Low-density lipoprotein particle size was measured using nondenaturing 2-16% polyacrylamide gradient gel electrophoresis as previously described [4].

Statistical analyses

The Framingham risk score was calculated using a previously reported algorithm, which takes into account age, sex, total cholesterol, high-density lipoprotein cholesterol, systolic and diastolic blood pressure, smoking and the presence of diabetes [5]. Because the Framingham risk score overestimates CHD risk in Europeans, and more specifically, in the EPIC-Norfolk study population, we recalibrated the Framingham risk score as previously described [6]. To compare the discrimination of the recalibrated Framingham risk score as well as the combination of the recalibrated Framingham risk score and hypertriglyceridemic waist, the areas under the receiver-operating characteristic curves were calculated for the recalibrated Framingham risk score alone and for the recalibrated Framingham risk score with the hypertriglyceridemic waist phenotype. The areas under the receiver-operating characteristic curves were also compared using a nonparametric algorithm. Participants were also categorized into three groups according to their calculated ten-year Framingham risk score: low (<10%), intermediate (10-20%) and high (>20%) risk.

Results

Men and women were also classified into tertiles of the recalibrated Framingham risk score and further classified according to the presence or absence of the hypertriglyceridemic waist phenotype. Figure 2 in the main article shows that men with the lowest Framingham risk score with the hypertriglyceridemic waist phenotype were at increased risk compared to men with a low Framingham risk score without the hypertriglyceridemic waist phenotype.

Appendix to: Arsenault BJ, Lemieux I, Després JP, et al. The hypertriglyceridemic-waist phenotype and the risk of coronary artery disease: results from the EPIC-Norfolk Prospective Population Study. *CMAJ* 2010. DOI:10.1503/cmaj.091276.

Similarly, Figure 2 shows that in women with a low Framingham risk score, those with the hypertriglyceridemic waist phenotype were at increased coronary heart disease risk compared to those without the hypertriglyceridemic waist phenotype. This observation was also valid for women classified at high coronary heart disease risk.

However, adding the hypertriglyceridemic waist phenotype to the recalibrated Framingham risk score did not result in a significant increase in the area under the receiver-operating characteristic curve. For men, the c-statistics were 0.716 (95%CI 0.702 to 0.729) and 0.715 (95%CI 0.701 to 0.729), respectively before and after inclusion of the hypertriglyceridemic waist in the recalibrated Framingham risk score. For women, the respective c-statistics were 0.771 (95%CI 0.756 to 0.785) and 0.771 (95%CI 0.756 to 0.786).

References for appended supplementary material

[1] Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 18: 499-502

[2] Albers JJ, Marcovina SM, Kennedy H (1992) International Federation of Clinical Chemistry standardization project for measurements of apolipoproteins A-I and B. II. Evaluation and selection of candidate reference materials. Clin Chem 38: 658-662

[3] Bruins P, te Velthuis H, Yazdanbakhsh AP, et al. (1997) Activation of the complement system during and after cardiopulmonary bypass surgery: postsurgery activation involves C-reactive protein and is associated with postoperative arrhythmia. Circulation 96: 3542-3548

[4] Arsenault BJ, Lemieux I, Despres JP, et al. (2007) Cholesterol levels in small LDL particles predict the risk of coronary heart disease in the EPIC-Norfolk prospective population study. Eur Heart J

[5] Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB (1998) Prediction of coronary heart disease using risk factor categories. Circulation 97: 1837-1847

[6] D'Agostino RB, Sr., Grundy S, Sullivan LM, Wilson P (2001) Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. JAMA 286: 180-187

Appendix to: Arsenault BJ, Lemieux I, Després JP, et al. The hypertriglyceridemic-waist phenotype and the risk of coronary artery disease: results from the EPIC-Norfolk Prospective Population Study. *CMAJ* 2010. DOI:10.1503/cmaj.091276.