1-Low-density lipoprotein cholesterol, C-reactive protein, and lipoprotein(a) universal one-time screening in primary prevention: the EPIC-Norfolk study

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Abstract

Background and Aims Recent data from a large American cohort of women strongly support universal one-time screening for LDL cholesterol, high-sensitivity C-reactive protein (hsCRP), and lipoprotein(a) [Lp(a)] in primary prevention. This study addresses the validity and generalizability of this novel primary prevention strategy in a large prospective European cohort of initially healthy men and women. Methods Plasma levels of LDL cholesterol, hsCRP, and Lp(a) were measured at study entry in 17 087 participants from the EPIC-Norfolk study who were subsequently followed over a period of 20 years for major adverse cardiovascular events (MACEs). Competing risk- and multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for incident MACE across quintiles of each biomarker and sought evidence of independent as well as additive effects over time were calculated. Results During the 20-year follow-up, a total of 3249 MACEs occurred. Increasing quintiles of baseline LDL cholesterol, hsCRP, and Lp(a) all predicted 20-year risks; the multivariable-adjusted HRs in a comparison of the top to bottom quintile were 1.78 (95% CI: 1.57-2.00) for LDL cholesterol, 1.55 (95% CI: 1.37-1.74) for hsCRP, and 1.19 (95% CI: 1.07-1.33) for Lp(a). Compared with individuals with no biomarker elevations, the multivariable-adjusted HRs for incident MACE were 1.33, 1.68, and 2.41 for those with one, two, or three biomarkers in the top quintile, respectively (all P < .001). Each biomarker demonstrated independent contributions to overall risk and findings were consistent in analyses stratified by sex. Conclusions A single combined measure of LDL cholesterol, hsCRP, and Lp(a) among initially healthy European men and women was predictive of incident MACE during a 20-year period. These data replicate findings from a recent American cohort and strongly support universal screening for all three biomarkers in primary prevention.

Keywords

Author Keywords

Atherosclerotic cardiovascular diseasePrimary preventionLDL cholesterolHigh-sensitivity C-reactive proteinLipoprotein(a)

Keywords Plus

PERIPHERAL ARTERY-DISEASECORONARY

2-Inflammation, Cholesterol, Lipoprotein(a), and 30-Year Cardiovascular Outcomes in Women

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Abstract

Background

High-sensitivity C-reactive protein (CRP), low-density lipoprotein (LDL) cholesterol, and lipoprotein(a) levels contribute to 5-year and 10-year predictions of cardiovascular risk and represent distinct pathways for pharmacologic intervention. More information about the usefulness of these biomarkers for predicting cardiovascular risk over longer periods of time in women is needed because early-life intervention represents an important risk-reduction method.

Methods

We measured high-sensitivity CRP, LDL cholesterol, and lipoprotein(a) levels at baseline in 27,939 initially healthy U.S. women who were subsequently followed for 30 years. The primary end point was a first major adverse cardiovascular event, which was a composite of myocardial infarction, coronary revascularization, stroke, or death from cardiovascular causes. We calculated the adjusted hazard ratios and 95% confidence intervals across quintiles of each biomarker, along with 30-year cumulative incidence curves adjusted for age and competing risks.

Results

The mean age of the participants at baseline was 54.7 years. During the 30-year follow-up, 3662 first major cardiovascular events occurred. Quintiles of increasing baseline levels of high-sensitivity CRP, LDL cholesterol, and lipoprotein(a) all predicted 30-year risks. Covariable-adjusted hazard ratios for the primary end point in a comparison of the top with the bottom quintile were 1.70 (95% confidence interval [CI], 1.52 to 1.90) for high-sensitivity CRP, 1.36 (95% CI, 1.23 to 1.52) for LDL cholesterol, and 1.33 (95% CI, 1.21 to 1.47) for lipoprotein(a). Findings for coronary heart disease and stroke appeared to be consistent with those for the primary end point. Each biomarker showed independent contributions to overall risk. The greatest spread for risk was obtained in models that incorporated all three biomarkers.

Conclusions

A single combined measure of high-sensitivity CRP, LDL cholesterol, and lipoprotein(a) levels among initially healthy U.S. women was predictive of incident cardiovascular events during a 30-year period. These data support efforts to extend strategies for the primary prevention of atherosclerotic events beyond traditional 10-year estimates of risk.

Keywords

C-REACTIVE PROTEINPRIMARY PREVENTIONRISKDISEASE