

# **Comparison of C-Reactive Protein and Low-Density Lipoprotein Cholesterol Levels in the Prediction of First Cardiovascular Events**

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## FROM ABSTRACT:

### Background

Both C-reactive protein and low-density lipoprotein (LDL) cholesterol levels are elevated in persons at risk for cardiovascular events.

However, population-based data directly comparing these two biologic markers are not available.

### Methods

C-reactive protein and LDL cholesterol were measured at base line in 27,939 apparently healthy American women, who were then followed for a mean of eight years for the occurrence of myocardial infarction, ischemic stroke, coronary revascularization, or death from cardiovascular causes.

We assessed the value of these two measurements in predicting the risk of cardiovascular events in the study population.

### Results

Although C-reactive protein and LDL cholesterol were minimally correlated, base-line levels of each had a strong linear relation with the incidence of cardiovascular events.

Overall, 77 percent of all events occurred among women with LDL cholesterol levels below 160 mg per deciliter (4.14 mmol per liter), and 46 percent occurred among those with LDL cholesterol levels below 130 mg per deciliter (3.36 mmol per liter).

By contrast, because C-reactive protein and LDL cholesterol measurements tended to identify different high-risk groups, screening for both biologic markers provided better prognostic information than screening for either alone.

### Conclusions

These data suggest that the C-reactive protein level is a stronger predictor of cardiovascular events than the LDL cholesterol level and that it adds prognostic information.

THESE AUTHORS ALSO NOTE:

"Because of its critical importance in atherogenesis, low-density lipoprotein (LDL) cholesterol is the focus of current guidelines for the determination of the risk of cardiovascular disease."

"However, atherothrombosis often occurs in the absence of hyperlipidemia."

**[IMPORTANT]**

C-reactive protein is a marker of inflammation that has been shown to be associated with an "increased risk of myocardial infarction, stroke, sudden death from cardiac causes, and peripheral arterial disease."

Markers of inflammation, including C-reactive protein, have prognostic value for the detection of first vascular events. **[IMPORTANT]**

Hormone-replacement therapy affects levels of both C-reactive protein and LDL cholesterol. **[IMPORTANT]**

Of all events in the study participants, 77% occurred among those with LDL cholesterol levels below 160 mg per deciliter (4.14 mmol per liter), and 46% occurred among those with LDL cholesterol levels below 130 mg per deciliter (3.36 mmol per liter).

"Increasing levels of C-reactive protein were associated with increased risk of cardiovascular events."

Also, "increasing C-reactive protein levels were associated with increased risk of cardiovascular events at LDL cholesterol levels below 130, 130 to 160, and above 160 mg per deciliter."

## DISCUSSION

"The current study suggests that C-reactive protein, a marker of systemic inflammation, is a stronger predictor of future cardiovascular events than LDL cholesterol."

"In this study, C-reactive protein was superior to LDL cholesterol in predicting the risk of all study end points."

"C-reactive protein and LDL cholesterol levels were minimally correlated."

"The combined evaluation of both C-reactive protein and LDL cholesterol proved to be superior as a method of risk detection to measurement of either biologic marker alone."

Large proportions of first cardiovascular events occur at LDL cholesterol levels below the threshold values for intervention and treatment in the current guidelines of the National Cholesterol Education Program.

"C-reactive protein in women can be used regardless of their status with regard to hormone-replacement therapy."

"Women in the high C-reactive protein-low LDL cholesterol subgroup were at higher absolute risk than those in the low C-reactive protein-high LDL cholesterol subgroup."

"Unlike other markers of inflammation, C-reactive protein levels are stable over long periods, have no diurnal variation, can be measured inexpensively with available high-sensitivity assays, and have shown specificity in terms of predicting the risk of cardiovascular disease."

Other biological risk factors for CHD are triglycerides, and homocysteine levels.

Other "risk factors, such as high blood pressure, smoking, obesity, diabetes, low levels of physical activity, and use of hormone-replacement therapy, may be more or less important for individual patients."

**THIS ARTICLE GENERATED THE FOLLOWING EDITORIAL, in part**

### **C-Reactive Protein — To Screen or Not to Screen?**

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Lori Mosca, M.D., M.P.H., Ph.D.

The traditional risk factors do not fully account for the occurrence of CHD.

"Only about half of patients with CHD have hypercholesterolemia."

"Important advances in understanding the pathophysiology of atherosclerosis have been made in recent years, and inflammatory mechanisms are now believed to play a central part in the origins and complications of CHD." **[IMPORTANT]**

"C-reactive protein is an acute-phase reactant that markedly increases during an inflammatory response."

"Minor elevations of C-reactive protein are predictive of cardiovascular events in patients with CHD."

C-reactive protein levels are a marker of low-grade chronic systemic inflammation.

This article "adds to the growing body of evidence that C-reactive protein is an independent predictor of cardiovascular disease."

"The results showed that C-reactive protein levels predicted the risk of cardiovascular disease."

"C-reactive protein levels predicted subsequent cardiovascular disease more strongly than did the levels of low-density lipoprotein (LDL) cholesterol."

"The data lend support to the inflammatory hypothesis of the pathogenesis of coronary heart disease."

"C-reactive protein has been associated with mortality from all causes in the elderly, suggesting that it is a nonspecific marker of clinical outcomes." **[VERY IMPORTANT]**

"C-reactive protein is correlated with central adiposity and insulin resistance." **[IMPORTANT]**

#### KEY POINTS FROM DAN MURPHY

- (1) C-reactive protein is a biological marker for systemic inflammation.
- (2) Inflammation plays a central part in the origins and complications of CHD.
- (3) C-reactive protein level is a stronger predictor of cardiovascular events than the LDL cholesterol levels.

#### COMMENTS FROM DAN MURPHY

The central theme in many of the articles we have been reviewing is:

- (1) Inflammation, particularly chronic systemic inflammation, is very bad.
- (2) The primary cause of systemic chronic inflammation is prostaglandin E2 (PGE2).
- (3) PGE2 is derived from the omega-6 fat arachidonic acid (AA).
- (4) Excess omega-6 fats in the diet are therefore bad.
- (5) Omega-3 fats, especially eicosapentaenoic acid (EPA, or 20:5n-3), are powerfully anti-inflammatory and block the conversion of AA to PGE2.
- (6) Omega-6 fatty acids are ideally balanced (1:1 ratio) with omega-3 fatty acids.
- (7) Average Americans have a ratio of about 30:1 omega-6 over omega-3.
- (8) This gross imbalance is largely responsible for joint degeneration, painful arthritis, immune system dysfunction, vascular disease, cardiac electrical abnormalities, and potentially for neurodegenerative diseases and brain dysfunction.