

High Sensitivity C-Reactive Protein (hsCRP)

Methodist Medical Center Laboratory began providing an in-house assay for high sensitivity CRP (hs-CRP) on July 1, 2002. At that time the reference range was reported in quintiles of risk for atherosclerosis. Published data from 2003 suggests that the predictive risk reporting can be simplified into a three-tier system.

Reporting of hsCRF by Methodist Medical Center Reference Laboratory MMCI reports the hs-CRP in mg/L along with an interpretative comment based on the following table plus the additional comment based on recommendations of the American Heart Association and the CDC.

hs-CRP Result	Comment
< 1.0 mg/L	Based on this marker, the risk of developing coronary heart disease and having adverse cardiac events is very low.
1.0 – 3.0 mg/L	Based on this marker, the risk of developing coronary heart disease and having adverse cardiac events is average.
> 3.0 mg/L	Based on this marker, the risk of developing coronary heart disease and having adverse cardiac events is high.

Additional Comment

** hs-CRP should be measured twice (averaging results), optimally two weeks apart, fasting or nonfasting. If the hs-CRP is > 10.0 mg/L the test should be repeated and the patient examined for source of inflammation.

Background

C-reactive protein (CRP) is one of the first acute-phase proteins to become elevated in inflammatory disease. CRP is synthesized primarily by the liver and functions by binding a variety of polysaccharides, phosphatidylcholines and polycations in the presence of Ca⁺⁺. Once complexed CRP activates the classic complement pathway and eliminates the bound compounds from the blood. Historically CRP measurements have been used to monitor a wide variety of inflammatory conditions. Recent studies suggest that subtle changes in CRP levels within the traditional reference range are indicative of inflammatory processes that may play a role in the atherosclerotic plaque formation. Assays capable of measuring these low levels are referred to as “high-sensitivity CRP” (hs-CRP).

hs
CRP

Cardiac
Marker



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CRP as cardiac risk factor

In recent years the high sensitivity CRP assay has been used to assess risk of future cardiac adverse events in otherwise healthy individuals. The reference or normal range is divided into 3 parts with the risk increasing with each division from 0 to 10 mg/L. Publications over the last 2 years have documented that CRP is a powerful predictor of future first coronary events in apparently health men and women. In a study (reference 6) of young patients with premature MI, CRP was a strong predictor of mortality in these patients. The report of the workshop convened by the CDC and the American Heart Association (reference 1) advised that hs-CRP be measured twice optimally 2 weeks apart, fasting or nonfasting in metabolically stable patients. If hs-CRP level is greater than 10 mg/L the test should be repeated and patient examined for sources of infection or inflammation.

Since HDL is also a risk factor for adverse coronary events, some authors have proposed a combined risk. Since this type of interpretation is dependent on the local population and specific assays, we have not included this analysis in the interpretative remarks. Articles are available for a proposed estimation of cardiac risk based on both the HDL and hsCRP values. The recent study by P.M. Ridker et.al. published in the New England Journal of Medicine in the November 14, 2002 issue suggested that hs-CRP might be a stronger predictor of cardiovascular events than the LDL level. In the brief article they show an algorithm for risk assessment using both LDL and hs-CRP levels.

Notes:

- * Reporting units of hs-CRP should be mg/L not the old units for CRP of mg/dl.
- * Current research shows that there is not a significant circadian variation in an individual's hs-CRP levels and the within person variability is slight having the same degree of variability as the cholesterol measurement.
- * Several authors have shown that serum is equivalent to using heparinized plasma with EDTA being 3-5 % less and citrate plasma 10 % less than serum..

Selected References:

1. Pearson, TA et.al., "Markers of Inflammation and Cardiovascular Disease" *Circulation* 107:499-511 (2003).
2. Ridker PM, Rifai N, Rose L, Buring JE and Cook NR, "Comparison of C-Reactive Protein and Low-density Lipoprotein Cholesterol Levels in the Prediction of First Cardiovascular Events" *N Engl J Med*, Vol. 347, November 4, 2002.
3. Rifai N & Ridker PM. *Clin Chem* 2001;47:403-411.
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6. Retterstol L, Eikvar L, Bohn M, Bakken A, Erikssen J, Berg K. "C-reactive protein predicts death in patients with previous premature myocardial infarction - A 10 year follow-up study", *Atherosclerosis* 2002;160:433-440.
7. Rothkrantz-Kos S, et.al. *Clin. Chem.* 2002;48:359-362.