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P: In patients with chest pain
 I: does measurement of CRP
 C: compared to CKMB and troponin
 O: improve detection of cardiac ischemia?

Clinical Scenario:

A fifty-two year old non-smoking, non-diabetic male with an isolated history of hypercholesterolemia presents to the ED for 2 hours of ill-defined substernal chest pain. An EKG shows no acute s-t changes, initial CPK, CK-MB, and troponin levels are normal. Aspirin and nitroglycerin provide only minimal change in his symptoms. Management for this patient includes blood pressure control if necessary, admission to the observation unit, and any of a variety of stress imaging modalities. An accurate, reliable test to rule in or out ischemia in patients with an inconclusive clinical picture could be very useful.

Author	Study Group	Study Type	Key Results	Weaknesses
Potsch, et al	980 consecutive chest pain patients without st-t segment elevation	Prospective, cohort from 1/1/02-12/31/03	Serum s-PCR values were 1.31 ± 2.90 (median =0.47) in patients diagnosed with AMI and 0.79 ± 1.39 (0.30) in patients without AMI ($p = 0.031$, Mann-Whitney) The s-CRP > 1.0 showed 30% sensitivity and 80% specificity, plus negative and positive predictive values of 6.1% and 96.7%, respectively, for AMI diagnosis Therefore, s-CRP <1.0 has good negative predictive value for acute MI	Small number of adverse events in inpatient group (40), with most events in the middle quartiles (22)
Huang, et al	205 consecutive patients suspected of CAD referred for cardiac cath	Prospective, cohort	Patients with elevated hsCRP and elevated NT-ProBNP were at greater risk of cardiovascular events within 4 years than those with low values of either or both of the above. Unlike NT Pro BNP, hsCRP was independent of age, Framingham risk score, or LVEF	Sample was 90% male, small sample size, no analysis of predictive value over short term
Boekholdt, et al	1108 participants who developed CAD during 6 years of follow-up matched with 2164 controls	Nested case-control among participants in EPIC-Norfolk	The odds ratio (OR) for future CAD incidence was 1.66 (95% CI = 1.31–2.12, p for linearity <0.0001), after adjustment for classical cardiovascular risk factors, for top versus bottom quartile of the CRP distribution. The predictive value was substantially stronger for fatal CAD (OR = 2.92, 95% CI = 1.83–4.67, p for linearity <0.0001) than for non-fatal CAD (OR = 1.25, 95% CI = 0.93–1.66, p for linearity = 0.06). CRP levels were among the strongest predictors of CAD incidence and mortality. CRP levels remained a statistically significant predictor of future CAD, even after adjustment for the Framingham risk score.	Negative results based on death or hospital admission. May miss minor events. No analysis of short term adverse outcomes.

Shah, et al	Retrospective analysis of 31 studies	Mathematical calibration of area under ROC curve to standardize reported values of CRP and associated heart disease	Comparison of CRP value with and without Framingham Risk score showed small variation between CHD and non CHD groups. Additionally, there was significant overlap in coronary events among those with average CRP values. Authors conclude that CRP does not perform better than the Framingham risk equation for discrimination. The improvement in risk stratification or reclassification from addition of CRP to models based on established risk factors is small and inconsistent.	Retrospective mathematical analysis. Does not address high sensitivity CRP
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Clinical bottom line:

High sensitivity CRP, while controversial, has been demonstrated to carry an independent risk of adverse cardiac events when given a threshold of 1.0. Levels of hs-CRP greater than 1.0 confer an increased risk of cardiac events within the next 6 months to 4 years, depending on the study. A negative hs-CRP, or level <1.0 has good negative predictive value for cardiac events. Hs-CRP cannot definitively distinguish between cardiac and non-cardiac causes of chest pain. However, a clinician may feel more confident about conservatively managing the patient with an unclear clinical picture for coronary disease, negative troponin and CK-MB if that patient also has an hs-CRP <1.0. Further study is warranted in the acute setting, to determine the rate of rise of hs-CRP in the setting of cardiac insult. With appropriate data, it may be possible to discharge low to moderate risk patients with negative CRP without obtaining stress imaging and necessitating overnight ED stays.

Potsch, A. Filho, A. Tura, B. Gamarski, R. et al. "C-Reactive Protein Diagnostic and Prognostic Value in Patients Presenting at the Emergency Room with Chest Pain" Arquivos Brasileiros de Cardiologia - Volume 87, N° 3, September 2006.

Boekholdt, S. Hack, C. Sandhu, M. et al. "C-reactive protein levels and coronary artery disease incidence and mortality in apparently healthy men and women: The EPIC-Norfolk prospective population study 1993–2003" Atherosclerosis 187 (2006) 415–422.

Huang, P. Lu, T. Wu, T. et al "Usefulness of combined high-sensitive C-reactive protein and N-terminal-probrain natriuretic peptide for predicting cardiovascular events in patients with suspected coronary artery disease" Coronary Artery Disease 2008, 19:187–193

Shah, T. Casas, JP. Cooper, JA. et al. "Critical appraisal of CRP measurement for the prediction of coronary heart disease events: new data and systematic review of 31 prospective cohorts" International Journal of Epidemiology. 38(1):217-31, 2009 Feb.