C-reactive protein: a predictive marker, not a causal factor, for cardiovascular disease

Elevated plasma levels of C-reactive protein (CRP) are associated with an increased risk of ischemic vascular disease, but whether CRP promotes this disorder or is simply a marker of increased cardiovascular risk is unclear.

Zacho and colleagues investigated whether CRP polymorphisms were associated with plasma CRP levels, and whether the polymorphisms were associated with ischemic heart disease and ischemic cerebrovascular disease. The team also assessed whether the relationship between CRP polymorphisms and risks of cardiovascular events was consistent with expected results correlated to changes in CRP levels. Data from patients from four independent study cohorts were analyzed.

Data from the Copenhagen City Heart Study revealed that, compared with plasma CRP levels below 1 mg/l, plasma CRP levels above 3 mg/l increased the risk for ischemic heart disease 1.6-fold, and the risk for ischemic cerebrovascular disease 1.3-fold. An analysis of different genotype combinations for four CRP polymorphisms, performed in the Copenhagen General Population Study cohort, showed rises in CRP levels of up to 64%. This CRP-polymorphism-associated increase in plasma CRP levels was predicted to increase risks of ischemic heart disease and ischemic cerebrovascular disease by up to 32% and up to 25%, respectively. Analysis of combined data from the Copenhagen City Heart Study, the Copenhagen General Population Study, the Copenhagen Ischemic Heart Disease Study and the Copenhagen Carotid Stroke Study, however, revealed that CRP polymorphisms were not associated with a significant increased risk of ischemic heart or cerebrovascular disease. The authors conclude that these data suggest increased CRP levels act only as a marker, rather than a causal factor, for ischemic vascular disease.

Another study by Ridker *et al.* has shown the importance of incorporating high-sensitivity CRP measurements and parental history of myocardial infarction before 60 years of age into traditional cardiovascular event risk prediction models for men. The authors have previously shown an improvement in the accuracy of risk classification in women using this algorithm, which is known as the Reynolds Risk Score. Traditional cardiovascular risk prediction models assess total cholesterol, high-density lipoprotein cholesterol, blood pressure, age, and smoking status.

A total of 10,724 initially healthy, nondiabetic men (median age 63 years) from the US were followed-up prospectively (median period 10.8 years). During follow-up, 1,294 cardiovascular events were recorded. Assessment of cardiovascular event risk was performed using both the traditional risk prediction model and the Reynolds Risk Score. The latter reclassified risk for 17.8% of participants overall and for 20.2% of those at intermediate (5% to 20%) 10-year risk, with significantly improved accuracy among reclassified individuals ($P<0.001$).

The superior global cardiovascular risk prediction achieved by Reynolds Risk Score, in comparison with the traditional risk model, could lead to improved targeting of preventative therapies to individuals at the highest levels of risk. Ridker and colleagues added that such individualized treatment could enhance the net benefit and decrease the toxicity of these therapies.

Original articles Zacho J *et al.* (2008) Genetically elevated C-reactive protein and ischemic vascular disease. *N Engl J Med* **359:** 1897–1908
Ridker PM *et al.* (2008) C-reactive protein and parental history improve global cardiovascular risk prediction: the Reynolds Risk Score for men. *Circulation* **118:** 2243–2251

Fondaparinux: a promising alternative to heparin treatment for acute coronary syndromes

A study has revealed that fondaparinux, a synthetic inhibitor of coagulation factor Xa, is a promising treatment option for patients with acute coronary syndromes.

Mehta *et al.* performed a combined analysis of the Fifth and Sixth Organization to Assess Strategies in Ischemic Syndromes (OASIS 5 and 6) trials. Data were assessed from a total of 26,512 patients with acute coronary syndromes who were randomly assigned to receive either fondaparinux 2.5 mg daily (13,270 patients, mean age 65.5 years) or to treatment with a heparin (unfractionated heparin or enoxaparin; 13,242 patients, mean age 65.4 years). Treatment strategies were invasive in 19,085 patients, and conservative in 7,427 patients.

Fondaparinux treatment was superior to heparin therapy in terms of reducing mortality,