Is C-Reactive Protein a Predictor of Perioperative Events Before Coronary Artery Bypass?

Yoshitaka Okamura, MD

The concept that “atherosclerosis is a chronic inflammatory disorder of the vessels” is widely accepted with considerable published evidence in support. Since Ridker reported that C-reactive protein (CRP), a marker of systemic inflammation, is a stronger predictor of future cardiovascular events than low-density lipoprotein-cholesterol in healthy persons, the predictive value of CRP in patients with coronary artery disease has undergone numerous investigations.

In a study of patients with acute myocardial infarction (AMI), CRP appeared a potential determinant of both death and major adverse cardiovascular events. As well as that study of AMI, the predictive value of preoperative CRP has been emphasized in percutaneous catheter intervention (PCI) and coronary artery bypass grafting (CABG). However, until now, studies of the predictive value of CRP have been limited to on-pump CABG.

In the past decade, off-pump CABG, which can reduce the systemic inflammatory response caused by cardiopulmonary bypass, has become popular, but there is little data about the relationship of preoperative CRP and the outcome of off-pump CABG.

In this issue of the Journal, Kim et al report an initial study concerning the predictive value of preoperative CRP in off-pump CABG. This information will be invaluable because they performed a prospective and observational study using a high-sensitivity nephelometric method and set the cut-off point at 0.3 mg/dl according to the American Heart Association guidelines. Most previous reports have been retrospective and some were not performed with high-sensitivity CRP and had relatively high cut-off points.

Kim and colleagues demonstrate that an elevated preoperative CRP level is a significant independent predictor of major postoperative complications, especially renal dysfunction in patients undergoing off-pump CABG. Although the difference was predominant only as regards renal dysfunction, the authors conclude the predictive value of preoperative CRP is applicable to major postoperative complications from a statistical viewpoint.

This study has some notable results. First, preoperative CRP was recognized as having significant predictive value for postoperative complications, even though off-pump CABG, a less invasive procedure, eliminates the unfavorable influences of extracorporeal circulation. Second, a significant difference was observed in the immediate perioperative phase. To validate the evidence, we need to compare it with previous reports.

There are some problematic areas. Most of the previous reports have had low case numbers from a single center. Clinical outcomes of CABG, either on or off pump, have improved recently, so the incidence of postoperative complications has decreased, and a small patient number has weak statistical power. There is a controversial report that claimed that elevated preoperative CRP cannot be a marker of increased surgical risk. Another showed that patients with elevated preoperative CRP were exposed to higher inhospital mortality and sepsis, but there was no difference in the incidence of renal dysfunction.

In the study by Biancari et al, the patient group with elevated preoperative CRP had significantly higher preoperative incidences of history of MI, diabetes, lower limb ischemia, and low left ventricular ejection fraction! However, the baseline patient characteristics were quite similar between the high and low CRP groups in the study by Kim et al. Biancari’s group also reported long-term results: they found no significant impact on the occurrence of major immediate postoperative morbidity and mortality, against a possible impact on 12-year outcomes.

Another issue is the influence of preoperative medication. In Kim’s study, statin and aspirin were administered to 70% of the patients. These anti-inflammatory drugs are thought to decrease the CRP level, so some patients could be allocated to the high or low CRP group by either being on or off this medication. Moreover, the number of patients with left main trunk disease was much less than in other reports, which might relate to the indication of CABG or the expansion of PCI, or even racial differences.

There are several inflammatory markers for atherosclerotic cardiovascular disease. In the same fashion as CRP, serum amyloid A (SAA), interleukin-6, soluble VCAM-1, soluble ICAM-1, low-density lipoprotein-cholesterol, homocysteine, and p-selectin were investigated for their predictive value of future cardiovascular events. Among these, SAA was suggested to have a similar predictive value as CRP for patients with AMI.

The mechanism of CRP is not a direct action against the arterial wall, but rather a pleiotropic action, such as activation of complement, promotion and inhibition of immune cells, or an opsonin effect on macrophages. Thus, a synergistic effect would be expected to increase the predictive value of preoperative CRP associated with any other factors.

It is very important to preoperatively assess the risks
associated with cardiac surgery, not only for decisions about surgical indication (patient selection, timing of surgery), but also for those related to the selection of surgical procedure and risk stratification of surgical results. EuroSCORE, STS score and Parsonette score are well-known methods of evaluating surgical risk, but all the listed risk factors in those systems of calculation are macroscopic and there are no biomarkers. It might be feasible to add biomarkers into the system for calculating the risks of cardiac surgery, especially if a prospective multicenter study with large patient numbers is performed.

References