FilterWire; if this is not possible, pre-dilate with a 1.5 mm balloon. Second, deploy the FilterWire before any major side branch or 2–3 cm beyond a total occlusion. Patients from an existing database were case matched according to infarct-related artery, pre–percutaneous coronary intervention, Thrombolysis in Myocardial Infarction (TIMI) flow grade, gender, and age.

The FilterWire was primarily successful in 89% of the patients. If seven patients who required pre-dilation are included, the success rate increases to 94%. Macroscopic particles were visually detected in 34% of the cases. Most of these particles were composed of fresh thrombus, platelets, and red blood cells. Foam cells, smooth muscle cells, cholesterol clefts, and calcifications were not observed.

Compared with the matched group, the FilterWire group had less IIb/IIIa inhibitor use, a 5-minute longer needle-to-balloon time, higher TIMI 3 flow grade (98% vs 85%, $P = .03$), lower frame counts (22 vs 31, $P = .005$), and higher percentage of grade 3 myocardial blush score (66% vs 36%). The FilterWire group also had greater ST segment resolution and lower peak creatine kinase levels. Multivariate analysis showed that FilterWire use is the only independent predictor of effective reperfusion markers.

This study certainly showed that the use of FilterWire is feasible and safe in primary angioplasty in ST elevation myocardial infarction. Fifty-eight percent of the interventions were in the left anterior descending or circumflex artery, dispelling the notion that distal protection may only be important in the right coronary artery. The authors did not discuss TIMI flow rate in the unprotected side branches, which may be important when the side branch is large; "kissing" filters may be possible for balloon angioplasty but not for stenting.

It is likely that in the future we will be using distal protection devices in many of our patients who present with acute coronary syndrome. One of the major concerns Gruentzig had when he first performed percutaneous transluminal coronary angioplasty (PTCA) 25 years ago was distal embolization. Fortunately, he did not perform the initial angioplasty in patients with saphenous vein grafts or acute myocardial infarction; otherwise, there would be no PTCA as we know it today. ■

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Atherosclerosis

The Relationship Between Inflammation and Atherosclerotic Events

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It is now recognized that atherosclerosis is an inflammatory disease.[1] Chronic, subclinical inflammation appears to be one mechanism explaining the increased risk of atherosclerotic events, regardless of the amount of obstruction produced by a given atherosclerotic lesion. In the inflammatory model of atherosclerosis, it is the degree of inflammation, not the degree of obstruction, that causes acute atherosclerotic events, such as unstable angina and myocardial infarction. If, indeed, inflammation underlies acute coronary syndromes, then inflammatory cytokines, such as interleukin-6 (IL-6), interferon-γ (IFN), and C-reactive protein (hsCRP) should be elevated in patients with acute coronary syndromes and in patients at risk for future cardiovascular events. Two recent articles address this phenomenon and are reviewed below.

Concentrations of Interleukins, Interferon, and C-Reactive Protein in Stable and Unstable Angina Pectoris

Yamashita H, Shimada K, Seki E, et al.
Am J Cardiol 2003;91:133–136.

In this study, 131 Japanese subjects were evaluated. Of these, 79 subjects had known atherosclerosis, and 52 were age- and gender-matched control subjects. Of the 79 individuals with known atherosclerosis, 40 patients presented with unstable angina, and 39 patients had stable atherosclerotic disease. All patients had blood drawn by peripheral venipuncture for measurement of interleukins, IFN, and hsCRP. All three groups were of similar age, gender distribution, and body mass index; however, the prevalence of cardiac risk factors was significantly greater in both the stable and unstable atherosclerosis groups. There were no significant differences in risk fac-

tors between the stable atherosclerosis group and the unstable angina group.

Concentrations of hsCRP and IL-6 were highest in the unstable angina group, intermediate in the stable atherosclerosis group, and lowest in the control group. Concentrations of IFN did not differ between the three groups. These data suggest that in patients with stable atherosclerotic disease and unstable angina, a proinflammatory state is present. They further suggest that inflammation is greatest in the patients with unstable angina.

This study makes an association between the presence and degree of inflammation and the presence of atherosclerosis. It further makes an association between the degree of inflammation and the instability of that atherosclerosis, by noting an increase in inflammatory cytokines in the unstable angina group compared with the stable atherosclerosis group. Therefore, this study supports the inflammatory theory of atherosclerosis.

This study makes an association between the presence and degree of inflammation and the presence of atherosclerosis.

One limitation of this study was a lack of control for the overall plaque burden. It might be that the increase in inflammatory cytokines in the unstable angina group is more a reflection of overall plaque burden rather than of plaque instability. A second limitation, as the authors correctly note, is that this study cannot demonstrate a causal association between inflammatory cytokines and acute coronary syndromes.

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

Ridker PM, Rifai N, Rose L, et al.

N Engl J Med 2002;347:1557–1565.

In this second study, the concentration of the inflammatory cytokine hsCRP was compared with the concentration of low-density lipoprotein (LDL) as a risk predictor for a first cardiovascular event among 27,939 apparently healthy American women enrolled in the Women's Health Study, an ongoing evaluation of aspirin and vitamin E for the primary prevention of cardiovascular events among women 45 years of age or older. Current epidemiologic evidence suggests that LDL concentrations are strongly related to cardiovascular events, and these data have formed the basis of our current national guidelines, which stress LDL determination in risk prediction and LDL lowering for risk reduction.[2] The authors of the current study, however, note that atherothrombosis often occurs in the absence of elevated LDL levels, thus data on other potential risk predictors is needed. The inflammatory marker hsCRP had been shown in several smaller, prospective, nested case–control studies of short-term follow-up to be predictive of future cardiovascular events. But because of inherent limitations in these earlier studies and because a direct comparison between the predictive ability of hsCRP and the predictive ability of LDL has never been conducted, the authors chose to perform the current study.

Blood samples from all 28,345 women initially randomized in the Women's Health study were obtained. Of these, 27,939 samples were found to be evaluable for both hsCRP and LDL. The women in the study have now been followed for a mean of 8 years for the occurrence of myocardial infarction, ischemic stroke, coronary revascularization, or death from cardiovascular causes. The authors used the blood samples collected at randomization to prospectively assess the value of hsCRP and LDL measurements in predicting the risk of cardiovascular events in this study population.

Both the hsCRP levels and the LDL levels were expressed and analyzed according to baseline quintiles. For both hsCRP and LDL, a strong linear relationship was observed. Using a multivariate analysis after adjustment for age, smoking, and hormone replacement therapy use, the relative risk for suffering a first cardiovascular event associated with being in the highest quintile of hsCRP was 2.3, whereas the relative risk associated with being in the highest quintile of LDL was 1.5. The authors further analyzed the interaction between hsCRP and LDL, by dividing the study participants into four groups on the basis of whether they were above or below the median hsCRP value and the median LDL value. As expected, the lowest risk occurred in the low hsCRP/low LDL group. Compared with this group, the relative risk associated with being in either the low hsCRP/high LDL group or the high hsCRP/low LDL group was 1.5. The relative risk associated with being in the high hsCRP/high LDL group was 2.1. Thus, this study suggests that hsCRP, a marker of inflammation, is a stronger predictor of future cardiovas-

Although these and other data are compelling in identifying hsCRP as a risk predictor and risk marker, hsCRP has yet to reach the status of official "risk factor."

cular events than is LDL.

This study offers what appears to be a superior risk predictor than LDL; however, it does not have corresponding data to suggest that reducing this risk marker improves cardiovascular outcomes.

Commentary

These two studies both address the question of inflammation in atherosclerotic events. The first finds a correlation between atherosclerosis, unstable angina, and inflammation, the second finds that the inflammatory marker hsCRP is a better risk predictor than our standard marker, LDL. Although these and other data are compelling in identifying hsCRP as a risk predictor and risk marker, hsCRP has yet to reach the status of official "risk factor." Before adopting widespread use of a new risk factor, I believe at least two criteria must be met: 1) the factor in question must be demonstrated to be associated with future cardiovascular events; and 2) there must be data demonstrating that reduction of this factor reduces the occurrence of cardiovascular events. We have ample data that LDL fulfills both of these criteria. Thus far we have data demonstrating that hsCRP fulfills only the first criterion.

Future studies must address the question of whether reducing hsCRP levels will reduce the incidence of future cardiovascular events. The forthcoming JUPITER trial will address precisely this question. It will be a double-blind study that will randomize 15,000 patients with high levels of CRP and low levels of LDL (< 130 mg/dL) to either placebo or 20 mg/day of rosuvastatin to determine whether statin therapy has a primary preventive role in reducing CRP levels and subsequent cardiovascular risk.

In the interim, I believe hsCRP can be used as an additional test to assist the clinician in risk stratification and, if elevated, may prompt the physician to intensify those risk reduction therapies that have been documented to improve cardiovascular outcomes, such as LDL lowering, blood pressure lowering, and use of antiplatelet agents. It must be remembered, however, that we do not yet have definitive data to assure us that the hsCRP value actually helps assess risk on an individual basis. It may be that this assay is more valuable as a population-based clinical research tool.

We must further remember that hsCRP is affected by any inflammatory or infectious state (recent cold, surgery, joint inflammation, etc). Thus, many physicians advocate taking at least two measurements separated by several weeks to minimize the possible influence of these other factors. ■

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Coronary Artery Disease

Gender Differences in Coronary Revascularization: Does Age Make a Difference?

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Numerous and remarkably consistent studies have noted gender differences in the demographic characteristics of patients with acute myocardial infarction.[1] Gender differences have also been found in the clinical, angiographic, and procedural characteristics in patients undergoing coronary revascularization where, in particular, a disturbingly higher mortality rate in women than in men has been noted.[2] Much, although not all, of this difference in mortality rate has been explained by the older age and higher prevalence of comorbid factors in women at the time of presentation. Recently, however, a disparity in gender differences in outcomes has been noted, surprisingly in younger rather than in older women. Two recent studies highlight this finding.

Biology or Bias: Practice Patterns and Long-Term Outcomes for Men and Women with Acute Myocardial Infarction

Alter DA, Naylor CD, Austin PC, Tu JV.
J Am Coll Cardiol. 2002;39:1909–1916.

To determine how age and gender affect the use of coronary angiography and the intensity of cardiac follow-up within the first year after acute myocardial infarction (AMI), and to evaluate the association of age, gender, and intensity of treatment with survival at 5 years after AMI, 25,697 patients hospitalized with AMI in Ontario, Canada,