Inflammatory Biomarkers for Prediction of Outcomes After Unprotected Left Main Coronary Intervention

Seung-Jung Park, MD, PhD

Unprotected left main coronary artery (ULMCA) lesions are candidates for coronary artery bypass surgery because of the high risk of serious adverse periprocedural events and long-term complications associated with percutaneous coronary intervention (PCI). Although coronary stents have improved initial outcomes of PCI with coronary balloon angioplasty, the outcomes of coronary stenting in ULMCA remain mixed, even with the use of drug-eluting stents. \(^1\)\(^2\)\(^3\) Periprocedural safety and long-term outcomes are excellent in patients at low risk \(^1\)\(^2\)\(^3\); however, long-term mortality associated with ULMCA stenting is \(\approx 25\%\) in patients at high risk. \(^3\) These variations have resulted in studies that evaluated factors influencing ULMCA stenting outcomes. The recent Unprotected Left Main Trunk Investigation Multicenter Assessment (ULTIMA) registry report involved 279 patients, 46% of whom were deemed inoperable or at high surgical risk. \(^3\) For the latter patients, the in-hospital mortality rate was 14%, whereas the 1-year incidence rates were 24.2% for all-cause mortality, 20.2% for cardiac mortality, and 9.8% for myocardial infarction (MI). In that study, decreasing left ventricular function (<30%) was inversely related to events. In contrast, for the low-risk ULTIMA registry subset of 89 patients, the 1-year actuarial death rate was 3.4% and the MI rate was 2.3%. Likewise, we reported that the procedural success rate was 99.1%, with no incidence of cardiac death or MI during the follow-up period in selected patients with normal left ventricular function and who were good surgical candidates. \(^1\) The risk factors analyzed by these studies, such as low left ventricular ejection fraction, older age, and comorbidity, have been useful in selecting candidates for elective ULMCA stenting. The impact of these patient and angiographic risk factors on long-term outcomes is not always consistent, however. Moreover, these risk factors are not amendable before and after PCI. Given these facts, identifying systemic biomarkers that may predict ULMCA intervention outcomes would be valuable in selecting appropriate candidates and for accurately predicting prognosis.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea.

Correspondence to Seung-Jung Park, MD, PhD, Dept of Medicine, University of Ulsan College of Medicine, Asan Medical Center, 388-1 Poongnap-dong, Songpa-gu, Seoul 138-736, Korea. E-mail sjpark@amc.seoul.kr

(Circulation. 2005;112:2226-2227.)

© 2005 American Heart Association, Inc.

Circulation is available at http://www.circulationaha.org
DOI: 10.1161/CIRCULATIONAHA.105.574798

In this issue of Circulation, Palmerini et al report on the association between preprocedural inflammatory severity and ULMCA stenting prognosis. \(^5\) The severity of systemic inflammation was assessed by measuring levels of C-reactive protein (CRP), fibrinogen, and leukocytes. The study found that elevated levels of CRP and leukocytes were associated with an increased risk of death and death/MI after ULMCA stenting in 83 patients (drug-eluting stents in 42 patients and bare-metal stents in 41 patients). Death and death/MI occurred in 19% and 31%, respectively, of 59 patients with high CRP serum levels (>3 mg/L), but in 0 of 24 patients with normal CRP levels (for death, \(P=0.02\), for death/MI, \(P=0.006\)). Multivariate analysis showed the highest tertiles of CRP (\(P=0.028\)) and leukocyte (\(P=0.002\)) levels were predictors of death, independent of traditional cardiac risk factors. The findings of this article are in line with emerging evidence that inflammatory biomarkers such as CRP are useful for identifying high-risk patients. \(^9\)\(^-\)\(^11\) Previous reports documented that high preprocedural CRP levels were associated with unfavorable long-term outcomes \(^8\)\(^-\)\(^11\) as well as poor initial procedural results. \(^11\) Chew et al reported that elevated baseline CRP levels before PCI were associated with a progressive increase in death or MI at 30 days (lowest quartile, 3.9%, versus highest quartile, 14.2%; \(P=0.002\)) in 727 consecutive patients. \(^11\) This finding was in agreement with another large population study of 1458 PCI patients showing an association between death or MI rate and CRP levels (>3 mg/L (6.1% versus 15.5%, \(P<0.0001\)). \(^9\) The odds ratios for elevated CRP as an independent risk factor for death and MI were 3.69 and 3.7, respectively.

The Palmerini et al study extended the application of inflammatory markers, in particular in relationship to CRP and PCI of ULMCA lesions. \(^8\) Compared with other studies using low-risk ULMCA patients, \(^1\) this study included relatively high-risk patients, with 75% having acute coronary syndromes and 71% having elevated CRP levels (>3 mg/L). Therefore, despite a small study population of 83 patients, they identified an association between CRP levels and death or MI rate. Previously, high CRP levels were linked to worse clinical outcomes in studies that observed that coronary atherothrombosis was not limited to the focal culprit lesion but was diffusely involved \(^12\) or involved multiple plaque ruptures in the culprit and nonculprit lesions. \(^13\) We examined the incidence of multiple plaque ruptures using intravascular ultrasound examination of all 3 coronary vessels in patients with acute MI and stable angina. \(^13\) In that study, 17% of acute MI patients had ruptured plaques both in the culprit and nonculprit vessels. In addition, CRP was independently associated with plaque rupture in acute MI patients (\(P=0.035\); OR, 2.139; 95% CI, 1.053 to 4.343).
Taking into account the previous suggestion that in-stent restenosis at the ULMCA may be the main cause of long-term adverse cardiac events,4 the predictive role of CRP in ULMCA intervention may be explained by an association between CRP and restenosis occurrence. In contrast to the strong evidence of the relationship between CRP and death or MI rates, however, the association between preprocedural inflammatory markers and subsequent restenosis has been confusing. Some studies report that preprocedural CRP levels can predict late occurrence of clinical and angiographic restenosis,10,14 whereas others state that CRP levels are not associated with restenosis.9,15 Although the Palmerini et al study hinted at an association between CRP level and restenosis rate, this connection was not statistically significant.8 They found that restenosis rates in high- (>3 mg/L) and low-CRP level patients were 30% and 13%, respectively. Conclusive interpretation of this result was limited by the small study population, low angiographic follow-up rate (61%), and heterogeneity in the stents used (drug eluting and bare metal). Two recent studies failed to demonstrate an association between postprocedural CRP increase and restenosis rate after drug-eluting stent implantation, which contrasted with bare-metal stent implantation.16,17 Data linking CRP levels and cardiac events will aid in identifying high-risk coronary intervention patients and assist in the selection of specific therapies that will reduce cardiac risk.18,19 Statin therapy may ameliorate the risk of adverse cardiac events such as periprocedural MI and long-term adverse cardiac events in patients with high preprocedural CRP.20 Moreover, recent evidence in regard to statin therapy suggests that 10 mg/d of lovastatin and 40 mg/d of pravastatin can reduce the incidence of MI, which is associated with a 4% decrease in the 9-month mortality after coronary angioplasty for the treatment of unprotected left main coronary artery stenosis.21

In summary, this interesting study showed that preprocedural CRP measurement in ULMCA interventions is useful in predicting outcomes of PCI for ULMCA stenosis. High preprocedural CRP levels were associated with unfavorable long-term outcomes with regard to death and death/MI. The data also suggested an association between CRP levels and restenosis rate. Despite the study limitations, the report adds valuable information to the clinician’s knowledge base. In ULMCA interventions, we should bear in mind information about systemic inflammation, in addition to patient and lesion characteristics. High systemic inflammatory activity based on CRP measurement or other biomarkers may assist in making decisions about both the revascularization strategy and adjunctive medication in ULMCA intervention patients.

References

Key Words: Editorials | stent | coronary disease | inflammation
Inflammatory Biomarkers for Prediction of Outcomes After Unprotected Left Main Coronary Intervention
Seung-Jung Park

Circulation. 2005;112:2226-2227
doi: 10.1161/CIRCULATIONAHA.105.574798
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/112/15/2226

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at: http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at: http://circ.ahajournals.org/subscriptions/