Hemostatic Function and Coronary Artery Disease

To the Editor:

The lack of an independent relationship between fibrinogen level and recurrent coronary events reported by Moss et al in their recent article is at variance with previous evidence linking fibrinogen to coronary artery disease in individuals with and without preexisting cardiovascular disease. The fibrinogen levels reported by Moss et al are high in both patients who had recurrent events (387 ± 112 mg/dL) and in those who did not (350 ± 85 mg/dL; P < 0.05; upper limit of normal for the method used, 300 mg/dL). These high values may be due, in part, to the acute phase reaction of the index infarction. If so, these values obtained 2 months after the event do not accurately represent fibrinogen levels during the mean 26-month follow-up. A strong relationship between fibrinogen and reinfarction was observed when fibrinogen was measured an average of 23.5 months after the index event. These findings are further supported by the consistency of previous reports linking fibrinogen to coronary artery disease and the biological plausibility of such an association (increased blood viscosity, platelet aggregation, coagulation, etc). Fibrinogen is a risk factor for infarction and reinfarction in both population-based studies and those performed on patients with preexisting cardiovascular disease.

John B. Kostis, MD
Clifton R. Lacy, MD
Department of Medicine
UMDNJ-Robert Wood Johnson Medical School
New Brunswick, NJ


Response

We thank Drs Kostis and Lacy for their comments and focus on fibrinogen. Our post-myocardial infarction cohort differed considerably from the one reported by Kostis et al in terms of size of population (1045 versus 147 patients), number of cardiac end points (81 versus 20), average enrollment time after infarction (2 months versus 23.5 months), follow-up duration (26 months versus 38 months), use of adjustment for confounding covariates (yes versus no), use of life-table survivorship analysis (yes versus no), and time frame (1990s versus 1970s), respectively. Our cumulative cardiac event rate was somewhat higher for the top fibrinogen quartile than for the lower 3 quartiles (P = 0.07; see Figure 1), but this effect was markedly diminished after adjustment for relevant covariates (diabetes mellitus, prior myocardial infarction before the index infarction, infarct type by ECG, pulmonary congestion on chest x-ray, sex, and ejection fraction ≤0.30). Of note, in the meta-analysis by Danesh et al, 5 of the 6 studies evaluating patients with coronary heart disease had calculated 99% confidence intervals for fibrinogen that touched on or overlapped the null risk ratio of 1.0.

We agree with Drs Kostis and Lacy that elevated fibrinogen levels have some association with recurrent coronary events, but the strength and significance of this association in our prospective study were weak at best, and the causality is less than clear cut. After adjustment for covariates, fibrinogen level was not a significant risk factor for recurrent cardiac events in our 1990s cohort. Elevated levels of D-dimer and apoB and reduced levels of apoA-I were the only independent risk factors in our study.

Arthur J. Moss, MD
University of Rochester Medical Center
Rochester, NY

Robert E. Goldstein, MD
Victor J. Marder, MD
Charles E. Sparks, MD
David Oakes, PhD
Henry Greenberg, MD
Jarvey J. Weiss, MD
Wojciech Zareba, MD, PhD
Mary W. Brown, MD
Chang-Seng Liang, MD
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William C. Little, MD
John A. Gillespie, MD
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Judith Hochman, MD
Edward M. Dwyer, Jr, MD
Rohit Arora, MD
Frank I. Marcus, MD
Luc F. Miller Watelet, PhD
Robert B. Case, MD

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Circulation. 2000;101:e195
doi: 10.1161/01.CIR.101.18.e195
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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:
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