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LETTERS TO THE EDITOR

Effect of Smoking Status on Response to Thrombolytic Therapy

Barbash et al. (1) analyzed the relation between smoking status and outcome after thrombolytic therapy for acute myocardial infarction in the GUSTO-1 trial. The authors concluded that the superior survival of smokers is mostly accounted for by their younger age. However, in their analysis of the entire cohort, smoking remained an independent predictor of survival after age had been accounted for, which is in agreement with similar observations by the same authors using the international study data (2). It was only in their analysis of the angiographic substudy of GUSTO that smoking status was no longer predictive of survival after correction for age and gender. However, this may have resulted from inadequate correction for Thrombolysis in Myocardial Infarction (TIMI) flow grade.

We recently reported data from the TIMI-4 trial (3) showing that smokers more frequently have TIMI grade 3 flow in their infarct-related arteries 90 min after initiation of thrombolysis. This observation, previously reported by Gomez et al. (4) and now confirmed in the larger GUSTO data base, may explain in part the superior outcome of smokers after thrombolysis. Because improved early reperfusion may be a mechanism linking smoking and improved survival, it may be inappropriate to correct the observed mortality for the TIMI flow grade. We believe that younger age, as well as a better response to thrombolytic therapy, explain the superior outcome of smokers in acute myocardial infarction.

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Reply

We appreciate the comments made by Zahger and Shah regarding the effect of smoking status in response to thrombolytic therapy.

Smokers have numerous favorable clinical as well as angiographic characteristics compared with nonsmokers. The multivariable logistic regression helps us to define the correlation among these variables. Although age clearly plays an important role, we agree that the better outcome in smokers may well be related to the observed higher rate of Thrombolysis in Myocardial Infarction grade 3 flow in this group as well as overall less extensive coronary disease. The mechanism for the apparent better response to thrombolysis remains unclear and, as stated in the report, may derive from a different underlying pathogenic mechanism of the coronary lesions in these patients.

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Prognostic Value of Coronary Calcification—I

Inexplicably, Detrano et al. (1) have excluded coronary revascularization procedures from their analysis of coronary events in 491 symptomatic adults undergoing coronary arteriography for clinical indications. This omission is serious, for it assumes that coronary revascularization procedures fail to prevent nonfatal myocardial infarction or coronary death. The decision to exclude coronary revascularization procedures also raises a series of questions:

1. How were procedure-related deaths and myocardial infarctions analyzed?
2. Did any patients undergo either coronary angioplasty or bypass surgery between the time of coronary arteriography and electron beam computed tomographic (CT) scanning?
3. Was this a study of patients undergoing elective cardiac catheterization, or were patients admitted to the hospital for unstable angina, acute myocardial infarction or congestive heart failure also included in the study?
4. How do angiography and electron beam CT compare when revascularization procedures are included?

A statement in the methods section ("scan results did not generally influence the decision to perform coronary angiography") raises two other questions related to the appropriateness of the decision to exclude coronary revascularization procedures from the analysis:

1. How often and under what circumstances did scan results influence the decision to perform coronary angiography?
2. Given the novelty of electron beam CT scanning for the diagnosis of coronary disease and the paucity of prognostic information avail-

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able at the time that these patients underwent scanning, is there any reason to believe that scan results influenced any decisions to perform revascularization procedures?

Finally, the last paragraph of the discussion section suggests a bias against electron beam CT scanning as a screening test. The stated purpose of the report is to "assess the relation of coronary calcifications and angiographic stenoses and the relative contribution of both of these to future coronary heart disease events in symptomatic patients referred for angiography," yet the authors conclude that "clinical application of electron beam computed tomographic screening should be restricted to the evaluation of symptomatic patients only." Because none of their patients were asymptomatic, why have the authors concluded the discussion section with a statement that has nothing to do with their study?

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Reference

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Prognostic Value of Coronary Calcification—II

The correlation between coronary atherosclerosis and coronary calcification has given rise to the concept that detection of calcium in coronary arteries may serve as a useful screening technique. Detrano et al. (1) suggest that electron beam computed tomographic (EBCT) coronary calcium scores are a good screening marker for the prediction of coronary events in symptomatic patients undergoing angiography.

We fully agree with these authors that simple fluoroscopic imaging is incapable of demonstrating the real distribution and amount of calcium deposits in coronary arteries. Although Margolis et al. (2) could show a relation between fluoroscopic calcifications and coronary end points, the distribution of calcium, as well as the active calcification process in atherosclerotic lesions, is highly underestimated by fluoroscopic imaging. Although we accept intravascular ultrasound (IVUS) as a better reference standard for visualizing intracoronary calcium—in complete accordance with Detrano et al.—we have shown that different histologic types of calcific deposits in the coronary artery wall may be undetectable even by the IVUS technique (3).

Therefore, we suggest that not only is the actual amount of calcification underestimated by EBCT, but, furthermore, no information is provided about the distribution of intralesional calcium within the vessel wall (which affects the likelihood of plaque rupture). In addition, we do not know the correlation between plaque rupture and the amount of coronary calcium in nonstenotic coronary segments. Recent studies (4) have shown the large impact of intralesional calcium on coronary interventions. This interaction reflects the biomechanical process of severe stenotic coronary segments exposed to important shear stress effects.

Furthermore, we have shown that calcification in coronary segments does not significantly influence the remodeling process of the coronary vessel. We found a large variety of compensatory responses to atherosclerotic disease that were independent of plaque composition (5). Even with the results of experimental studies showing a higher likelihood of plaque rupture in the presence of vessel calcification (6), we suggest that besides the volume of calcified plaque there are still unidentified variables involving the type and distribution of calcium that contribute to the failure of compensatory enlargement of coronary arteries and subsequent plaque disruption.

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6. Demer L. Effect of calcification on in vivo mechanical response of rabbit arteries to ballon dilation. Circulation 1991;83:2083–93.

Reply

Guerci directs his comments to our study (1) of 491 symptomatic patients undergoing electron beam computed tomography (EBCT) for assessment of coronary calcification and coronary angiography for various indications, including those enumerated in his letter. The research team assessed clinical status 30 months after angiography and found a sixfold increase in events in patients with calcium scores higher than the median. This finding suggests that EBCT can be helpful in the decision to perform angiography for a symptomatic patient. Numerous others (2,3), including Guerci (4), have found that coronary calcium tests can be helpful in managing these patients.

End points were determined by phone call followed by acquisition of hospital records for all incident hospital admissions and transcripts of conversations with next-of-kin in cases of out-of-hospital deaths. Only acute infarction and coronary heart disease death were considered by the three cardiologists who reviewed these records in blinded manner to adjudicate event occurrence.

Many of these patients underwent revascularization during the hospital period during which angiography was performed. One patient who died during this index hospital period was excluded. Infarctions occurring during the index hospital period were also excluded from analysis. There were no procedure-related deaths or infarctions during later hospital periods.