We did not choose this recording as an example because of the variability in the A-wave signal. Note that E-wave peak velocities in the two recordings, at 100 beats/min and 92 beats/min, are both nearly equal at ~100 cm/s, different from the example of E-A fusion in their letter, where the fused signal has a substantially higher peak velocity than the nonfused E-wave. However, we agree that E-A fusion must be considered in the recording in Figure 4 of our article and regret the ambiguity in the recording. We commend the authors of the letter for their clever and instructive “detective work” in pointing this out.

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REFERENCE

Vasospastic Angina and Hemodynamic Injury

In their study of optical coherence tomography (OCT)-defined morphological characteristics of coronary artery spasm sites in vasospastic angina, Shin et al. (1) found thrombi at only 23 (29%) of 80 sites of spasm in patients with vasospastic angina and in only one-half of patients with a diagnosis of acute myocardial infarction. They reported a reduction in coronary flow at only 40 (50%) of 80 sites of spasm in patients with vasospastic angina and in only 31% of patients with acute myocardial infarction.

The authors point out that it is thought that thrombosis is the result of grossly reduced blood flow secondary to critical vascular constriction and suggest that the lack of a correlation between frequency of thrombus and clinical presentation in their study may be related to the relatively small size of the thrombi as seen on OCT. Triple therapy with aspirin, clopidogrel, and unfractionated heparin and “spontaneous” fibrinolysis should be considered among the possible explanations for the low number and/or size of the thrombi in these patients.

They then cite our animal study that showed, by scanning electron microscopy and arterial flow monitoring, that endothelial damage and thrombosis can occur even in circumstances of partial arterial constriction (40% to 60% luminal diameter reduction), especially if superimposed on pre-existing arteriosclerosis (2). However, they did not mention a critically important controlled finding of that study that the hemodynamic forces at such sites of partial coronary constriction can be sufficiently severe to exceed what has been calculated to be the “yield stress” of the endothelial lining. This hemodynamically induced damage was found to range from focal vascular injury to cellular fragmentation and desquamation with exposure of highly thrombogenic subendothelial tissues. These animal studies suggested that coronary spasm may cause myocardial ischemia not just by total obstruction of the artery at the site of spasm, but also by endothelial damage and thrombus formation that may occur at sites of spasm even, and perhaps particularly, when the reduction in luminal diameter is insufficient to reduce the rate of distal coronary flow (2, 3). Indeed, the endothelial damage, whether hemodynamically or otherwise induced, would also be expected to promote or exacerbate underlying atherosclerosis.

By showing with correlative quantitative angiography that blood flow at sites of coronary spasm was reduced in only one-half of patients with angina and in less than one-third of patients with acute myocardial infarction, the study by Shin et al. (1) provides strong clinical support for the experimentally demonstrated role of hemodynamic forces in vascular damage and thrombosis in patients with vasospastic angina.

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We would like to express our admiration of the remarkable experiment by Gertz et al. (1) 35 years ago and agree with their findings wholeheartedly. Their animal study proved that endothelial damage and thrombus formation occurred just at the proximal site of partial obstruction without reduction in coronary flow based on the electron microscopy findings. They reported that for this reason, vasospasm could cause not only angina pectoris but also acute myocardial infarction (AMI) and furthermore suggested that the possibility that atherogenesis could start at the site of spasm because of endothelial damage.

In our study (2), which was an in vivo study, we presented optical coherence tomography findings in study subjects who had >90% diameter stenosis during spasm and had symptoms of angina accompanied by electrocardiographic changes. Nevertheless, we found thrombus in only 29% of subjects. However, a luminal irregularity suspicious for plaque damage was found in 61% of subjects even when thrombus was not found. It is postulated that the prevalence of thrombus in our study compared with thrombus observed in the animal study by Gertz et al. (1) can be underestimated due to the reason itself that the resolution of optical coherence tomography is much lower than that of electron microscopy. Certainly it is highly possible that the presence of thrombus could be lowered by endogenous thrombolysis as well as pre-treatment with aspirin, clopidogrel, and heparin. Although it may look as if the degree of coronary flow reduction during spasm is neither associated with the prevalence of thrombus nor with AMI clinically, this could be due to the small number of subjects (Table 1). We are in the process of finalizing our next study on the comparison of thrombus and plaque erosion at coronary spasm sites and nonspasm sites in patients with suspicious vasospastic angina using optical coherence tomography. In this study, all thrombi were observed in the areas with plaques, and thrombus was also observed at the nonspasm sites. In fact, however, thrombus was found 4 times more frequently at spasm sites than at nonspasm sites. Although endothelial damage and thrombus were found at the proximal stenosis sites due to arterial constriction in the animal study, the cause-and-effect relationship is not clear in the in vivo study. The effects that spasm has on the natural history of plaque are a future research subject of great interest to us.

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THE AUTHOR REPLIES:

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