previous work [1] listed in the letter are, however, in vitro studies, three of which refer to aortic stenosis. As stated in our article, pressure recovery has indeed been demonstrated by other investigators and by us in experimental studies. However, all the extensive clinical work that has been done so far on the Doppler assessment of aortic stenosis has generally neglected pressure recovery as a source of discrepancy between Doppler and catheter gradients. To the best of our knowledge, our study was the first to demonstrate that pressure recovery can indeed cause clinically relevant "overestimation" of catheter gradients by Doppler echocardiography in the clinical setting of aortic stenosis. The referenced study of Lemler et al. (2) (two authors of the letter contributed to this report) may be another one, but has apparently not been published yet.

It is correct that Doppler and catheter measurements should ideally be obtained simultaneously. However, accurate measurement of maximal transvalvular velocities in aortic stenosis needs careful interrogation of the jet from various windows (apical, right parasternal, suprasternal), requiring various patient positions including the left and right lateral (sometimes extreme) position. Conditions that allow for such demanding Doppler examinations, however, can hardly be provided in the catheterization laboratory while simultaneously performing proper invasive pressure measurements. Thus, invasive and noninvasive studies were performed within 24 h at stable conditions in all patients, and special care was taken to collect the data at comparable heart rates with all patients being in sinus rhythm. Nevertheless, we agree that nonsimultaneous measurement remains a limitation, as discussed in our article. However, simultaneous measurement would have suffered from the limitations discussed earlier.

Of course, we agree that all well-known sources of error for invasive pressure measurements with fluid-filled catheters and echocardiographic measurements, such as Doppler gradients, orifice areas and dimensions of the ascending aorta, remain limitations for such clinical studies. Nevertheless, it was possible to clearly demonstrate the effect of pressure recovery on the relation between Doppler and catheter gradients despite the acknowledged limitations of measurement techniques currently used in clinical practice. Finally, we cannot agree that our article should have included more information on previous data regarding discrepancies between Doppler and catheter gradients across aortic stenosis. As far as pressure recovery is concerned, these published reports comprise only in vitro studies. As a matter of fact, these studies (including our own work [1]) are extensively discussed and form the basis of this clinical study, which sought to confirm previous in vitro findings.

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Can Angiography Predict the Vulnerable Lesion That Progresses to Myocardial Infarction?

Ledru et al. (1), in their interesting study, attempted to identify the most powerful angiographic predictors of a future acute myocardial infarction with known coronary anatomy. They showed that the symmetry index and the outflow angles were the two independent predictors of infarction at three-year follow-up. Stenosis severity predicted only those infarctions occurring within one year of angiography.

The identification of predictive markers for acute myocardial infarction remains a challenge. Many attempts have been made, and different markers have been proposed. Biochemical markers have been found—for example, serum C-reactive protein level, which is higher in those patients with unstable angina who subsequently develop acute myocardial infarction (2). Other investigators have proposed different angiographic markers. Ambrose et al. (3,4) found that on the initial angiogram the lesion responsible for the infarction had <50% stenosis in one-half of cases and <70% stenosis in more than two-thirds. They showed that the morphologic characteristics of the plaque may also be useful predictive markers for an acute coronary syndrome. Stenoses with an eccentric outline and a narrow neck and those with overhanging edges, scalloped borders or multiple irregularities often progressed to acute myocardial infarction. Little et al. (5) also reported that the artery that subsequently occluded had only mild stenosis (<50%) on the first angiogram in two-thirds of patients and <70% stenosis in the vast majority of patients. They also showed that the stenoses that progressed to acute myocardial infarction usually were of complex morphology. By contrast, Taeymans et al. (6) showed that stenoses that progressed to total occlusion were the more severe, and the inflow and outflow angles were steeper than those of lesions that did not occlude. Similarly, Ledru et al. (1) showed that culprit lesions had steeper outflow angles and were longer than control nonculprit lesions. However, it is difficult to properly evaluate steepness of the outflow angle and symmetry index from only one projection, because they are both inextricably dependent on the angle of projection.

A recent study from our group (7) also showed that the development of myocardial infarction cannot be predicted from the severity of preexisting stenosis, but is related to lesion morphology. A preexisting irregular, eccentric morphology is significantly more common in infarct-related than in non–infarct-related stenoses. For acute myocardial infarction, therefore, stenosis morphology seems to be more predictive than stenosis severity. We have also analyzed the morphologic characteristics of stenoses using a computerized angiographic analysis system (CASS system, Pie Medical Data), and we found that stenoses with a symmetrical, smooth diameter function shadow are likely to remain stable (Fig. 1A), whereas stenoses with an asymmetrical, irregular diameter function shadow (Fig. 1B) often progressed to acute myocardial infarction. Thus, computerized analysis may allow for the identification of vulnerable lesions.

Although complex lesions appear to increase the risk of future myocardial infarction (8,9), the majority of complex lesions remain
studies, the stenosis diameter borders are irregular and symmetrical; (B) the stenosis diameter borders are smooth and symmetrical; (non-severe lesions. (A) the stenosis diameter borders are smooth and asymmetrical.

stable for years (10). Therefore, new noninvasive and invasive (e.g., ultrasound, thermographic catheter) diagnostic modalities and new biochemical markers will be necessary in the future to enable early identification of vulnerable atherosclerotic plaques and to prevent acute myocardial infarction.

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REPLY

We read with interest the comments by Tousoulis and colleagues. They stressed the importance of coronary lesion morphology in predisposing to acute occlusion and myocardial infarction. Indeed, in our study (1), we also found a greater prevalence of border irregularity or ulceration in the 84 culprit as compared with the 291 nonculprit lesions (40% vs. 22%, p < 0.001). It was not mentioned in the published report, however, because this description is visual, subjective and highly dependent on the quality of the radiologic equipment and angiograms, and above all, the intraobserver and interobserver reproducibility in our experience is as low as 60%. Visual assessment of lesion eccentricity has the same limitations. We believe that such visually assessed variables should be analyzed cautiously.

We are also less optimistic than Tousoulis and colleagues in the ability of coronary angiography to identify potentially vulnerable lesions. Indeed, we found strong evidence that the symmetry index, the outflow angle and, to a lesser extent, the percent diameter severity separated future culprit stenoses from stable lesions within the following 36 months, using a univariate approach. However, use of various multivariate models to stratify the risk of individual stenoses and to predict the vulnerable lesion among stenoses of intermediate severity (40% to 70% diameter stenosis) yielded disappointing results, with positive predicting values (PPV) <50% (1). By contrast, stable lesions could be predicted with greater accuracy (PPV 87%). We infer that the occurrence of a future acute occlusion cannot be accurately predicted by angiography, even with the help of quantitative coronary analysis. We therefore certainly agree with Tousoulis and colleagues that use of other invasive or noninvasive techniques, such as those they mentioned, is mandatory to reach this goal and to help improve patient survival and care.