Assessment of Coronary Flow Reserve by Contrast-Enhanced Second Harmonic Echo Doppler

To the Editor:

With regard to the recent article by Caiati et al on the use of echo Doppler for the noninvasive determination of coronary flow reserve, several issues regarding this methodology should be clarified to ensure correct interpretation of the data. The authors used contrast-enhanced Doppler to determine blood flow velocity in coronary arteries of patients with and without significant stenosis of the left anterior descending coronary artery. Irrespective of the Doppler device, the calculation of coronary flow reserve is based on velocity information only. Furthermore, these measurements are performed on the assumptions that (1) the shape of the velocity profile is an invariant one and (2) the cross-sectional area of the vessel remains constant both at rest and under hyperemia.

The authors cited previous work by Rossen et al, who compared effects of intravenous dipyridamole and adenosine on blood flow velocity in patients with and without coronary artery disease. These data were validated by demonstrating that proximal coronary artery diameter was unchanged during infusion, as demonstrated by quantitative coronary angiography. In contrast to that study, in which blood flow velocity was measured proximally, Caiati et al used the distal or the middle part of the left descending coronary artery for flow-reserve assessment after infusion of dipyridamole without determining coronary artery diameter, which is likely to be affected. Based on the assumptions mentioned above, coronary flow reserve will be underestimated. Furthermore, assessment of coronary flow reserve may be complicated by changes in the velocity profile, yielding an error as high as 12%, and alterations of the epicardial coronary artery cross-sectional area, which may cause errors up to 40%. Because measurements of coronary flow reserve include both parameters, these errors have to be taken into account. The use of average peak velocity for the calculation of coronary flow reserve in most cases leads to a considerable underestimation of the actual values, as correctly stated by the authors. One way to prevent such interference would be to cause maximal dilatation before stimulation of coronary flow.

Although the work by Caiati et al represents an interesting approach for noninvasive determination of coronary flow reserve from a methodological standpoint, we strongly believe that further studies are required to validate this method and to eliminate interference of variables such as velocity profile and cross-sectional area before this method can be reliably applied in clinical practice.

Jenni et al have pointed out that a source of error in assessing coronary flow reserve with our new Doppler method can be the flow-mediated dilation of the epicardial vessel during hyperemia and the hyperemia-induced variation of blood flow velocity profile. Regarding the first point, the data in the literature are controversial and scanty. An animal study, in fact, using intravascular echocardiography has shown no variation of epicardial coronary vessels during intracoronary adenosine. In another study conducted in patients with and without left coronary artery disease, intravenous adenosine did not increase the angiographic luminal diameter in the mid and distal segments (control 3.39 ± 0.85 to 3.53 ± 0.98 mm after adenosine; percent change −1 ± 12%) compared with the proximal epicardial vessel diameter (control 3.72 ± 0.99 to 3.72 ± 0.86 mm after adenosine; percent change 1.2 ± 6%). The data cited by Jenni et al refer mostly to preliminary data (abstracts) of small series of patients and to studies that tested the action of an intracoronary bolus of adenosine or papaverine. In our study, however, intravenous dipyridamole was used.

It can be hypothesized that a vasodilator agent administered intravenously would have less effect on the conductance vessel (only an indirect effect, if any, through an increment of flow) than one administered through the intracoronary route (a direct effect of the bolus and indirect flow-mediated action). In addition, in our study, flow-mediated vasodilation, if any, should have affected the assessment of coronary flow reserve only in the non–coronary artery disease subgroup (thus decreasing a little the specificity in predicting coronary artery disease) and not in the coronary artery disease subgroup, because in coronary artery disease, atherosclerosis impairs flow-mediated dilation of coronary arteries. Further studies are needed to shed more light on this issue.

Regarding the second point, the hyperemia-induced blood flow velocity profile variation is a minor limitation (relatively small source of error [12%]) of any Doppler method that thus affects not only our new noninvasive method but also the intracoronary Doppler flow wire method.

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Response

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