EDITORIAL COMMENT

Coronary Artery Function: Out of the Cath Lab and Into the Magnet*

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Exclusive dependence on invasive angiography to image coronary artery anatomy is now a thing of the past, thanks to the success of coronary computed tomography angiography (CTA). But evaluation of coronary artery function has remained largely invasive despite the development of cardiac magnetic resonance (CMR) methods to image coronary artery lumens and flow in the 1990s (1,2). Invasive studies of coronary flow reserve with the use of intracoronary Doppler or pressure measurements and of coronary endothelial function, assessed from changes in angiographic lumen size and flow after intracoronary acetylcholine or cold pressor stimulation, have largely defined our understanding of coronary artery function (3–5).

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In this issue of the JACC: Cardiovascular Imaging, Terashima et al. (6) describe the use of CMR to assess the coronary vasodilator response to sublingual nitroglycerin (NTG) in relation to atherosclerotic plaque burden. The study population consisted of 212 predominantly male subjects age 60 to 72 years who underwent both coronary artery calcium scoring, as an index of atherosclerotic plaque burden, and spiral coronary magnetic resonance angiography to assess the coronary vasodilator response. The results, based on analysis of proximal right coronary artery lumen cross-sectional area before and after sublingual nitroglycerin, show that coronary vasodilation is independently related to plaque burden by multivariable logistic regression, with a significant difference between subjects with calcium scores ≥400 Agatston units and those with lower scores, so that a score ≥400 was associated with reduced coronary vasodilator response. When subjects with negative and positive right coronary artery calcium scores were compared, those with positive scores also had impaired vasodilator responses.

Although similar CMR methods have been previously described both by Pepe et al. (7) and Terashima et al. (8), the effects of coronary atherosclerosis were not specifically addressed. The present findings provide a potential explanation for earlier invasive studies demonstrating an association between impaired coronary vasodilator response to NTG and adverse outcomes (9). More important, they open a new door for noninvasive imaging and can be viewed as a harbinger of things to come: an era in which noninvasive evaluation of coronary function, using repeated imaging before and after perturbations, comes to the fore. In the wings is CMR evaluation of coronary endothelial function at both epicardial coronary and microvascular levels with CMR coronary lumen area and flow imaging with the cold pressor test—already the subject of several preliminary reports (10,11). Further, newer more quantitative methods for myocardial perfusion reserve with adenosine stress perfusion CMR and myocardial blood flow quantitation with either dual bolus or dual-echo first-pass saturation-recovery imaging show great promise for evaluation of the physiologic significance of stenoses (12,13). This issue is made more pressing by the impact of coronary CTA itself because the properties of CTA stenoses that impair perfusion reserve are not well defined and cannot be extrapolated from earlier work with invasive quantitative coronary angiography because of the substantial differences in temporal and spatial resolution.
REFERENCES


between CTA and invasive angiography. Thus, in practice, CTA identifies many coronary lesions of uncertain physiologic significance, as well as many heavily calcified lesions in which the lumen cannot be well visualized.

With regard to the findings in the present study, NTG evokes nonendothelium dependent vasodilation by providing a surrogate source of nitric oxide directly to vascular smooth muscle. Although invasive studies have suggested that impaired NTG vasodilation has adverse prognostic significance, the association with plaque burden, an important “missing” link, has not previously been recognized, because invasive angiography does not directly assess plaque burden. Although an impaired NTG response has been shown to be associated with adverse outcomes, its significance and mechanisms, relative to those of impaired coronary endothelial function, are not well understood. The availability of a noninvasive approach will permit far wider exploration of coronary NTG responsiveness. In addition, the time-course of the NTG response is of note. The central hemodynamic effects of sublingual NTG, both arterial and venous, can be detected within 1 min (14). However, the authors have found that coronary lumen size peaks at 3 min and beyond, which may indicate that peak dilation occurs when an element of flow mediated dilation is added to the initial direct effect of administered NTG. The study has a few limitations. First, patient variability required a large sample size to demonstrate plaque burden effect. Thus, there is little prospect of prognostic utility of the method in individual patients. Second, the paucity of women with high calcium scores in the population precludes definitive statements about effects in women or gender differences. Third, it is also unknown whether these findings are applicable to a younger population. Fourth, neither CTA nor invasive angiographic data are provided so that the contribution of asymptomatic coronary stenoses to the results, if any, cannot be determined.

Despite these limitations, the authors are to be congratulated both for their success with this technically challenging imaging study and for their success in demonstrating the continuing progress in development of CMR techniques for the assessment of coronary artery function. Their findings also raise a number of questions worth pursuing. What is the relationship between abnormalities of endothelial-dependent vasodilation and abnormal response to direct vasodilation with NTG? Do interventions known to improve coronary endothelial dysfunction improve NTG response as well? Is the relationship between plaque burden and NTG response in part due to mechanical splitting of the arterial wall by plaque? Do calcified and “soft” plaque differ in their effects? Is some apparent endothelial dysfunction in response to intracoronary acetylcholine or the cold pressor test really smooth muscle dysfunction? The sheer number of open questions suggests a robust future for studies of this type.

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