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EDITORIAL COMMENT

What Will it Take to Retire Invasive Coronary Angiography?*

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The techniques of cardiac catheterization and coronary angiography have changed little since their beginnings in the late 1950s. Aside from the coronary arteries, most conventional angiographic procedures have been largely replaced by computed tomography (CT) scanning, magnetic resonance imaging (MRI), or ultrasound imaging to avoid risks from invasive testing. Furthermore, tomographic methods, such as CT scans and MRI, allow examination of vasculature with unlimited projections and 3-dimensional viewing compared with the limited, 2-dimensional techniques of conventional angiography. Cross-sectional vascular lumen assessment has been shown to be more accurate than 2-dimensional viewing in numerous studies using the standards of intravascular ultrasound and histopathology (1). Most importantly, conventional angiography does not directly assess the condition of interest (i.e., atherosclerotic disease) but merely allows assumptions on its presence and extent based on lumen obstruction (2). Atherosclerotic disease burden is frequently underestimated by conventional angiography compared with intravascular ultrasound or optical coherence tomography, particularly in cases of external vascular remodeling (3).

In recent years, advancements in CT and MRI technologies have overcome the enormous difficulty in imaging the small and fast-moving coronary arteries. With its superior spatial resolution and fast image acquisition, CT scanning has emerged as the strongest challenger to conventional angiography for the default imaging modality of coronary arteries. Compared with quantitative (invasive) coronary angiography (QCA), CT scans yield high (although not perfect) agreement for the diagnosis of coronary artery disease (CAD) in patients (4); disagreement on individual lesion severity is particularly considerable. Conversely, QCA also does not agree well with intravascular ultrasound on severity of stenosis (5). Indeed, agreement between intravascular ultrasound and CT scanning regarding lumen area is greater than that by intravascular ultrasound and QCA (6,7). This should not be surprising because both CT scans and intravascular ultrasound allow comprehensive vascular assessment in contrast to the limited, 2-dimensional projections available by conventional angiography.

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In this issue of *iJACC*, Budoff et al. (8) report a head-to-head comparison of QCA and coronary computed tomography angiography (CTA) for detecting hemodynamically significant CAD as defined by coronary artery lesions with associated abnormal fractional flow reserve (FFR) values. The authors report similar, although modest, diagnostic accuracy for both techniques in this context. These results are important because they demonstrate yet again that conventional angiography is not superior to CT scanning for the diagnosis of CAD (in this case, hemodynamically significant CAD) compared with an independent reference standard (9). Strengths of the analysis by Budoff et al. (8) include the multicenter study design and the independent core laboratory analysis. Their results are even more impressive when considering that the authors used only visual lumen assessment for their analysis whereas the conventional angiography method used quantitative evaluation. Rossi et al. (10) have shown that quantitative assessment yields greater diagnostic accuracy versus FFR than visual evaluation alone. Furthermore, Budoff et al. (8) only used percent stenosis estimates by CT scanning but did not take advantage of the abundant options for CAD assessment (e.g., lumen area, area stenosis, lesion length, plaque burden assessment). Thus, CT scanning sent only its

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"B" team and still held its own compared with our current gold standard for the diagnosis of CAD.

The larger question, however, is what imaging characteristics matter most for patient management (11). The assessment of hemodynamic significance clearly is of value when percutaneous coronary intervention (PCI) is considered for relief of angina in patients with stable CAD. For the benefit of improved survival, however, current practice guidelines still stipulate anatomic criteria for class I indications of (surgical) revascularization: left main disease, 3-vessel disease, or 2-vessel disease, including the proximal left anterior descending artery (12). There is strong evidence of worse patient outcomes with increasing coronary atherosclerotic disease burden, which appears independent of associated hemodynamic significance of the disease (13). Indeed, there is increasing focus on atherosclerotic disease burden as the main determinant of risk for assessment and management of patients with CAD (14). In contrast to conventional angiography, CT scans are capable of providing fast, accurate assessment of the atherosclerotic disease burden (15).

Recent years have also seen the reporting of many results on the prognostic value of CAD assessment by CT scan. A large meta-analysis found a negative likelihood ratio of 0.01 for myocardial infarction or cardiac death at follow-up in patients presenting with suspected CAD but normal coronary CTA (16). Conversely, patients with obstructive CAD are at high risk of subsequent adverse events. Unfortunately, no data are available on direct comparison of conventional and coronary CTA for establishing prognosis in patients. Using simple categories of normal, nonobstructive, and obstructive CAD, historic comparisons of patient outcome evaluation by CT scanning and conventional angiography seem to yield similar results. Because CT scanning allows direct visualization of atherosclerotic disease, it detects disease that is not apparent by conventional angiography, which may be of additional prognostic value. Conversely, CT scans are capable of delineating atherosclerotic plaque characteristics and estimating total disease burden, which show promise for advanced risk stratification in patients (17).

Given this impressive portfolio for CT scans, why is it then that we still puncture arteries and advance catheters in the aortas of >1 million patients every year for the diagnosis of CAD? We do so simply because we have no data on patient management based on a CT scan-guided approach directly compared with the standard approach of invasive angiography. The ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial (NCT01471522) is breaking the ice by using myocardial perfusion imaging to guide management decisions. Importantly, CT scans play a critical role in the trial by excluding patients with left main disease before randomization. To convince practitioners, payers, and patients that coronary CTA is equivalent to diagnostic cardiac catheterization, we need to demonstrate that management decisions based on CT assessment yield the same (or better) results for patients across the entire spectrum of management options. This task is daunting and will take us years to accomplish. At the same time, it opens the door for enormous opportunities. Aside from the many promising assessment options in addition to mere stenosis assessment, noninvasive angiography will allow disengagement of diagnosis and treatment of CAD in patients in stable condition. Too often, decisions about PCI are made in the catheterization laboratory only seconds after the patient is confronted with his or her diagnosis, whereas a more reflected evaluation (involving family and the primary cardiologist) may have resulted in a different approach. It is conceivable that many thousands of PCIs that are performed without good justification can be avoided, reducing risks to patients and costs to society. Despite some improvements in vascular access and catheter designs, major complication rates from invasive coronary angiography still average between 1% and 2% (18).

Noninvasive coronary angiography has come a long way and is ready for prime time. However, we have to complete the last—and most difficult—step; that is, proving its utility in patient management compared with the current standard of conventional angiography. In the meantime, the technology will further improve. The Achilles' heel of CT scanning (i.e., severe coronary calcification) is being addressed with dual-energy imaging and subtraction algorithms, with promising results (19). The latest generation of CT scanners are less vulnerable to suboptimal heart rate control and allow image acquisition with lower radiation and contrast doses compared with conventional angiography (20). Discrepancies between technology and experience available in the community compared with major laboratories will diminish over time. Patients prefer CT scanning over conventional angiography for CAD testing (21). We are almost there.

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