LIMITATIONS OF COMPUTED TOMOGRAPHY CORONARY ANGIOGRAPHY* 

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It seems so simple and elegant. Fifty years after the introduction of coronary angiography, advances in technology allow imaging of the coronary arteries noninvasively using multidetector computed tomography (CT) scanners (1). Within a few short years, these imaging systems have begun appearing everywhere, first in hospitals and clinics, then in individual doctors’ offices, offering the promise of safe and painless detection of coronary obstructions (2). Weekend courses allow the members of our profession to “learn” this new technology and apply it routinely to patient care (3). The manufacturers of the equipment, all large multinational providers of radiological imaging devices, are quite pleased to show practitioners how they can rapidly recoup their million-dollar investments (4,5). What could possibly be wrong with this picture? Medical progress to the betterment of patients (and practitioners).

In this issue of the Journal, an interesting and important paper by Meijboom et al. (6) provides data that should give us pause. When applied routinely in symptomatic patients at risk of coronary disease, in more than 50% of subjects, CT angiography “detected” coronary obstructions that simply were not there. Strikingly, of 98 patients in whom CT angiography diagnosed 3-vessel coronary artery disease (CAD), only 19 actually were found to have it, a false-positive rate of 81%. This high false-positive rate has potentially serious implications, leading to unnecessary and potentially risky procedures that threaten to accelerate already-excessive health care costs. Now that our national health care expenditures exceed 16% of the gross national product, we must ask ourselves critical questions about the introduction of any costly new technology. Does it improve quality of care compared with existing methods? Does it prolong life or improve quality of life? Does it reduce costs? Is it cost-effective? Are there important safety concerns? Despite its rapid adoption, for all of these metrics, CT coronary angiography has yet to show that it can deliver on its promise.

Routine application of CT angiography is largely based on flawed assumptions about the nature of CAD. After the introduction of angiography by Sones in 1957, a generation of practitioners came to believe that coronary disease could best be defined by the presence or absence of obstructive lesions. This view was reinforced by the introduction of bypass surgery in 1968. Coronary disease was simple. If you had enough obstructions, you carried a high risk for morbidity and mortality, and would benefit from surgical revascularization. If there were no obstructions, CAD was not present. Then, a decade later, Andreas Gruntzig introduced balloon angioplasty, and luminal obstructions could be readily treated without surgery. Within a few years, an entirely new discipline, interventional cardiology, was created, rapidly growing into the dominant approach used to treat stable CAD.

LIMITATIONS OF ANGIOGRAPHY

Then came disquieting research. Most myocardial infarctions did not occur at the sites of significant coronary narrowing, and percutaneous treatment of coronary obstructions in patients with stable angina did not reduce the risk of myocardial infarction or death (7,8). Whether performed invasively or via multidetector CT, angiography is confounded by the phenomenon of coronary remodeling, first described in 1987 by Glagov et al. (9). The remodeling process is observed histologically as the outward displacement of the external vessel wall overlying the atheroma. The adventitial enlargement opposes luminal encroachment, thereby concealing the presence of disease. Thus, the vessel wall may contain a large atheroma, despite an angiogram that shows little or no luminal narrowing. Although remodeled lesions do not restrict blood flow, clinical studies have shown that these low-grade lesions represent the most important source of acute coronary syndromes (10). Accordingly, an absence of luminal narrowing does not preclude a risk of plaque rupture, resulting in myocardial infarction or sudden cardiac death. It must be acknowledged that a potential advantage of CT angiography is detection of these nonobstructive plaques, but the clinical utility of such assessments remains unproven.

Beginning soon after the introduction of coronary angiography, studies began to question the accuracy and reproducibility of angiography. Carefully performed investigations demonstrated that visual interpretation of angiog-

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raphy showed clinically significant intraobserver and interobserver variability (11). Other investigators documented major differences between the apparent angiographic severity of lesions and the extent of disease at post-mortem examination (12). Then, using functional testing, studies showed a prominent discordance between the apparent angiographic severity of lesions and the physiological effects of stenoses (13). We learned the difficult lesson, now apparently forgotten, that the silhouette or luminogram is a relatively poor representation of coronary anatomy and a limited standard on which to base therapeutic decisions (14).

**Functional Testing**

Accordingly, cardiovascular medicine evolved to use functional testing to assess the likelihood that symptoms were related to impaired coronary blood flow. Because luminal narrowing alone did not accurately identify patients who would benefit from revascularization, practitioners began routinely evaluating symptomatic patients for the presence of physiological abnormalities associated with these obstructions. This approach was logical, although its cost effectiveness has not been rigorously studied. If there was good exercise capacity and no ischemia, angiography and intervention could be safely deferred. In some cases, functional testing was performed after angiography, rather than before, to determine whether a lesion observed by angiography actually represented a flow-limiting stenosis. Two competing imaging technologies developed, first exercise nuclear scintigraphy, and subsequently, stress echocardiography. For patients who could not exercise, elegant pharmacological approaches were developed to substitute for exercise testing. Of equal importance, the exercise capacity and magnitude of the ischemic burden provided valuable prognostic information that could be used to guide therapy. Unfortunately, the rapid proliferation of CT angiography threatens to take us back to the overly simplistic approach of our predecessors, once described as “our preoccupation with coronary luminology” (14). Just find the stenosis and treat it aggressively, an approach sarcastically described as the oculostenotic reflex (14).

**CT Angiography: A Step Backward**

Compared with conventional angiography, the angiograms produced by multidetector CT scanners are much lower in quality and are suboptimal for diagnostic purposes. To understand the deficiencies in CT angiography, it is important to review the physics of the technology used for coronary angiography. The resolution of modern angiographic equipment is surprisingly modest, only about 4 or 5 line pairs per millimeter. Prudence limits radiation exposure, resulting in an image flaw known as quantum statistical noise that can be reduced only by increasing radiation doses. Angiographic resolution is also compromised by rapid coronary artery motion, which is reduced in impact for conventional angiography by using pulse-mode radiography. The translational velocity of the right coronary artery can reach 50 mm/s. A coronary artery moving at 50 mm/s will produce a motion blur of approximately 0.35 mm during a typical 7-ms X-ray pulse width, an acceptable temporal resolution for high-quality angiographic imaging.

CT angiography represents a step backward in image quality. The spatial resolution is only about 2 line pairs per millimeter, about one-half that of conventional angiography (15). The temporal resolution of CT angiography is very poor, currently about 20-fold worse than a typical conventional angiogram (>150 ms) (15). To overcome the limitations in temporal resolution, electrocardiographic gating is used, but rarely represents a perfect solution and precludes successfully imaging in patients with arrhythmias such as atrial fibrillation. Even more problematic, the presence of coronary calcium frequently obscures the underlying lumen, rendering the imaging of specific stenoses unreliable. Accordingly, CT angiography retains all of the limitations of conventional angiography, including the absence of physiological information and poor correlation with histology, but it is further constrained by poor image quality. With these limitations, it is not surprising that CT angiography performed poorly in the current study.

To overcome quantum statistical noise and other quality limitations, large radiation dosages are used, typically averaging >15 mSv, with specific organ systems receiving substantially higher exposure levels, about 5 to 7 times the dosage used by prudent practitioners in an optimal invasive angiogram (16). Recent studies suggest a small but important risk of inducing malignancy, ranging as high as 1 in 150 for breast cancer in a younger woman (16). Practitioners also must consider the likelihood that many patients will endure multiple CT scans during their lifetime, amplifying the radiation risk.

**Coronary Flow Reserve (CFR)**

Why should we prefer functional testing to anatomical methods such as CT angiography? In chronic ischemic coronary disease, symptoms result principally from the ability of stenoses to blunt increases in blood flow in response to metabolic demands. This phenomenon is commonly called CFR (17). Animal studies show that CFR remains normal (typically a 5- to 7-fold increase in flow) until the stenosis approaches 75%. Between 75% and 95%, CFR decreases progressively. Accordingly, the angiographic differences between moderate and severe lesions may be only a few tenths of a millimeter. Such differences are difficult to discern given the limitations in resolution of the best conventional angiography and impossible to resolve with CT angiography. Other factors impair the correlation between angiographic lesion severity and CFR, including the presence of ventricular hypertrophy, the metabolic state of the myocardium, and microvascular disease. Thus, the epicardial stenosis represents only one factor responsible for a reduction in flow reserve in patients with clinical symp-
toms. A stenosis incapable of producing angina in one patient may result in severe functional limitation in another. Accordingly, testing for the presence of ischemia, rather than the presence of a stenosis, is essential for good clinical decision making.

Some ardent advocates will point out that CT angiography and physiological testing are not mutually exclusive. This advocacy ignores the issue of cost-effectiveness. Testing via multiple imaging modalities has shown neither superior effectiveness nor cost savings over current diagnostic paradigms. Proponents also emphasize the negative predictive value of the test. However, we must consider the implications and costs of a false-positive study, which, in many cases, will lead to additional costly testing or procedures. Therefore, we are now left with a conundrum. CT coronary angiography is being deployed rapidly, and there exist no incentives for industry or physician advocates to seek the clinical trial data we need to effectively use this imaging modality. Accordingly, we need a restricted use of CT angiography until adequate clinical evidence becomes available showing the cost-effectiveness and safety of this approach (18,19). We need real-world trials that use this technology, not just in carefully selected patients who generate optimal images, but in all comers, including patients with a low, medium, and high risk of CAD. Finally, we need outcome studies to show whether this new approach really improves what we care most about: patient outcomes.

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