A learned person has 7 traits, the Babylonian Talmud teaches. Among them, “He discusses first things first...[and] about something he has not heard he says, ‘I have not heard.’” Establishing proper priorities for inquiry and acknowledging ignorance are highly relevant in the ongoing debate raging around the rapid adoption of CT angiography.

Investigators from leading centers now promote CT angiography as a major advance in diagnostics, making it possible for many patients to avoid invasive coronary angiography. They provide 3 lines of evidence to make their case. First, in a number of cross-sectional patient-oriented studies, the diagnostic accuracy seems to be high, with claims of sensitivity and negative predictive value approaching or exceeding 95%. The most recent high-quality multicenter study using the more advanced 64-slice technology yielded less sanguine findings, though, with a reported sensitivity of 85% and a negative predictive value of only 83%; the investigators themselves concluded that “CT angiography cannot replace conventional coronary angiography at present.”

Second, preliminary investigations show that findings on CT angiography predict risk of major coronary events. Although not surprising, it is not clear whether prognostic information provided by CT is more or less accurate than that provided by conventional noninvasive tests, like measurement of exercise capacity or detection of myocardial scar or inducible ischemia by perfusion imaging or ultrasonography.

The third line of evidence is illustrated by the careful clinical epidemiological study presented by Chow et al in the current issue of Circulation Imaging. The investigators analyzed the proportion of normal findings among patients undergoing invasive coronary angiography at a single large Canadian institution before and after establishment of a cardiac CT program. Before the CT program was implemented, 32% of patients had normal findings on invasive angiography. The proportion decreased by a modest amount to 27% after the CT program was started. In 3 other geographically remote centers where cardiac CT was not offered, the proportion of normal coronary angiograms remained essentially constant, at 30% to 31%, during the same calendar period.

The investigation presented by Chow et al has a number of strengths. Because procedures like conventional and CT angiography are regionalized in Canada, the investigators were able to effectively perform a population-based outcomes study, even though they collected data from only 1 institution. Not all major centers in Canada adopted the new CT technology, making it possible to perform a properly controlled quasi-experimental analysis. This type of investigational approach has been used to assess the impact of population-based strategies like smoking bans, and it has particular promise for estimating effects of interventions in which randomized trial evidence is absent. The authors argue that implementation of CT angiography reduces the frequency of normal invasive coronary angiograms, a conclusion that is reasonable given the robust data they present.

Putting these 3 lines of evidence together, what can we say? CT angiography has high diagnostic accuracy, but not high enough to be considered a replacement for invasive coronary angiography. CT angiography can probably predict major cardiovascular events, but there is a much more robust literature for other noninvasive methods, in particular myocardial perfusion imaging. And now, given the data presented by Chow et al, we can say that implementation of CT angiography within health care systems reduces the prevalence of normal coronary angiograms, but only to a modest degree. Even with a CT angiography program, over 25% of invasive angiograms were normal. On all 3 lines of evidence there are reasons for pause, yet this technology is being widely adopted, even within Canada’s controlled health care system. What is wrong with this picture?

When a patient sees a physician complaining of symptoms suggestive of coronary artery disease, what is his/her main concern? Is it what an invasive coronary angiogram, if done, would look like? We would hope not, as it is now well known that the coronary angiogram often misses disease likely to cause major clinical problems. Is the patient worried about the proportion of coronary angiograms performed at the local hospital that show normal findings? Doubtful. Does he/she want to know the probability of suffering a major, possibly fatal, cardiovascular event if natural history were allowed to take its course? Or is he/she, working with his/her doctor, asking a more fundamental question—is there something to worry about, and if so, is there something that can be done that we can confidently say will reduce the probability of a major clinical event. In other words, will this test help?
Given existing evidence, can we answer this patient’s primary question? Can we tell him/her that performing a CT angiogram will reduce the risk of a premature death or myocardial infarction? The only honest answer must be, “I have not heard.”

CT angiography may well be a major advance in cardiovascular care. It is possible that widespread use of the technology may reduce the number of patients receiving unneeded medical treatments or undergoing unneeded invasive procedures. The intriguing data presented by Chow et al make this a viable hypothesis. But this is a supposition and a supposition only. It is also possible that CT angiography programs may lead to more patients undergoing angiography, even if the rate of normal findings is lower. Looking at the data presented by Chow et al (Figure 1 of Ref. 6), at the institution with the CT angiography program there were 253 invasive angiograms per month before the program was implemented and 316 per month afterward. In the 3 control hospitals, the corresponding invasive angiography rates were 445 per month and 440 per month—no change. Will the increased frequency of invasive coronary angiography associated with implementation of the CT angiography translate into better public health? The only honest answer must be, “I have not heard.”

CT angiography may also, by virtue of its sensitivity, enable diagnosis of early, nonobstructive disease. Treatment of previously unrecognized disease with intensive lifestyle changes, aspirin, statins, or revascularization may well reduce the risk of subsequent myocardial infarction, premature death, or costs of care. But this, too, is only a supposition. Just because a test is capable of detecting the presence of disease or increased risk better than older tests can does not necessarily mean that performance of the test will yield better outcomes.11 In some cases, it does; consider mammography,12 ultrasound of the abdominal aorta,13 or troponin.14 In other cases, it does not; consider urinary catecholamines for neuroblastoma.15 And in other cases, we simply do not know; consider nearly all of cardiovascular imaging or genomics.

At the heart of evidence-based medicine is a desire to know whether proposed strategies can safely prolong life, improve quality of life, or reduce costs. If we are claiming to practice evidence-based medicine, and want to be paid for it, we must put these “first things first.” For the vast majority of strategies that have modest effects, the only way to know is by performing randomized trials.

In cardiovascular medicine, we can proudly point to a number of advances in which we generated robust randomized trials and then implemented technologies. Large-scale trials demonstrated clear value for revascularization in patients with ST-elevation myocardial infarction.15 Stratified analyses within large-scale trials demonstrated the value of troponin testing for identifying which acute coronary syndrome patients should under coronary angiography.14 Other trials clarified the value of powerful antiplatelet inhibitors among patients undergoing percutaneous revascularization.17

Unfortunately, we cannot make the same claim for imaging. As eloquently stated by Bonow, “As an imaging community, we have failed to demonstrate the added value of cardiac imaging in terms of improved quality of care or improved outcomes.”18 We have no randomized trial evidence showing that CT angiography, or any other noninvasive imaging test, save lives, prevent myocardial infarctions, or reduce costs. We have not put first things first. We should care more about patient outcomes and public health than about normal angiography rates.

In the current crisis atmosphere of health care debates, much attention has been directed toward our widespread adoption of imaging technologies like CT angiography in the absence of evidence of improved outcomes.19 Fortunately, a number of cardiovascular leaders have come to recognize the importance of putting first things first and acknowledging that for one of the most fundamental questions in clinical cardiology, whether imaging technology actually helps patients, we have not heard. Some are calling for randomized trials.20 This is a welcome step. The time has long since come to reverse the paradigm of implement first and study later. Only then will our patients have the learned doctors they deserve.

Disclosures
Dr. Lauer is an employee of National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH).

References


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