MDCT Scores in Trial, But Critics Still Wary

BY MITCHEL L. ZOLER
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ORLANDO — CT angiography remains controversial after a report on the diagnostic accuracy of multidetector CT measured in 316 patients.

Noninvasive multidetector CT (MDCT) angiography had a 91% positive predictive value and an 83% negative predictive value, compared with conventional angiography, for identifying significant coronary stenoses in the "first large, multicenter trial of the 64-slice technology" for coronary angiography, Dr. Julie M. Miller said at the annual scientific sessions of the American Heart Association.

"This represents a high degree of diagnostic accuracy" for MDCT angiography, said Dr. Miller, a cardiologist at Johns Hopkins University, Baltimore.

But Dr. Miller's report of a high correlation between noninvasive and invasive angiography was immediately followed at the podium by strong comments from the invited discussant for the study, Dr. Michael S. Lauer. After criticizing the study's clinical relevance and questioning the technique's safety, he called for a moratorium on using MDCT angiography until its value for patients was better defined.

"This is a technology with no evidence of benefit and real concern for harm," said Dr. Lauer, a cardiologist and director of the division of prevention and population science at the National Heart, Lung, and Blood Institute. His safety concern was that the radiation dose from repeated scans could pose a significant cancer risk.

Routine use of MDCT should stop until results from large-scale, randomized studies prove that "this test saves lives or prevents heart attacks with an acceptable margin of safety," Dr. Lauer said.

His sharp critique contrasted with the response to Dr. Miller's report from other experts. "Dr. Miller's study is important because it shows that MDCT angiography gives you coronary anatomy outside the catheterization laboratory," said Dr. Daniel Mark, a cardiologist and professor of medicine at Duke University, Durham, N.C.

In an interview following Dr. Lauer's podium remarks, Dr. Miller contended that his criticism mostly applied to using CT to screen people for their coronary calcium scores rather than issues of MDCT angiography. She stressed that the study did not use MDCT for screening. A reliable, noninvasive image of coronary anatomy could help many patients avoid the cost and potential complications of catheterization, Dr. Miller said.

"Until now, there was no proof that MDCT angiography was accurate for making diagnoses. We proved that MDCT works." The next step is to compare noninvasive angiography with other noninvasive tests, she said.

On the issue of safety, the radiation dose each patient received, about 14-15 mSv, is comparable to the dose from conventional coronary angiography and less than the exposure during a nuclear perfusion scan, Dr. Miller said. The contrast volume also was similar to conventional angiography.

The Coronary Evaluation Using Multidetector Spiral Computed Tomography Angiography using 64 Detectors (CORE-64) trial enrolled patients older than 40 years (median age 59 years) who had been referred for conventional, quantitative coronary angiography at nine centers in seven countries. The study used equipment made by and was sponsored by Toshiba. Dr. Miller has received research support from Toshiba.

The patients' hearts were scanned with a 64-slice MDCT device that takes images at 0.5-mm intervals. The MDCT examination first was analyzed to get each patient's calcium score, and the study continued with 316 patients who had calcium scores of less than 600.

The images obtained from these patients were then analyzed at 19 locations throughout the coronary tree. Each location was at least 1.5 mm in diameter, and stented segments were excluded. All stenoses that blocked more than 30% of a vessel were quantified, and lesions that were 50% stenotic or greater were counted as significant. Patients underwent conventional quantitative angiography within the next 30 days.

A receiver-operator curve analysis showed that 93% of the patients with significant stenoses identified by conventional angiography were also spotted using the noninvasive method, the study's primary end point, reported Dr. Miller. The patients had a 56% prevalence of having at least one coronary artery with a significant stenosis.

A second analysis compared the noninvasive and invasive methods on a per vessel basis, with 868 individual vessels evaluated. By this measure, MDCT angiography identified 91% of the individual coronary vessels with a significant stenosis, compared with catheterization angiography, and produced a positive predictive value of 82% and a negative predictive value of 89%.

"We can define which patients need revascularization," Dr. Miller said in an interview. ■

Clinical Guidelines For Family Physicians

Venous Thromboembolism

BY NEIL S. SKOLNIK, M.D., AND MATTHEW R. GERSTBERGER, M.D.

Venous thromboembolic disease includes pulmonary embolus and deep vein thrombosis. The annual incidence of the disease in the United States is 600,000 cases. These new recommendations review the diagnosis and treatment of pulmonary embolus and deep vein thrombosis.

Guidelines are most useful when they are available at the point of care. A concise yet complete handheld computer version of this guideline is available for download, compliments of Family Practice News, *at www.redi-reference.com.*

Diagnosis

Clinical prediction rules should be used to estimate the pretest probability of venous thromboembolic disease, and thus to determine the best test to use next to diagnose it. The Wells Prediction Rules are validated methods for determining the clinical or pretest probability of disease. (See boxes.) These rules work best in young patients with no previous history of venous thromboembolism (VTE), and have less validation in older patients or patients with comorbidities.

If a patient has a low pretest probability of VTE, then a D-dimer—which has a sensitivity of 96%-100% for detecting clot formation—can be used as the initial laboratory test to diagnose the condition. In patients with a low clinical (pretest) probability of VTE, the D-dimer has high negative predictive value and can be used to effectively rule out VTE.

In patients with an intermediate to high pretest probability for VTE, the predictive value of the D-dimer is not sufficient to use as the sole test to rule out VTE, and an imaging study should also be obtained. In patients with suspected deep vein thrombosis (DVT), a lower-extremity ultrasound should be obtained to diagnose thrombosis in the proximal vein of the lower limb. It is important to recognize that ultrasound is not a sensitive test for isolated calf DVT, and if clinical suspicion is high enough, a repeat ultrasound may be indicated. In patients with an intermediate to high pretest probability for pulmonary embolus (PE), either a ventilation-perfusion (VQ) scan or a helical CT scan should be ordered (Ann. Intern. Med. 2007;146:454-8).

Management

For the initial treatment of DVT, low-molecular-weight heparin (LMWH) is superior to unfractionated heparin. LMWH has a lower incidence of heparin-induced thrombocytopenia, and patients have significantly fewer episodes of bleeding and lower mortality. For PE, more evidence is needed to make clear recommendations, but the evidence to date is highly suggestive that LMWH is at least as effective as unfractionated heparin for the initial treatment of PE.

The initial treatment of DVT—and possibly PE—in carefully selected patients who are able to comply with recommendations and who have no serious comorbidities may be carried out safely and cost effectively on an outpatient basis. Rates of PE, bleeding, and death do not differ between inpatient versus outpatient treatment, and outpatient treatment is often more convenient for patients.

The duration of anticoagulation after VTE has been an area of active research. Patients with VTE secondary to transient risk factors should be anticoagulated with warfarin for 3-6 months. Patients with recurrent or idiopathic VTE should be treated with a vitamin K antagonist (warfarin) for at least 12 months, with consideration for extended-duration treatment. In trials lasting as long as 4 years, extended therapy decreases the incidence of recurrence by 64%-95%. The goal INR (international normalized ratio) should be 2.0-3.0.

To prevent the development of postthrombotic syndrome, compression stockings should be prescribed beginning within a month of the diagnosis of a proximal vein DVT and continuing for a minimum of 1 year. Evidence indicates that the use of compression stockings reduces the incidence of postthrombotic syndrome by more than 50%.

Additional recommendations address specific circumstances. In pregnant patients, vitamin K antagonists should be avoided because they cross the placenta and can cause fetal bleeding and embryopathy at 6-12 weeks' gestation. In contrast, LMWH and unfractionated heparin do not cross the placenta, and neither is associated with embryopathy or fetal bleeding. For patients with cancer, LMWH is safe and efficacious for the long-term treatment of VTE, and may be safer and more effective than vitamin K antagonists at preventing recurrence (Ann. Intern. Med. 2007;146:204-10).

The Bottom Line

Clinical assessment, preferably with a well-validated clinical prediction rule, should be the first step in determining the best approach to making a diagnosis of VTE. In patients with a low clinical probability of VTE, a D-dimer may be used as the initial test; a negative result would make VTE unlikely. Patients with a moderate to high risk of VTE should receive an imaging study (ultrasound for DVT, and either a CT or VQ scan for PE). LMWH is superior to unfractionated heparin for the initial treatment of VTE, and consideration can be given to the initiation of treatment for selected patients in an outpatient setting. For patients with idiopathic VTE, consider long-term treatment with a vitamin K antagonist to decrease the risk of recurrent VTE.

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