Drugs, Methods Poised To Change Imaging

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW YORK — New agents and imaging methods will change the way that hearts are scanned in coming years, researchers said during the annual meeting of the American Society of Nuclear Cardiology.

Myocardial Hyperemia Drugs

Adenosine and dipyridamole are the current mainstays of pharmacologic stress during nuclear imaging, but both agents cause many adverse events. Serious side effects include atrioventricular block in up to 8% of patients and bronchospasm in a small but significant fraction. Bothersome adverse effects such as flushing, chest pain, and dyspnea occur in 50%-80% of patients, according to Robert C. Hendel, M.D., of the Rush University Medical Center in Chicago.

These features sparked an interest in developing more specific agonists for the A_{2A} receptor that is responsible for coronary vasodilation. These agents have a reduced affinity for the A_1, A_{2B}, and A_3 receptors that are the source of the adverse effects caused by adenosine and dipyridamole.

More specific agents can be administered as an intravenous bolus rather than as the continuous intravenous infusion needed for adenosine and dipyridamole.

Another big plus for the more specific agents is that they can be administered as an intravenous bolus rather than as the continuous intravenous infusion now needed for adenosine and dipyridamole.

Two new drugs are now in phase III trials: binodenoson, developed by King Pharmaceuticals Inc., and regadenoson, developed by CV Therapeutics Inc. A third agent, BMS068645, developed by Bristol-Myers Squibb Co., is in phase II clinical studies.

Results from a phase II study with binodenoson that involved 203 patients showed that the new drug had "very good concordance with adenosine" for myocardial perfusion but with a "clear decrease in the overall adverse event profile," Dr. Hendel said.

In this study, adenosine triggered a 92% rate of adverse effects, compared with a 33%-80% rate among patients treated with binodenoson, depending on the dosage.

At a dosage of 1.5 mcg/kg, the dosage being used in phase III studies, binodenoson produced no atrioventricular block and a "minimal" incidence of tachycardia in this small study, Dr. Hendel said.

Regadenoson was tested in a crossover study with 36 patients, where it showed about an 85% concordance with the effect of adenosine on myocardial ischemia. A dosage of 400 mcg produced a 61% rate of adverse effects, compared with an 83% rate when adenosine was used.

Ischemic Memory

A radionuclide that's just entering clinical testing in the United States has the potential to open a new avenue of cardiac imaging by tagging regions of the myocardium that were ischemic hours earlier. Known as BMIPP, this radioiodine tracer is a fatty acid analogue that takes advantage of the disturbed fatty acid metabolism that persists in tissues for a relatively prolonged period following ischemia, said James E. Udelson, M.D., director of the nuclear cardiology laboratory at Tufts–New England Medical Center in Boston. BMIPP has been used for several years in Japan.

The results from initial clinical studies in the United States have confirmed that BMIPP can selectively tag myocardium that has had ischemic stress more than 24 hours previously. "This agent may extend the time window for imaging ischemia beyond what we can do with a perfusion image," he said.

One especially attractive prospect is to use BMIPP simultaneously with a standard radionuclide marker of myocardial perfusion such as thallium-201 or technetium-99m sestamibi. This would allow physicians to get information on both metabolic ischemia and resting perfusion "in one spin of the camera," Dr. Udelson said.

Neuronal Imaging

Imaging the heart using a nuclear-tagged norepinephrine analogue, metaiodobenzylguanidine (MIBG), allows researchers to assess myocardial innervation and the abnormal denervation that's associated with pathology.

Results from pilot studies show that MIBG imaging can give new insights into both primary and secondary cardioneuropathies, said Mark I. Travin, M.D., a cardiologist at Montefiore Medical Center in New York. Cardiac imaging with MIBG can identify dysautonomias and may allow early detection and definitive diagnosis of Parkinson's disease. MIBG abnormalities also occur in patients with idiopathic ventricular tachycardia and fibrillation. MIBG imaging may be a way to identify patients who are at high risk for sudden cardiac death and are the best candidates for receiving an implantable cardioverter defibrillator. MIBG imaging can also follow the progress of cardiac transplants.

The most important potential use for MIBG may be as a means to assess coronary artery disease and heart failure. Neuronal imaging may be a way to detect the early stages of coronary disease before it becomes clinically apparent, Dr. Travin said. Patients with congestive heart failure usually have MIBG-uptake abnormalities. ■

Coronary Calcium Screening Backed for High-Risk Patients

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW YORK — Coronary calcium scanning followed by myocardial perfusion imaging looks like it may be an effective approach to screening for coronary disease, John J. Mahmarian, M.D., said at the annual meeting of the American Society of Nuclear Cardiology.

"Further investigation needs to focus on the complementary role of CT scanning [for coronary calcium] and SPECT [single-photon emission computed tomography] for more precisely defining patient risk and recommending who should receive aggressive, antiatherosclerotic treatments," said Dr. Mahmarian, medical director of the nuclear cardiology laboratory at the Methodist Hospital, Houston.

Screening for coronary calcium by electron beam CT or by multislice CT is well suited for selected, asymptomatic people because it has a relatively low cost and because conventional risk factors are not foolproof for identifying asymptomatic people who have coronary disease, he said.

"About 25% of people with three, four, or five risk factors for coronary disease have very little coronary calcification, and about 25% of patients with very high calcium scores have zero or one risk factor," Dr. Mahmarian noted. In addition, the results from several studies have shown that people with high coronary calcium scores have a markedly increased risk of having myocardial perfusion defects and significant coronary disease. Therefore, he said, screening for coronary calcium makes sense for people with an intermediate or high risk for coronary disease based on their risk factor profile.

Dr. Mahmarian proposed that people with an intermediate or high risk based on their risk factors who have a calcium score of less than 100 do not need additional, immediate testing but should be managed for risk factor reduction and treated with aspirin and a statin.

People with a calcium score of 100-399 should be placed on an aggressive, risk-factor reduction regimen and are potential candidates for further, noninvasive testing by myocardial perfusion imaging using SPECT. Whether myocardial perfusion imaging is used on people in this category or not should depend on the severity of their risk factors as well as their age and gender. These people should have follow-up screening for coronary calcium every 1-2 years. Dr. Mahmarian said that about 15% of people screened could be in this category.

Those with a calcium score of more than 400—about 10% of the screening population—should receive aggressive risk-factor management plus noninvasive testing by SPECT. People who show a large perfusion defect on myocardial perfusion imaging are candidates for coronary angiography. Those who are negative for a significant perfusion defect should be rescreened with SPECT annually, Dr. Mahmarian said. ■

Normal Stress Echo Good for 18 Months in Patients With Prior MI

BY BRUCE JANCIN
Denver Bureau

NEW ORLEANS — The "warranty time" of a normal stress echocardiogram in patients with a history of MI is about 18 months, Sripal Bangalore, M.D., reported at the annual scientific sessions of the American Heart Association.

At that point, it's a good idea to obtain a repeat stress echo exam for further risk stratification, said Dr. Bangalore of St. Luke's-Roosevelt Hospital, New York City.

"Up until about 18 months, the event rate is pretty benign, but after that, it exponentially rises," he explained.

Stress echocardiography is a well-established tool for risk stratification in patients with known or suspected coronary artery disease. But the reliability and durability of a normal stress echo exam in the high-risk setting of patients who have already had an MI has not been clearly defined.

To investigate this issue, Dr. Bangalore evaluated 251 consecutive patients with a history of nonrecent acute MI who were referred for stress echocardiography. The average time since the MI was 6.5 years, with a maximum of 12 years. Dobutamine stress echocardiography was used in 83% of the patients, and the patients who were remaining were stressed on a treadmill.

Overall, 64% of patients were classified as low-risk on the basis of a normal stress echo exam free of reversible ischemic left-ventricular-wall motion abnormalities. During the full follow-up, which lasted a mean of 2.9 years and a maximum of 5 years, these low-risk patients had a rate of another MI or cardiac death of just 0.8% per year, compared with 4.2% per year among patients with an abnormal stress echo exam.

No cardiac end points occurred in the normal stress echo group during the first 18 months of follow-up, thus the approximate 18-month "warranty time."

Of the patients with an abnormal stress echo exam, 30 underwent coronary artery bypass graft surgery, and 20 had a percutaneous coronary intervention during the full follow-up, compared with just 1 and 13, respectively, with a normal stress echo.

Standard cardiovascular risk factors did not predict which patients were likely to have another cardiac event, and this finding underscored the value of stress echo in the high-risk context of a prior MI.

Similarly, stress ECG parameters were unable to distinguish those patients who had a cardiac event during follow-up from the ones who didn't, he said. ■