

Advances in Nuclear Cardiology

New Pharmacologic Agents

Manuel Cerqueira, MD, Cleveland Clinic, Cleveland, OH, provided an overview of pharmacologic stress agents, focusing on the identification and development of agents that can maximize overall laboratory efficiency and improve patient satisfaction. One of the most common stress agents currently used (adenosine) stimulates all adenosine receptors and has several disadvantages, most notably, undesirable side effects and inconvenient administration.

Dr. Cerqueira described the ideal features of a pharmacologic stress agent, noting that a selective adenosine agonist (A_{2A} agent) could reduce the frequency and intensity of side effects caused by adenosine, such as atrioventricular node (AV) block and bronchoconstriction, thus allowing its use in a broader range of patients. The ideal agent also would selectively vasodilate the coronary circulation without affecting the peripheral circulation, thus minimizing the decrease in systemic blood pressure. Agents that have a rapid onset and termination of action would reduce the duration of side effects and allow rapid reversal without the need for intervention. Lastly, he said, the ability to administer a bolus rather than a continuous infusion would increase the ease of use.

Three A_{2A} agents are currently in development: CVT-3146 (regadenoson), MRE-0470 (binodenoson), and BMS-068645 (apadenoson). All of these agents can be administered as a bolus infusion and produce the desired augmentation in coronary arterial blood flow without the undesirable side effects due to stimulation of the other adenosine receptors. Dr. Cerqueira noted that early studies have shown these agents to be comparable with adenosine for the detection of ischemia. In addition, regadenoson has been evaluated in two phase 3 studies (ADVANCE MPI 1 and 2), and the agent is comparable with adenosine in assessing the extent of reversible perfusion abnormalities and in detecting the defect type while being associated with significantly fewer occurrences of first-degree AV block and with lower overall summed symptom scores.

Regadenoson administered in a standard dose of 400 μ g achieves a >2.4-fold increase in coronary blood flow in 33 seconds and maintains it for 2.3 minutes. Treatment with aminophylline returns coronary blood flow to the baseline level.

“New vasodilatory pharmacologic stress agents may simplify the stress SPECT MPI procedure and extend its use to a greater number of patients,” said Dr. Cerqueira.

Hybrid Imaging

Marcelo Di Carli, MD, Brigham and Women’s Hospital, Boston, MA, discussed the limitations of computed tomography angiography (CTA) and myocardial perfusion imaging (MPI) and then presented several case examples of how integration of the two modalities could offer benefits in terms of diagnosis, risk assessment, and treatment guidance. Dr. Di Carli pointed out that the frequency of abnormalities on CTA in patients with an intermediate likelihood of CAD is >50%, and this modality will be an inefficient “gate-keeper” for this cohort because of the low prevalence of normal results. MPI is limited because it underestimates the extent of anatomic CAD, and it cannot detect atherosclerosis. Integrating CTA and MPI offers better identification of culprit coronary stenosis, because MPI provides improved detection of CAD in small vessels (<2 mm), while CTA provides assessment of multivessel disease.

Hybrid imaging can also enhance risk assessment. MPI is an excellent tool for identifying ischemic burden and assessing endothelial health, and when coupled with CTA’s ability to delineate multivessel disease, plaque characteristics, and subclinical atherosclerosis, the combined use of these two modalities, which integrate structure and function, will allow for a more personalized approach to management, said Dr. Di Carli.



*Highlights from the
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Dr. Di Carli noted that both of the key diagnostic objectives of identification of ischemic burden that requires revascularization and elucidation of the detailed anatomic burden, thus determining the goals and intensity of medical therapy, can be achieved with hybrid imaging. “It is likely that future approaches to CAD management will evolve toward more individualized strategies that better match patients’ risk with intensity and goals of therapy,” said Dr. Di Carli. He added that the hybrid approach is most apt to benefit individuals with an intermediate to high likelihood of CAD, with CT offering the best approach for individuals with a low likelihood of disease.

Innovations in Cardiac Imaging

The field of diagnostic cardiac imaging has experienced many exciting innovations and advances in recent years. Each modality has clinical advantages and disadvantages and their use in clinical practice varies greatly. The main imaging modalities include echocardiography, magnetic resonance imaging (MRI), nuclear cardiology and multi-slice computed tomography (MSCT).

Echocardiography is the most commonly used imaging technique in clinical cardiology due to its reliability and practicality. This technique is highly reproducible, mobile and available bedside. It provides an accurate evaluation of cardiac dimensions and function, valvular anatomy and function, cardiac pressures, and the pericardium without the use of radiation.

Stress echocardiography (physiological exercise or pharmacological stress) is used for detection of myocardial ischemia as a marker of coronary artery disease (CAD). Intravenous contrast can be used to enhance left ventricular border opacification, as well as to evaluate myocardial perfusion.

Magnetic resonance imaging (MRI) produces information similar to echocardiography but with a higher resolution. With contrast-enhanced imaging, high precision imaging of scar tissue is possible without radiation. The most significant drawbacks to this technique are claustrophobia, the presence of cardiac pacemakers and defibrillators, and limited availability of equipment.

Nuclear cardiology includes imaging with PET and SPECT, the two most frequently used techniques for assessment of myocardial ischemia. Radioactive tracers are used to visualize cardiac biology and functional processes. The main focus of SPECT imaging is assessment of myocardial perfusion (Figure 1A); in addition, assessment of cardiac innervation is also possible. The main advantage of PET imaging is the option of absolute quantification of

physiological processes such as perfusion, metabolism and innervation.

The most recent advance in imaging is MSCT. This technique provides assessment of coronary atherosclerosis (a calcium score) and permits non-invasive angiography (Figure 1B). It provides anatomic imaging, without information on the hemodynamic consequences of the observed coronary lesions (ie, no information on the presence/absence of ischemia secondary to the detected atherosclerosis is provided). This technique utilizes contrast agents and radiation. The main advantage is that CAD can be assessed at a very early stage (ie, atherosclerosis without significant coronary artery stenoses). It is clear that MSCT has a high diagnostic accuracy for detection/exclusion of CAD, but its precise role in clinical evaluation and patient work-up remains to be determined.

Figure 1A. SPECT Perfusion Study.

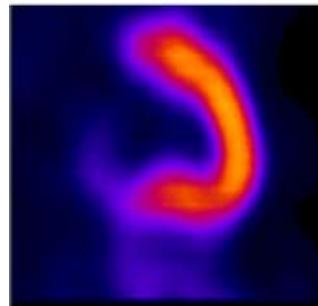
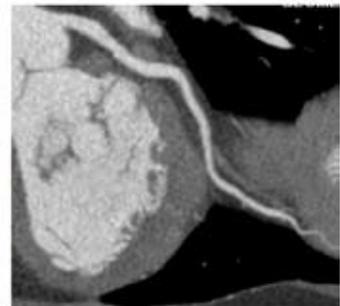


Figure 1B. MSCT Angiography.



Accordingly, the current era is characterized by a large variety of non-invasive imaging techniques, and the (near) future will determine the precise roles of these various imaging techniques.

The upcoming Annual Meeting of the European Society of Cardiology (Aug 30 -Sept 3, 2008, Munich, Germany; <http://escardio.org/congresses>), will emphasize clinical cardiology and imaging. Presentations including “Expert Imagers” and Live-Case Imaging sessions will specifically address imaging technology and how it can be integrated to support and enhance clinical care. One of the most exciting new features being introduced this year is the “Everything You Wanted to Know About Cardiovascular Imaging but were Afraid to Ask” session. This new interactive session will allow attendees to post questions on the ESC website prior to the meeting which will then be answered by our expert panel during the live session, providing a wonderful opportunity for attendees to interact with our experts. I look forward to seeing you in Munich this August!

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