Clinical considerations in cardiac stress testing

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Stress testing is an established part of investigation in the patient with known or suspected cardiac disease. Traditionally, it has been combined with the electrocardiogram (ECG); but various forms of stress are now used in myocardial perfusion imaging (MPI) and in echocardiography.[1-5] Guidelines for exercise testing with dynamic exercise are well established,[6,7] but none has yet considered stress testing during MPI specifically. The aims of this article are to review stress procedures used during MPI, to consider best clinical practice, and to review recent advances.

The training and nature of staff performing stress tests vary considerably between centers. Most commonly, technicians or dedicated stress nurses have taken on the responsibility of supervising stress, and medical supervision is becoming less common, at least in the United Kingdom. We have used trained and dedicated stress nurses to run MPI stress sessions for 5 years. The success of this strategy has arisen not only from the experience and training of the nurses but also from aspects of organization such as the clinical environment of the department, its layout, and the screening of referrals to assign the ideal stress and imaging protocol.

CHOICE OF STRESS

Dynamic exercise has been used in the stress testing of the cardiovascular system for more than 6 decades, and it is a powerful method of provoking myocardial ischemia in patients with hemodynamically significant coronary artery disease. It is, however, important to maximize the amount of work performed; it is usually necessary for patients to achieve at least 85% of the maximum age-predicted heart rate because up to one half of abnormalities occur only at heart rates in excess of this value.[8] Inadequate exercise is a major cause of false-negative exercise test results.[9,10] Reasons for inadequate exercise include peripheral vascular disease; neurologic, muscular, and skeletal disease; chronic pulmonary conditions; poor physical conditioning; and poor motivation.[11]

Pharmacologic stress can be a valuable alternative to dynamic exercise, particularly when used during MPI. We use pharmacologic stress almost exclusively (Figure 1). In a recent study that randomly selected 2529 patients to receive either thallium, sestamibi, or tetrofosmin, the stress agent was chosen according to a clinical algorithm; the authors used adenosine with dynamic exercise in 81% of patients, adenosine alone in 8.5%, dobutamine in 10.5%, and exercise alone in only 0.5%.[12]

Adenosine

Adenosine is a natural purine that causes arteriolar dilatation by activation of the A2 receptor of the arteriolar smooth muscle. Its main site of action is the coronary arteriole. A 6-minute intravenous infusion at 140 μg/kg/min leads to maximal coronary vasodilation, with flow increasing to 4.4 mL/min/g compared with dipyridamole at 4.3 mL/min/g (0.56 mg/kg), dobutamine at 2.3 mL/min/g (40 μg/kg/min), and exercise at 1.5 mL/min/g (Figure 1). The peripheral vasodilation leads to a small increase in heart rate and a fall in systolic blood pressure; this vasodilation also causes many of the side effects of adenosine, such as facial flushing, chest pain, headache, dyspnea, nausea, and dizziness. However, the plasma half-life of adenosine is very short, and the side effects, although common (80%), are short-lived and well tolerated. Adverse effects also include atrioventricular conduction block, sinus node dysfunction, and bronchospasm. For this reason, adenosine should not be used in patients with heart block without pacemaker protection, in those with sick sinus syndrome, or in those with asthma.

The adenosine infusion is prepared by drawing 25 mL of adenosine 3 mg/mL into one syringe for a patient of average weight (75 kg). The usual protocol involves a 6-minute infusion at 140 μg/kg/min, with radiopharmaceutical injection between the third and fourth minutes. Although some centers use separate cannulas for adenosine and radiopharmaceutical injection, it is feasible to inject both through a single cannula with use of a 3-way tap to ensure that the tracer is injected without interrupting the flow of adenosine. The ECG and patient should

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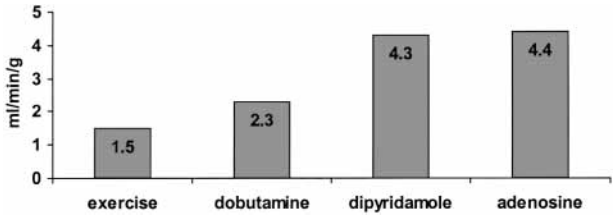

Figure 1. Comparison of maximum coronary flow during exercise and pharmacologic stress. (Data from Pennell DJ et al. Thallium myocardial perfusion tomography in clinical cardiology. London: Springer-Verlag; 1992. p. 5-21.)

be monitored closely at the time of tracer injection in case of adverse effects.

Dipyridamole

Dipyridamole is also a coronary arteriolar dilator; it acts by increasing interstitial levels of native adenosine. It is given intravenously as an infusion at a dose of 0.56 mg/kg for 4 minutes, with radiopharmaceutical injection 4 minutes after the end of the infusion. The side effects of adenosine and dipyridamole are similar in nature, although they are longer lasting for dipyridamole because of its longer half-life of about 30 minutes. Serious side effects can be counteracted by aminophylline (250 mg) given intravenously for 1 minute; although this is rarely necessary.

Adenosine has superseded dipyridamole stress testing in a number of centers because of its practical advantages, although it is considerably more expensive in the United Kingdom. The accuracy of MPI with adenosine is similar to that of MPI with dipyridamole; it is also high, with an average sensitivity and specificity between 80% and 90% reported in multiple studies (Figure 2).

Dobutamine

Dobutamine is a β-sympathetic agonist that also has a primary action to dilate coronary arterioles. When used during perfusion imaging, it is this primary vasodilation effect that is most important; hence its mode of action is similar to that of adenosine. It also has positive inotropic and chronotropic effects, thus increasing myocardial oxygen demand. This leads to secondary coronary dilatation. In general terms, though, it is a less powerful vasodilator than adenosine.

The infusion is prepared from 250 mg of dobutamine in a 20-mL vial, which can be added to 105 mL of 0.9% saline solution to make 125 mL at a concentration of 2 mg/mL. This is infused into a peripheral vein in 3- to 5-minute stages starting at 5 or 10 μg/kg/min and increasing to 15, 20, 30, and 40 μg/kg/min. Radiopharmaceutical

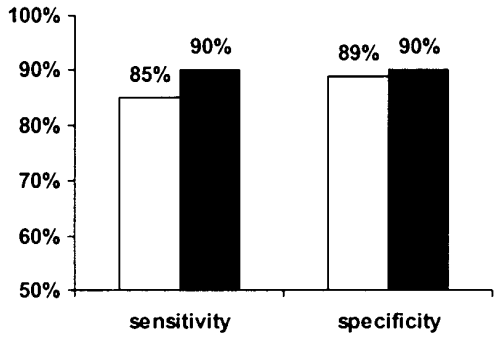

Figure 2. Sensitivity and specificity of dipyridamole *(open bars)* and adenosine MPI *(filled bars).* (Data from Pennell DJ et al. Thallium myocardial perfusion tomography in clinical cardiology. London: Springer-Verlag; 1992. p. 5-21.)

tracer is injected at the peak infusion rate, and the infusion is continued for 1 minute after injection.

The practical advantages of dobutamine are that it has a short half-life of approximately 2 minutes, it is not expensive, and it is relatively well tolerated. It can be given by peripheral intravenous injection and is associated with fewer arrhythmias than other β-agonists.[13] The disadvantages are that the infusion protocol may last up to 15 minutes and that the incidence of adverse events is higher than with adenosine, particularly at high doses. Possible side effects include hypotension from peripheral vasodilation, chest pain, palpitation, headache, flushing, dyspnea, other pain, nausea, and dizziness.

FACILITIES

The stress room should be easily accessed and should be large enough for general and resuscitation equipment. It should be clean, bright, and well ventilated with humidity and temperature control, and it should have a clock and curtains for privacy. It is also helpful to have the stress and camera rooms in close proximity, with a window between the rooms to aid communication between the stress and technical staff.

Electrocardiographic recording is essential, but a single lead is adequate to monitor rhythm. Some departments record a full 12-lead ECG, but this is relatively cumbersome and is not essential. A 12-lead ECG machine should, however, be available in the event of more serious complications. Manual blood pressure monitoring is better than that of automated machines because of inaccuracies caused by motion.

We use an electrically braked bicycle ergometer on a couch with an adjustable backrest and pedals. This is suitable both for maximal dynamic exercise and for submaximal exercise used as an adjunct to pharmacologic stress, and it is preferable to a treadmill because infusions

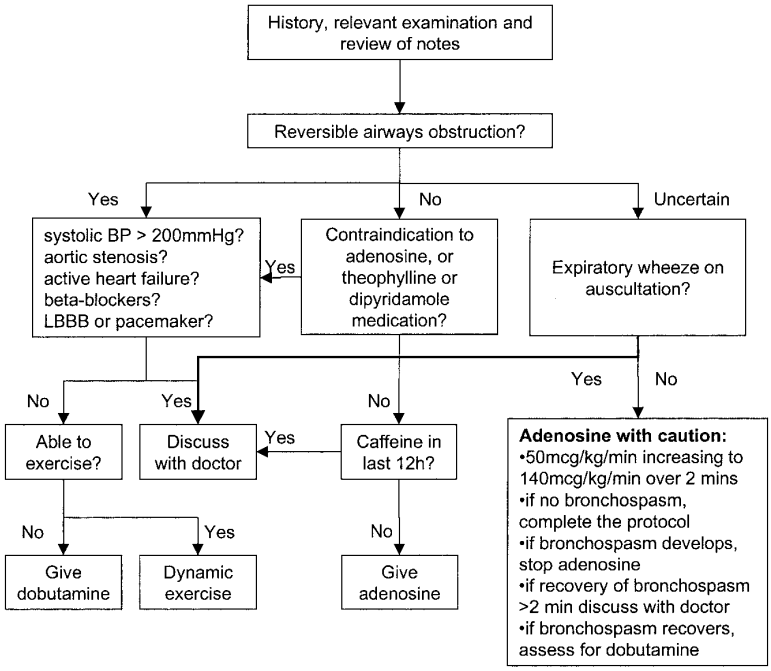

Figure 3. Algorithm used by stress nurses at Royal Brompton Hospital for selection of stress protocol. *LBBB,* Left bundle branch block; *BP,* blood pressure.

are more easily managed when the patient is relatively immobilized. The ergometer should have the capability to adjust the workload in increments, both automatically and manually.

GUIDELINES FOR STRESS TESTING IN MPI

Guidelines for the clinical competence of medical[6] and technical staff[3,7] involved in stress testing exist. Staff should understand exercise physiology and ECG interpretation, and they should have experience in care of the cardiac patient, preferably including coronary or intensive care. They should be trained and currently certified in advanced life support.[3,6,7,14] Doctors and many nurses, especially cardiac or intensive care nurses, possess this experience. Cardiac technicians have also established themselves as competent supervisors of treadmill exercise testing in the United Kingdom.[15,16] In our center and in some other centers, supervision of dynamic and pharmacologic stress has been handed over to nurses from doctors; this is an important extension of the nursing role. Nurses have advantages over persons in other nonmedical professions because they are legally able to give prescribed drugs and they are able to work without direct medical supervision.

In the United Kingdom, the role of the stress nurse is relatively new, and national guidelines for competent practice have not yet been published. We do, however, have our own guidelines.[17] These have been devised by nursing and medical staff with the assistance of clinical managers, pharmacists, and solicitors. These guidelines form a legal document required by the United Kingdom Central Council for Nursing, the English National Board of Nursing, and the Medicines Act of 1968. They allow nurses to prescribe and administer medicines under defined conditions.[18] Professional qualifications required of the stress nurse include a postregistration qualification in a cardiac speciality or intensive care, advanced ECG interpretation, advanced life support certification, and a course in radiation protection and handling of unsealed radioactive sources. Stress testing is taught by practical demonstration and supervision, formal and informal discussion, and daily review until competence is achieved. This is reinforced during daily reporting sessions and more formally at 6 monthly intervals, if required.

Guidelines for nurse-led stress testing have been documented in Australia by Zecchin et al[14] and in the United States by Zielinski et al.[19] Zecchin et al studied 17,467 patients over a 12-year period. Of these patients, 97% had angiographically proven coronary heart disease or recent acute myocardial infarction and were termed moderate- to high-risk patients. All patients had stress tests supervised by nurses without direct medical supervision. The patient mortality rate was 0%, which is simi-

lar to the mortality rate of less than 0.01% for physician-supervised stress testing.[2] Zielinski et al studied 343 patients who had dobutamine stress testing performed by nurses without direct medical supervision during echocardiography. Although the outcome measures were less clear than those in the Australian study, the authors concluded that the nurses were competent and that complication rates were acceptable with no deaths.

MANAGEMENT OF REFERRALS

When patients are referred for MPI, it is important to consider and plan the best stress and imaging protocol, as well as scheduling of the test. Considerations include the state of health of patients, concomitant diseases such as diabetes and asthma, their ability to travel and need for a companion or helper, their weight and build, medication, and nutrition (eg, caffeine intake). It is also important to know whether information on myocardial function, viability, or hibernation is required. This is most easily handled with the aid of set protocols; we review all referrals by a doctor or an experienced stress nurse to allocate stress and tracer technique according to clinical need (Figure 3). Clinical urgency is assessed and appointments are allocated according to 4 categories of urgency: routine, soon, urgent, and immediate. We use adenosine with submaximal exercise as the default form of stress and thallium as the default tracer, but we use dynamic exercise or dobutamine in patients with contraindications to adenosine; we use technetium tracers in obese patients or in those in whom gated single photon emission computed tomography is planned to assess myocardial function or hibernation. It might be ideal to perform gating in all patients, but many practical constraints conspire against this, including hard disk space and the extended times required for acquisition and processing.

Another concern in managing a busy department is to maximize attendance rates. The United Kingdom national nonattendance rate for outpatient appointments is 12%, and this costs the National Health Service £300 million (approximately $450 million) annually.[20] We have adopted a number of procedures to maximize attendance. First, all appointments are sent with a postage-paid reply card on which the patient can confirm planned attendance and provide important information such as weight and telephone number. This has the advantage of improving communication between department and patient and has been shown to reduce nonattendance. Second, patients who do not confirm their appointments are reminded by letter, and the appointment is ultimately canceled if positive contact is not made after 2 attempts. Third, patients are asked if they are available at short notice and are called to fill vacant slots if another patient cancels at short notice. Patients may even be called on the day of an appointment to fill a slot if a scheduled patient fails to attend.

These 3 aspects give greater control to the patient and have all helped to reduce nonattendance. The system is not infallible, but it has reduced our nonattendance rate from 8% to 4% and our cancellation rate from 3.1% to 2.2% and has saved £2900 (approximately $4350) per year.[21]

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