Treadmill exercise echocardiography: methodology and clinical role

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Exercise echocardiography using treadmill exercise and immediate post-exercise imaging is an accurate means for detecting and stratifying coronary artery disease. It is applicable to patients with chest pain syndromes in whom the initial diagnosis is being contemplated and also in follow-up of patients after myocardial infarction or interventional procedures. Numerous studies have demonstrated that its accuracy is equivalent to that of competing radio-nuclide imaging techniques and that it has particular relevance in patients with non-diagnostic electrocardiograms.

In addition to evaluating patients for the presence of coronary artery disease, because of the highly versatile nature of the imaging modality utilized (two-dimensional echocardiography), stress echocardiography is an excellent tool for evaluating atypical symptoms such as dyspnoea and fatigue.

Key Words: Coronary artery disease, exercise echocardiography, stress testing.

Introduction

Stress echocardiography has evolved over the past 15 years into a widespread, clinically applicable and cost effective tool for evaluating patients with known or suspected coronary artery disease. Its role has evolved from the evaluation of chest pain syndromes to a highly versatile technique used to evaluate patients with valvular heart disease, cardiomyopathy and atypical symptoms such as fatigue and dyspnoea. Stress echocardiography is a family of examinations which includes post-treadmill imaging, imaging at the time of exercise with supine or upright bicycle ergometry and various forms of pharmacological and pacing stress (Table 1). All forms of stress echocardiography share the advantages of relatively low cost (compared to competing nuclear medicine techniques), tremendous versatility, enhanced yield when compared to exercise electrocardiography and the ease with which a stress echocardiography laboratory can be established.

Independent of the type of stress used, the underlying premise for the use of stress echocardiography is the same, and can be stated as: 'in patients with suspected ischaemic heart disease, cardiovascular stress will induce myocardial ischaemia which results in a wall motion abnormality. This wall motion abnormality is then detected by two-dimensional ultrasound imaging and serves as a marker for the presence and location of an obstructive coronary lesion'. This paper will review the basic methodology, clinical indications and utility of stress echocardiography performed in conjunction with treadmill exercise.

Post-treadmill echocardiography

Exercise testing methodology

Post treadmill exercise echocardiography represents a merger of routine treadmill exercise with echocardiographic imaging. Any of the traditionally employed exercise protocols can be utilized. The treadmill exercise portion should be tailored to the specific clinical question and the patient's ability to vigorously exercise. Typically, a standard Bruce protocol is used in male patients capable of exercise while a Cornell protocol may provide some advantages in female patients and in less well conditioned individuals. Modified and other protocols can be used in specific instances as well and may be particularly useful in patients with congestive heart failure or early following myocardial infarction. As long as appropriate exercise endpoints are attained the accuracy of the exercise echocardiogram is probably equivalent among the different protocols.

Routine, multiple lead ECG monitoring is undertaken as it would for a non-imaging study. However, it is frequently necessary to modify the lead position near the apex to accommodate echocardiographic imaging. In most instances, this does not substantially affect the accuracy of the electrocardiographic analysis,
Table 1  Relative value of peak stress, post stress and pharmacological stress echocardiography

<table>
<thead>
<tr>
<th>Aetiology of chest pain</th>
<th>Post-treadmill</th>
<th>Upright bicycle ergometry</th>
<th>Supine bicycle</th>
<th>Pharmacological</th>
</tr>
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<tbody>
<tr>
<td>Physiological significance of CAD</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Aetiology of dyspnoea</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Aetiology of fatigue</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Valvular stenosis</td>
<td>+</td>
<td>+++</td>
<td>++</td>
<td>?</td>
</tr>
<tr>
<td>Valvular insufficiency</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial viability</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>+++</td>
</tr>
<tr>
<td>Post infarct prognosis</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; 0 = no value; ? = insufficient data; +++ to + = increasing to decreasing clinical value.

Figure 1  Diagram of an exercise echocardiography laboratory which has been designed for maximum efficiency of motion of the patient, sonographer and monitoring physician. Note the very close proximity of the imaging bed to the treadmill. Fewer than three steps are required of the patient to move from the treadmill to the bed. Likewise all cabling is out of the path of motion and only one set of electrocardiographic leads is applied to the patient. (Modified and reprinted from Marcovitz P. In: The Practice of Clinical Echocardiography. M. Otto, ed. W. B. Saunders.)

and any decrement in accuracy is more than balanced by the increased diagnostic yield afforded by the echocardiographic imaging. The only other deviation from routine treadmill exercise protocols is that no 'cool down' period is allowed after exercise, rather the patient moves immediately from the treadmill to an imaging bed for repeat echocardiography.

As wall motion abnormalities can resolve quickly following cessation of exercise it is essential that patients move immediately from the treadmill to the imaging bed. This can be facilitated by appropriate laboratory design. Figure 1 is a typical layout of an exercise echocardiography laboratory which allows rapid and efficient movement of the imaging sonographer, the monitoring physician and the patient around the room with minimal steps required for the patient to move from the treadmill to the imaging bed. Additionally, efficiency can be enhanced by utilizing only one set of electrocardiographic leads. These typically are the leads used for the ECG monitoring console: an ECG lead is sent from the ECG monitoring console directly into the ultrasound machine and into the image digitizer. Utilizing this type of set-up with an exercise laboratory designed as suggested in Fig. 1, most patients can move from the treadmill to the exercise bed in no more than three steps. This can be accomplished within 5 s of terminating exercise. This allows immediate repeat scanning after exercise which can then be completed in under 60 s in the majority of patients.
For efficient high volume clinical exercise echocardiography, digital frame grabbing systems are essential. These allow capture of images which can then be edited, free of respiratory interference, and displayed side by side with comparative rest images. This facilitates detection of subtle wall motion abnormalities and improves interpretation efficiency.

Two-dimensional imaging
As noted above, it is essential that two-dimensional imaging be accomplished immediately after exercise. Depending on the clinical question a full echocardiographic study with colour flow and spectral Doppler may be a component of the baseline study. Typically, four views are utilized for digitizing and comparison at the time of stress. In the majority of instances the combination of parasternal short- and long-axis and apical four- and two-chamber views are recorded and digitally acquired. In specialized circumstances subcostal views, apical long-axis views or additional short-axis views may also be used. Subcostal views can be particularly advantageous in patients with chronic lung disease. For individuals in whom distal left anterior descending lesions are suspected, the apical long-axis view (with the transducer in a parasternal position lower on the chest) can visualize a critical area of the anterior septum. The standard protocol involves capturing these four views which are then put into memory in the digitizing system.

After acquisition of baseline views and recording a complete Doppler study (when indicated) exercise is then undertaken using any of the clinically indicated treadmill exercise protocols. Immediately at termination of exercise, which is determined by traditional exercise treadmill endpoints such as target heart rate, leg fatigue, cardiac symptoms or electrocardiographic changes, the treadmill is stopped and the patient immediately returns to the imaging bed. The same four views that were captured at rest are immediately captured and recorded on videotape. It is highly advantageous to have the patient briefly hold their breath in end- or mid-expiration. While this may initially appear difficult immediately following exercise, the majority of patients are capable of breath holding for six to eight cardiac cycles. This results in higher quality imaging with less respiratory interference. Immediately after several consecutive images are captured, the imaging sonographer then proceeds to capture the next view. Using digitizing equipment, post-exercise imaging typically is accomplished in under 60 s. Imaging at this point should not be interrupted for repeat electrocardiograms, blood pressure monitoring, etc. unless clinically indicated by an adverse event.

The order in which images are acquired following exercise can either be standardized or individualized to the clinical situation. The advantage of a predetermined order of imaging is that it results in fewer imaging or technical errors. In instances in which subtle wall motion abnormalities may be expected, imaging the view with the highest diagnostic yield first is an appropriate option. Instances in which this can occur are in individuals who have exercised to low levels or in whom the functional significance of a specific lesion is the target of the study. Following digital capture of the immediate post exercise images, the patient is then allowed to recover to baseline heart rate and blood pressure. At this point, echocardiographic imaging is again recorded on videotape to confirm that baseline left ventricular function has again been established.

Analysis of stress echocardiograms
Exercise echocardiograms can be analysed using several different levels of complexity. These range from a simple assessment of normal vs abnormal, to detailed quantitative wall motion schemes. The type of analysis undertaken should be tailored to the clinical indication for the study. It is often sufficient to simply identify wall motion as either being normal, hypokinetic, akinetic, dyskinetic in a coronary territory if the intent of the study is to diagnose coronary artery disease. For serial and follow-up studies, quantitative schemes using a wall motion score can be highly advantageous.

The response of normal myocardium, not perfused by a stenotic coronary artery, is for the wall to become hyperdynamic after adequate cardiovascular exercise. On occasion, if the magnitude of cardiovascular stress has been suboptimal, a hyperdynamic response may not be seen. This should not be construed as an abnormality in individuals who have not exercised to a maximum degree. The echocardiographic indicator of the presence of coronary artery disease is the presence of a resting or stress-induced wall motion abnormality. A resting abnormality implies prior myocardial infarction or chronically ischaemic, 'hibernating' myocardium. Induction of a new wall motion abnormality implies the presence of a stenotic coronary lesion sufficient to cause reduction in coronary flow reserve. The location of the wall motion abnormality can then be correlated with known coronary anatomy. Figure 2 provides a basic outline of the coronary distribution of different wall motion abnormalities.

Advantages and disadvantages of treadmill exercise
Stress echocardiography using post-treadmill imaging has distinct advantages and disadvantages compared to other modalities commonly used in conjunction with echocardiographic imaging. Perhaps the greatest advantage of post-treadmill imaging is that, in many countries (United States being the most obvious), walking or treadmill exercise is more familiar to patients than is bicycle exercise. As such, the ability of a patient to attain legitimate cardiovascular endpoints with treadmill exercise is frequently greater than with bicycle exercise. Additionally, prognostic databases with respect to exercise duration and ECG responses are more extensive and
Treadmill exercise echocardiography

Figure 2   Cardiac anatomy vs coronary artery territories based on a 16-segment model. The views are those typically acquired during exercise echocardiography. The distribution of the left anterior descending, right coronary artery and circumflex coronary arteries are as noted. □ = left anterior descending distribution; □ = right coronary artery distribution; □ = circumflex distribution; □ = left anterior descending/circumflex overlap; □ = left anterior descending/right coronary artery overlap. (Reprinted with permission.)

perhaps better validated with treadmill exercise than with bicycle ergometry.

The limitations of exercise echocardiography using post-treadmill imaging are that only baseline and immediate post-exercise images are available for analysis. As such, when a wall motion abnormality is detected in the post-exercise period, the interpreter is not afforded information regarding this stage of onset of the ischaemic wall motion abnormality. Potentially this information can provide valuable information regarding the severity of a coronary stenosis. Additionally, wall motion abnormalities which are due to relatively mild degrees of ischaemia may resolve rapidly and be missed in the post-exercise images, even if accomplished within the recommended 60 s time frame. As exercise is stopped for traditional endpoints such as target heart rate or symptoms, the full spectrum of abnormalities which could develop can often be missed using post-treadmill imaging. This has particular pertinence with respect to detection of patients with multivessel disease. While post-treadmill imaging identifies the vast majority of patients who have multivessel disease as having ischaemic heart disease, it may underestimate the number of vessels with stenotic lesions.

Accuracy of treadmill exercise imaging

Post-treadmill exercise imaging has been validated in numerous laboratories with respect to its ability to detect patients with coronary artery disease. Table 2 outlines results of the majority of previously published studies with respect to sensitivity, specificity, positive and negative predictive values. As with all imaging techniques, the sensitivity for detecting patients with single-vessel coronary artery disease is somewhat less than that for detecting patients with multivessel disease. Very few studies have assessed the accuracy at different thresholds of coronary stenosis. The limited data that are available suggest that sensitivity is higher for a 70% threshold for defining significant stenosis than with the lower and traditionally used 50% stenosis. Several studies have demonstrated that exercise echocardiography results may enhance the determination of functional significance of coronary lesions when quantitative coronary arteriographic techniques are utilized. The study by Sheikh et al. suggested that the majority of 'false-positive' studies could be resolved by quantitative coronary arteriography. However, when more detailed analysis of the coronary arteriogram was undertaken, many individuals with superficially false-positive
studies were subsequently found to have significant coronary stenoses.

When compared to peak exercise imaging with bicycle ergometry, post-exercise imaging often has a slightly lower sensitivity but slightly higher specificity\cite{19-21}. Perhaps more importantly, peak exercise imaging with a bicycle may have a higher specificity for the accurate detection of patients with multivessel disease\cite{12}. While both techniques identify patients with ischaemic heart disease, exercise echocardiography using bicycle ergometry with peak exercise imaging has a higher yield for accurate identification of patients with multivessel disease.

The overall accuracy of exercise echocardiography in identifying patients with coronary artery disease has been excellent and comparable to that of the more established radionuclide techniques. Several distinct patient subsets are known to effect the accuracy of exercise echocardiography. False-negative examinations will be seen in individuals who fail to attain appropriate cardiovascular workload. This is most commonly seen in deconditioned individuals incapable of 6 min or more of exercise on the treadmill. Additionally, as ischaemia, especially milder degrees, may resolve quickly following cessation of exercise, in individuals who are not capable of moving rapidly from the treadmill to the imaging bed the wall motion abnormalities may resolve before scanning. These individuals are frequently those incapable of vigorous exercise. Several studies have also demonstrated that induction of ischaemia is less likely in single-vessel disease and in patients with intermediate (50-70\%) degrees of coronary stenosis. Some individuals on effective anti-anginal therapy with calcium channel blockers and beta-blockers likewise will have 'false-negative' stress echocardiograms. These probably are not true false-negative studies but represent the effects of effective anti-anginal therapy.

False-positive stress echocardiograms likewise can be predicted in certain patient subsets. Many of these pitfalls can be avoided if the interpreting physician is forewarned. The wall motion abnormalities attendant with the post-operative state in patients who have undergone prior cardiac surgery as well as in the individuals with paced rhythms or intrinsic left bundle branch block has been well described and should not be confused with an ischaemic abnormality. In these instances, while septal motion is abnormal with respect to external landmarks, wall thickening is preserved. Secondly, as it is usually the left anterior descending coronary artery that is suspected of being ischaemic, when proximal abnormalities are seen (such as with left bundle branch block), if truly ischaemic the anterior wall and apex will also be involved. By adhering to these simple guidelines the majority of false-positives in these situations can be avoided. Finally, the proximal portions of the walls perfused by the posterior circulation (combined right and circumflex arteries) frequently have atypical responses and abnormal wall motion. It is prudent to have a conservative reading scheme in these areas and not to call single segment abnormalities as indicative of myocardial ischaemia.

**Comparison with radionuclide perfusion studies**

Very few studies have directly evaluated stress echocardiography and radionuclide perfusion imaging\cite{10,22}. The majority of these studies compared laboratories (echo or nuclear) of widely disparate levels of expertise and are of questionable validity. The single exception to this is the study of Quinones and colleagues\cite{10}. These authors provide an angiographic correlation in 112 patients who underwent both studies using the state of the art equipment and highly experienced readers in each discipline. The sensitivity for detection of single-, double- and triple-vessel disease was virtually identical with both techniques. However, there was a slight edge in specificity with exercise echocardiography compared to thallium scintigraphy.

**Prognostic information**

The majority of published prognostic information on stress echocardiography has utilized pharmacological

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**Table 2 Accuracy of post-treadmill exercise echocardiography**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Sens</th>
<th>SVD</th>
<th>MVD</th>
<th>Spec</th>
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<th>NPV</th>
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<td>123</td>
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<tr>
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<td>73</td>
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<td>82%</td>
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<tr>
<td>Crouse</td>
<td>1991</td>
<td>228</td>
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<td>92%</td>
<td>100%</td>
<td>64%</td>
<td>90%</td>
<td>87%</td>
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<tr>
<td>Marwick</td>
<td>1992</td>
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<td>79%</td>
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<td>88%</td>
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<td>82%</td>
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<td>93%</td>
<td>86%</td>
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<tr>
<td>Roger</td>
<td>1995</td>
<td>127</td>
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<td>—</td>
<td>—</td>
<td>72%</td>
<td>93%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Sens=sensitivity; SVD, MVD= single- and multivessel disease, Spec=specificity; PPV, NPV=positive and negative predictive values.
stress\textsuperscript{33–36}, and several studies have evaluated the prognostic significance of normal and abnormal exercise echocardiograms as well as the value of the exercise echocardiogram following myocardial infarction. Sawada and colleagues followed a cohort of 148 patients with normal exercise echocardiograms for 14 months and documented a 0-85% hard event rate following normal exercise echocardiography\textsuperscript{27}. The average age of these patients was 52-5 years and roughly half of them had an abnormal electrocardiographic response to exercise. Virtually all patients in this study had initially presented for evaluation of chest pain syndromes or other symptoms suggesting coronary artery disease. This hard event following normal exercise echocardiography is equivalent to that seen following normal thallium scintigraphy.

Several other investigators have looked at outcomes following a full range of echocardiographic responses\textsuperscript{28–29}. Krivokapich and colleagues reported a 12-month follow-up of 360 patients after post-treadmill exercise echocardiography\textsuperscript{28}. Individuals with an ischaemic response had a greater likelihood of having events than did individuals with a non-ischaemic response. A preliminary report from Usedom and colleagues was in concordance\textsuperscript{29}. These investigators evaluated 693 female patients and documented a hard event rate following normal exercise echocardiography of approximately 1-2% per year over a 28-month follow-up and a substantially greater event rate, defined as myocardial infarction and cardiac death, after any of the categories of abnormal exercise echocardiograms.

Exercise echocardiography has also been utilized to a limited degree for evaluation of patients following acute myocardial infarction\textsuperscript{30–32} or hospitalization for unstable angina\textsuperscript{30}. Ryan and colleagues evaluated 40 patients following non-intervened myocardial infarction and documented a statistically greater likelihood of subsequent cardiac events, defined as hospitalization for unstable angina, recurrent myocardial infarction or cardiac death in individuals with inducible ischaemia on exercise echocardiography\textsuperscript{30}. However, it should be noted that this study was performed in the non-interventional era and that these results may not directly extrapolate to contemporary patient populations in which lytic therapy or other reperfusion strategies have been employed.

Evaluation of patients following coronary angioplasty with exercise echocardiography has been incompletely evaluated. First it should be recognized that there is no clear clinical consensus as to which patients require surveillance echocardiograms or other stress studies following interventions. Certainly a normally active individual with typical angina prior to an interventional procedure does not benefit from routine surveillance studies of any type. Several studies using exercise echocardiography as well as pharmacological stress testing have demonstrated that ischaemia-mediated wall motion abnormalities are no longer present after successful angioplasty or that when present they are less severe or brought on by higher levels of stress\textsuperscript{33}. Likewise the ability to detect significant restenosis with stress echocardiography has been demonstrated, however the incremental yield over analysis of patient symptoms or other routine clinical parameters has never been demonstrated.

### Clinical role of post-treadmill imaging

Stress echocardiography using post-treadmill imaging can play a highly versatile and valuable role in evaluating patients. As noted above, this extends not only to detecting coronary disease in patients with suspected ischaemic syndromes but also for establishing a link between other forms of cardiac disease and exertional fatigue and dyspnoea. As treadmill exercise mimics the most common form of exercise or activity spontaneously undertaken by patients, it affords an excellent way to establish a link between cardiovascular disease, symptomatic response and underlying anatomy.

### References


