Use of first-pass radionuclide ventriculography in assessment of wall motion abnormalities induced by incremental atrial pacing in patients with coronary artery disease

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SUMMARY In order to show that stress-induced changes in ventricular function can be determined by radionuclide techniques, 13 patients with coronary artery disease were paced to angina. Changes in ejection fraction and regional wall motion were measured from contrast angiograms and first-pass nuclear angiograms performed using a multicrystal gamma camera. A count-volume method applied to the nuclear technique demonstrated a significant fall in ejection fraction on pacing. The area-length method was also applied to both techniques and a significant fall in ejection fraction was induced by pacing in both contrast and nuclear angiograms. There was a good correlation between ejection fraction on pacing derived from contrast and count-volume nuclear angiograms. Those patients with greater falls in ejection fraction were identified by both techniques. Changes in regional wall motion were assessed by a hemiaxial method. All six anterior and all four inferior pacing-induced zones of hypokinesis identified on contrast angiography were demonstrated by the nuclear technique. Of three apical regions of pacing-induced hypokinesis seen on contrast angiography one was shown by the nuclear method. All 11 zones of pacing-induced hypokinesis seen on nuclear angiography were in regions supplied by significantly stenosed coronary vessels.

Nuclear angiography is able to demonstrate changes in global and regional wall motion induced by ischaemia.

The non-invasive nature of radionuclide techniques allows them to play an important role in the assessment of ventricular function during stress. Before extending these methods to the dynamic exercise test, it is important to demonstrate that stress-induced changes in ventricular contraction seen on contrast angiograms could also be identified by radionuclide ventriculography.

Although left ventricular wall motion is known to be sensitive to ischaemia,1 most angiographic studies of left ventricular function in patients with coronary artery disease have been performed at rest. Rickards et al.2 have shown that ventriculograms performed under conditions of circulatory stress may demonstrate regional contraction abnormalities not seen in the resting state. In view of the fact that first-pass radionuclide ventriculography is capable of identifying localised wall motion abnormalities proven by contrast angiography,3 4 a study was undertaken to investigate the usefulness of the technique in the detection of stress-induced changes in ventricular function. Since Sowton et al.5 first described incremental atrial pacing as a method of inducing ischaemia, pacing has frequently been used for the assessment of ventricular function during pain.6–9

In this study we have investigated left ventricular function using both radionuclide and contrast angiography, at rest and at pacing-induced angina.

Patients and methods

The study group consisted of 12 male and one female patients aged between 37 and 62 years. All
were undergoing cardiac catheterisation for stable angina pectoris. Beta-blocking drugs were withdrawn 48 hours before the investigation and all patients received a premedication of 15 mg oral diazepam two hours before the procedure. Informed consent was obtained in every case.

**CONTRAST ANGIOGRAPHY**

Left heart catheterisation was carried out via a right brachial arteriotomy. A pacing catheter was passed into the right atrium via an antecubital vein. A resting left ventriculogram was performed in the 30° right anterior oblique projection with 20 to 30 ml of contrast medium. After three minutes, right atrial pacing was started at a rate of 100 beats per minute, increasing by 10 beats per minute every two minutes until the patient developed angina. When the pain had increased to moderate severity and persisted for one minute atrial pacing was discontinued and a second left ventriculogram performed at switch off using the same projection as at rest. Coronary arteriography was then carried out using the Sones technique.

**RADIONUCLIDE ANGIOGRAPHY**

Immediately after cardiac catheterisation the patient was transferred to the nuclear angiography laboratory and positioned under the detector of the multicrystal gamma camera (Baird-Atomic, System 77), in the right anterior oblique projection. After 30 minutes had elapsed from the end of coronary angiography, right atrial pacing to pain was restarted following the same procedure as above. At switch-off a 10 millicurie (mCi) bolus of technetium-99m as pertechnetate was injected into the right atrium through the pacing catheter, with a rapid saline flush. Counting was carried out for 50 seconds at a framing rate of 20 per second. Data were collected on to disc and stored on magnetic tape, correction having been made for the dead-time of the instrument and flood-field non-uniformity. Twenty minutes later a static background frame of residual intracardiac radioactivity was counted with the patient in the same position as previously. This frame was then stored on disc. Immediately afterwards a 15 mCi bolus was injected and the resting study performed. Before storage on magnetic tape, this was corrected for background activity as well as for dead time and non-uniformity.

**Data analysis**

**CONTRAST ANGIOGRAPHY**

From the cine angiogram, end-systolic and end-diastolic frames were visually selected, ignoring ectopic and post-ectopic beats. Using the catheter position as a guide, the perimeters were traced and superimposed. The aortic valve plane was also delineated. The areas and long axes of the ventricles were measured using a computerised pressure-pad technique as previously described.4 Ventricular volumes at end-systole and end-diastole were calculated by the area-length method modified for the right anterior oblique,6 and ejection fraction derived. Wall motion abnormalities were quantified by a hemi-axial method similar to that of Dwyer,10 and Leighton et al.11 The long axis of the ventricle at end-diastole was trisected and two points obtained one-third and two-thirds of the distance along it from the aortic plane to the apex. Perpendiculars were drawn from these points to the ventricular perimeters in systole and diastole. Thus, five hemi-axes were generated, as shown in Fig. 1, there being two anterior, two inferior, and one apical hemi-axis. The percentage shortening of each hemi-axis was calculated using the formula:

\[
\frac{\text{shortening of hemi-axis}}{\text{end-diastolic length of hemi-axis}}
\]

A shortening of less than 25 per cent was defined as hypokinesia5 and absence of inward wall motion as akinesis. All contrast angiograms, at rest and at pacing-induced angina, were analysed by this method.

**RADIONUCLIDE ANGIOGRAPHY**

After transferring the data from tape to disc, serial frames of each radionuclide study were summated over intervals of 1·5 seconds and the left ventricular phase identified. A region of interest was selected over the left ventricle using a magnetic pen and a grid array representing the 294 crystals of the detector. A time-activity curve from this region

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*Fig. 1  Hemiaxial model for wall motion analysis.*
was generated. A background frame was selected from the pulmonary phase and correction was automatically made spatially and temporally for the exponential decay of lung activity during all further data processing. The peaks and troughs of the laevophase, which represent end-diastolic and end-systolic counts, respectively, of individual cardiac cycles, were used to derive ejection fraction (count-volume method) and a representative cardiac cycle as previously described. From this representative cardiac cycle end-systolic, end-diastolic, and stroke volume images were obtained. End-systolic and end-diastolic perimeters were generated from these images using an edge enhancement technique whereby the band of counts from 25 to 30 per cent of the maximal count in any one cell (N max) was isolated, and returned to normal in each study to the image with the lower N max. These perimeters were then superimposed in each case so that wall motion could be assessed. The area-length formula was used to calculate ventricular volumes from the perimeters, and thus a geometric ejection fraction was obtained. Wall motion abnormalities were assessed by means of the same hemiaxial method as for contrast angiograms, both at rest and at pacing-induced angina. Normal values for shortening of each hemiaxis were obtained from the radionuclide angiograms of 22 patients with no evidence of cardiac disease. The means and the ranges of shortening for each hemiaxis are shown in the Table. Hypokinesis of a hemiaxis was objectively defined as a percentage shortening of less than two standard deviations below the mean percentage shortening of that axis in normals. Akinesis was defined as for contrast angiograms.

**CORONARY ARTERIOGRAMS**

Coronary artery stenoses were regarded as significant if they were greater than 50 per cent of the luminal diameter.

<table>
<thead>
<tr>
<th>Hemiaxis</th>
<th>Normal range of shortening (mean ± 2 SD)</th>
</tr>
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<tbody>
<tr>
<td>Anterior</td>
<td>52.7 ± 32.0</td>
</tr>
<tr>
<td>Apical</td>
<td>81.7 ± 31.2</td>
</tr>
<tr>
<td>Inferior</td>
<td>83.0 ± 36.5</td>
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<td></td>
<td>81.1 ± 36.0</td>
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<td>37.2 ± 37.6</td>
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**Results**

**CORONARY ANGIOGRAPHY**

Thirteen patients were studied. Six patients had triple vessel disease, five had double vessel disease, and two single vessel disease. Two of the patients had a significant left main stem stenosis.

**EJECTION FRACTION**

Fig. 2 shows the relation between the resting nuclear count-volume ejection fraction and the geometric ejection fraction derived from the contrast angiograms. Though there is a significant correlation (r = 0.636, p < 0.05), there was excessive scatter in the higher ejection fraction range. The method distinguished those patients with low ejection fraction. On pacing, the levels of ejection fraction obtained by the two methods are shown in Fig. 3. There is a better correlation (r = 0.801, p < 0.001)
and this is consistent with the lower values obtained during angina by both techniques.

The change in ejection fraction caused by pacing to angina was calculated by contrast angiography and both nuclear methods (count-volume and area-length). Mean ejection fraction fell significantly for contrast angiograms from 62·6 to 40·3 (p < 0·05). Geometric ejection fraction for nuclear angiograms fell from a mean of 71 to 55·1 (p < 0·02) and mean count volume ejection fraction from 59·3 to 51·15 (p < 0·05). Thus there was a significant fall in ejection fraction on pacing as judged by all three methods of analysis.

Fig. 4 shows the relation between the change in radionuclide ejection fraction assessed by the count volume and geometric contrast methods. There is a significant correlation between the two (r = 0·622, p < 0·05) and those patients with the larger falls in ejection fraction are identified by both methods.

There is a close relation between the area-length and count-volume methods which were applied to nuclear angiograms (Fig. 5a and 5b). There is a highly significant correlation at rest (r = 0·913, p < 0·001) and on pacing (r = 0·859, p < 0·001). Thus there was good evidence that either method may be applied to ejection fraction calculations and also that the perimeters used for the area-length method are valid.

Regional wall motion
All six pacing-induced anterior hypokinetic zones demonstrated by contrast angiography were identified by the nuclear technique also. Similarly, four of four inferior zones of pacing-induced hypokinesis assessed by contrast angiography were seen on nuclear angiography. One of three apical zones was demonstrated. Thus, of 13 zones of wall motion abnormality unmasked by pacing and shown by contrast angiography, 11 were seen by objective analysis of nuclear angiograms. The two cases which had apical abnormalities during pacing stress on contrast but not nuclear angiography had anterior hypokinetic segments demonstrated by the isotope technique.

The 11 zones of pacing-induced wall motion abnormality were seen in regions supplied by
Atrial pacing and nuclear angiography

Fig. 6  Change in ventricular contraction induced by pacing to angina. (a) Rest nuclear angiogram end-diastolic and end-systolic perimeters; (b) paced nuclear angiogram end-diastolic and end-systolic perimeters; (c) rest contrast angiogram end-diastole; (d) rest contrast angiogram end-systole; (e) paced contrast angiogram end-diastole; (f) paced contrast angiogram end-systole.
significantly stenosed coronary arteries. Seven akinetic segments seen on the contrast angiograms were shown to be abnormal by the nuclear method. Three were inferior in location, two anterior, and two apical. All eight patients who developed pacing-induced abnormalities seen in the contrast study also had zones of hypokinesia unmasked by pacing during the nuclear study. Fig. 6 shows the change in ventricular contraction caused by pacing to angina in one of the patients. In both contrast and nuclear angiograms there is a distinct fall in ejection fraction on pacing, and generalised hypokinesia develops when assessed by both methods.

Discussion

First-pass radionuclide ventriculography is an accepted technique for the assessment of ejection fraction at rest and has been correlated with contrast angiography. Dymond et al. have also reported its use in the assessment of regional dysfunction caused by left ventricular aneurysms both at rest and on moderate exercise.

The major alternative to the first-pass technique in radionuclide ventriculography is that of gated blood pool scanning. Though this method has been shown to be reliable for the assessment of ejection fraction an important limitation is that imposed by overlapping of cardiac chambers. For this reason, the projection usually used in gated studies is the left anterior oblique which is not ideal for assessing regional wall motion abnormalities of the left ventricle. Another problem is the length of time needed to collect data during a gated procedure. This has been reported as one to two minutes by Borer et al. and up to eight minutes by Folland et al. Therefore, it is extremely difficult to collect data representing the precise situation at the time of stress endpoint. Borer et al. using the gated technique, reported changes in ejection fraction and wall motion during exercise in patients with coronary disease, though there was no comparison with contrast angiography at angina in these patients and also no quantification of wall motion abnormalities.

This is the first report of an assessment of wall motion abnormalities induced by myocardial ischaemia in the right anterior oblique projection which also affords a direct comparison with a contrast method. Since Sowton et al. first described its use, atrial pacing has remained a useful tool for the induction of myocardial ischaemia in a relatively controlled situation. Dwyer, and Rickards et al. report the unmasking of wall motion abnormalities by pacing at the time of contrast angiography. Marshall et al. have shown good agreement between successive studies with the first-pass technique and Bodenheimer et al. also showed that the order in which the respective obliques were used in a biplane study did not affect the results obtained. Thus, there is no evidence that significant errors are introduced by the performance of sequential studies without intervention.

The hemiaxial method of wall motion analysis was developed by Leighton et al. for contrast angiograms, though Dwyer used a similar technique for an assessment of pacing-induced abnormalities. Bodenheimer et al. used the method in their assessment of wall motion abnormalities by first-pass radionuclide angiography at rest and found a good correlation between contrast and nuclear angiography in the right anterior oblique projection.

A possible criticism of our method is that, unlike Leighton et al. and Bodenheimer et al., no allowance is made for shift of long axis between end-systole and end-diastole, which might lead to errors in assessment of apical wall motion changes. In this study, the definition of normal wall motion is based on the results of 22 patients without heart disease who were studied at rest.

In addition, all changes are occurring in the same patient between rest and exercise and compared with contrast angiograms analysed in the same way. Leighton et al. who did allow for axis shift, noted the wide variation in apical wall motion and felt that akinesis was necessary before wall motion abnormalities of the apical region could be judged as significant.

Both methods of analysis showed the expected fall in ejection fraction on pacing to angina. The overestimation of ejection fraction by the nuclear techniques in the patients with higher ejection fraction may be the result of a tendency to underestimate end-systolic volumes when they are small and, therefore, contain less counts. Since edge detection is dependent on Poisson statistics, the error increases as the count diminishes. The radionuclide technique proved reliable in the identification of abnormally contracting segments. All patients who developed wall motion changes as detected by contrast angiography were identified by the nuclear technique. Only in the apical region were changes seen on contrast angiography but not by the first-pass study. In those two patients there were anterior regions of hypokinesia which developed on pacing identified by both techniques. Thus, the wide variation in apical wall motion seen on contrast angiography is paralleled by
Atrial pacing and nuclear angiography

the nuclear techniques, and stricter criteria should perhaps be applied to the assessment of wall motion abnormality in this region.

This study has shown that first-pass radionuclide angiography can demonstrate changes in wall motion induced by acute ischaemic stress. This suggests that the technique may be extended with confidence to the assessment of wall motion changes induced by other forms of stress, for example exercise. Any changes that occur may be assessed in terms of global or regional ventricular function and allow the effect of interventions such as surgery or drug treatment to be judged at times of stress as well as at rest. In combination with the other non-invasive techniques it may also be able to play an important part in the screening of patients with coronary disease.

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