

Detection of Coronary Stenoses by Stress Echocardiography Using a Previously Implanted Pacemaker for Ventricular Pacing: Preliminary Report of a New Method

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Summary

Background: The number of patients with pacemakers has been increasing and a large number of them will present with chest pain or symptoms suggesting angina pectoris. Myocardial ischemia and presence of coronary artery disease are difficult to detect and assess by noninvasive methods in patients with a pacemaker; the electrocardiogram (ECG) at rest and during exercise is usually very difficult to analyze in terms of ischemia or even presence of an acute myocardial infarction.

Hypothesis: To detect significant coronary stenosis in patients with previously implanted pacemakers, we tested a new stress echocardiography method using incremental ventricular pacing by already implanted pacemakers.

Methods: We studied prospectively 25 consecutive patients who underwent stress echocardiography with increasing ventricular pacing up to either 85% of the age-predicted maximal heart rate or chest pain. Positive tests were defined by new hypokinesia or worsening of a preexisting alteration in wall motion in at least two adjacent territories. All patients underwent coronary angiograms to define the presence and severity of coronary stenoses.

Results: Among the 25 tests, 11 (44%) were stopped for chest pain, 1 (4%) for moderate discomfort, 1 (4%) for a drop in blood pressure, and the target pacing rate was achieved in the tests of the remaining 12 patients (48%). There were no complications. Thirteen patients had significant stenoses. In 10 cases, stress echocardiography was a true positive test with respect to coronary angiography. There were 11 true negative, 1 false positive, and 3 false negative tests. The sensitivity was 77%, specificity was 90%, the positive predictive value was 91%, and the negative predictive value 79%. The accuracy was 84%.

Conclusions: This new stress echocardiography method appears feasible, easy, safe, and effective for detection of significant coronary stenoses in patients with pacemakers.

Key words: stress echocardiography, pacemaker, ventricular pacing, coronary artery disease

Introduction

The number of patients with pacemakers has been increasing and a large number of them will present with chest pain or symptoms suggesting angina pectoris. Myocardial ischemia and presence of coronary artery disease are difficult to detect and assess by noninvasive methods in patients with a pacemaker; the electrocardiogram (ECG) at rest and during exercise is usually very difficult to analyze in terms of ischemia or even presence of an acute myocardial infarction.¹ In fact, ECG tracings are often continuously paced, ventriculograms and repolarizations are not analyzable, or at least in spontaneous rhythm repolarization is severely altered by the Chatterjee phenomenon.^{2,3} However, echocardiography performed with either pharmacologic stress, especially dobutamine,⁴ or exercise stress^{5–7} has been demonstrated to be reliable in the detec-

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tion of coronary artery disease. Some studies have tested and validated stress echocardiography methods using atrial pacing via esophageal leads with either transthoracic^{8, 9} or transesophageal echocardiography;^{10, 11} however, there are no reports on the use of implanted pacemakers to apply an incremental ventricular pacing as stress. This prospective study was designed to assess the feasibility and ability of this kind of ventricular pacing to produce ischemic stress and to detect significant coronary stenoses in patients with previously implanted pacemakers.

Methods

Patients

Between May 1996 and December 1997, patients with a single-chamber ventricular pacemaker or a dual-chamber pacemaker referred to our cardiology department for coronary angiography because of a suspected or known coronary artery disease and chest pains in a stable condition underwent this new stress echocardiography method. All patients gave their informed consent to this study protocol. Patients with a recent myocardial infarction (< 2 months) or clinical signs of unstable angina or congestive heart failure were excluded. Thus, 25 consecutive patients were included.

Stress Echocardiography

All tests were performed after withdrawal of all antianginal medications for at least 48 h in patients who had been taking these medications. Stress echocardiography was performed by a single trained physician who was blinded to the clinical data. Stress echocardiography was performed using a commercially available Advanced Technology Laboratory HDI 3000 echograph (ATL Ultrasound, Inc., Bothell, Wash., USA), with a 2.5 MHz transducer linked to a digital work station (Mediasys Digital Systems, Gif sur Yvette, France) for computer-assisted analysis of digital sequences at different stages. The 16-segment model recommended by the American Society of Echocardiography¹² was used to score regional wall motion and to calculate the overall wall motion score index. A segment with a normal motion was scored 1, an hypokinetic segment 2, an akinetic segment 3, and a dyskinetic segment 4. In addition to segmental wall motion, normal myocardial thickening (or its absence) was considered to be a complementary criterion to classify the segments as normal or abnormal. Thus, for a segment to be scored as abnormal it had to have both a deficit in wall motion and parietal thickening. All pacemakers were converted in VVI mode at the beginning of the test; the ventricular pacing rate was usually started at 70 beats/min and then increased progressively. The reference stage considered as prestress was the first pacing rate with a 100% permanent ventricular paced rhythm (usually 70/min). This reference stage was chosen to distinguish between possible wall motion abnormalities induced by right ventricular pacing and those derived from the incremental rate of ventricular pacing as stress method. This was particularly important for apical sep-

tal and apical inferior segments, in which a frequent moderate asynchronous contraction,¹³ but with a normal thickening, was observed because of the ventricular paced rhythm. Then, the ventricular pacing rate was increased by 20 beats/min every 3 min until an endpoint criterion was reached: chest pain, complications or side effects, drop in blood pressure < 100 mmHg, elevation of systolic blood pressure \geq 220 mmHg, arrhythmia, or achievement of the target rate (85% of the age-predicted maximal heart rate). After 3 min at the maximal rate or when the endpoint was reached, the pacing rate was reduced to 70 beats/min. Patients who suffered typical anginal chest pain received sublingual nitroglycerin. In each patient, four usual views of the left ventricle (parasternal long- and short-axis papillary muscle, apical four- and two-chamber views) were recorded along with four continuous loop images of the stress echocardiograms in a quad screen format: (1) at basal rate considered as prestress, (2) at an intermediate stage, (3) at peak stress pacing rate, and (4) after 3 min of recovery at the basal ventricular pacing rate. Throughout the test, the ECG was monitored, a 12-lead ECG tracing was performed by a trained nurse, and blood pressure was measured at each stage during the first min and every min during the 5 min recovering period. The patients were monitored for 15 min after the end of the test and then were discharged after changing the pacing mode to the usual one.

Image Analysis and Interpretation

The stress tests were analyzed for the presence of a new significant wall motion abnormality, considered to be a marker of coronary artery disease, by the simultaneous reading by three experienced observers blinded to clinical data, as proposed by Mairesse *et al.*¹⁴ in the case of left bundle-branch block, which is quite similar to right ventricular pacing. The observers assessed the loop images of the four stages of each incidence to detect new wall motion abnormalities. The test was regarded as positive when a new alteration was observed in the case of basal normal kinetics or if there was a worsening of the basal wall motion abnormalities in at least two consecutive segments between basal and peak stress sequences. The wall motion score index was calculated at both prestress and peak stress stages. The arteries expected to have significant stenoses were diagnosed with the usual distribution of perfusion of the 16 segments by the three coronary arteries.¹²

Coronary Angiograms

Coronary angiograms were performed via femoral approach in all patients 24 or 48 h after stress echocardiography. Angiograms were analyzed by two experienced cardiologists independent of the echocardiographers to detect > 50% stenoses which were regarded as significant. In case of disagreement, a third physician joined the former two in a panel to reach a consensus. The presence of at least one coronary vessel with significant stenosis was used to define a patient with a significant coronary artery disease, while the absence of significant stenosis defined patients without coronary artery disease.

Statistical Analysis

The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the stress echocardiography method to detect significant coronary artery disease were calculated. The qualitative variables were compared using Fisher's exact test and quantitative variables using the Mann Whitney test to assess differences between patients with a positive and negative test. The Wilcoxon test was used for comparison of paired series.

Results

Patient Characteristics

There were 21 men and 4 women (mean age 71 ± 7 years); 12 were smokers, 5 were diabetics, and 9 had hypercholesterolemia. Five patients had had documented myocardial infarction and previous coronary angiography; of these, one had had a previous coronary angioplasty, one coronary bypass, and one both interventions. Two other patients without previous myocardial infarction but with known angina pectoris had had angioplasty for one and coronary bypass for the other. The pacemaker had been implanted for a mean period of 56 ± 35

months. The clinical and ECG data, and the characteristics of the pacemakers are presented in Table I. In 14 patients, an exercise test had been performed on a bicycle ergometer using a stepwise protocol of 30 W every 3 min and started at 30 W. It was stopped for muscular limitation in 13 and angina in 1. The exercise ECG was not analyzable in 13 patients, including the patient with angina. A 4-mm ischemic ST depression, without angina, was observed in a patient who recovered spontaneous ventriculograms when atrial fibrillation was accelerated.

Stress Echocardiography Examination

The starting pacing rate (for a 100% paced rhythm) was 70 beats/min for 22 patients and 80 beats/min for 3 patients. The maximal pacing rate reached was between 100 and 140 beats/min. Among the 25 tests, 11 (44%) were stopped for chest pain—at 85% of age-predicted maximum rate in 6 patients and at a lower level in 5 patients (typical anginal chest pain in 9 cases and atypical in 2 cases); for moderate discomfort in 1 patient (4%) with elevation of blood pressure; and an asymptomatic drop in blood pressure in 1 patient (4%). In the remaining 12 patients (48%), the test was stopped because the target pacing rate had been reached. The chest pains disappeared quickly after the return to a basal pacing rate at 70

TABLE I Clinical, electrocardiographic, and pacing characteristics of the patients

Patient No.	Age (years)	Sex	Known CAD	Atrial rhythm	Indications	Vent paced	PM	Time (months)
1	74	M	Yes	AF	Brady/tachy	Permanent	VVIR	60
2	76	M	No	Sinus	Atriovent B	Permanent	DDDR	48
3	68	M	Yes	Sinus	Atriovent B	Permanent	VVIR	84
4	76	M	No	Sinus	Atriovent B	Permanent	VDDR	24
5	68	M	Yes	AF	Atriovent B	Permanent	VVIR	72
6	75	M	No	AF	Brady	Permanent	VVIR	92
7	77	M	No	AF	Brady	Permanent	VVIR	2
8	77	F	No	Sinus	Brady/tachy	Permanent	DDDR	18
9	70	F	No	Sinus	Sick sinus	Intermittent	DDDR	48
10	77	M	No	Sinus	Brady/tachy	Permanent	DDDR	5
11	61	M	No	AF	Atriovent B	Permanent	VVIR	120
12	75	M	Yes	Sinus	Atriovent B	Permanent	DDDR	48
13	78	F	No	Sinus	Brady/tachy	Intermittent	VVIR	36
14	69	M	No	Sinus	Atriovent B	Permanent	VVIR	120
15	73	M	No	Sinus	Sick sinus	Intermittent	VVIR	36
16	71	M	No	Sinus	Brady/tachy	Intermittent	VVIR	72
17	79	M	No	Sinus	Sick sinus	Permanent	DDDR	96
18	65	M	No	Sinus	Sick sinus	Intermittent	DDDR	62
19	59	M	Yes	Sinus	Sick sinus	Permanent	DDDR	60
20	70	M	No	Sinus	Sick sinus	Permanent	DDDR	72
21	74	F	Yes	Sinus	Brady/tachy	Permanent	DDDR	48
22	53	M	No	Sinus	Atriovent B	Permanent	DDDR	3
23	68	M	Yes	Sinus	Sick sinus	Permanent	DDDR	96
24	74	M	No	AF	Atriovent B	Permanent	VVIR	1
25	56	M	No	Sinus	Sick sinus	Permanent	DDD	72

Abbreviations: M = male, F = female, AF = atrial fibrillation, Atriovent B = atrioventricular block, Sick sinus = sick sinus syndrome, Brady = bradycardia, Tachy = tachycardia, Vent paced = ventricular paced rhythm, PM = type of pacemaker, Time = time from implantation.

beats/min in seven patients and a few minutes after sublingual nitroglycerin in four patients. There were no major complications. No significant atrial or ventricular arrhythmia was detected. One patient (No. 18) had few isolated ventricular premature beats during 2 min at the last stage of the pacing stopped for moderate angina. Minor discomfort was noted with a moderate elevation in blood pressure (170/90 mmHg) in one patient (No. 14) at the last stage of the test and a drop in blood pressure (90/40 mmHg) in one patient (No. 22). These side effects rapidly disappeared on a prompt return to the basal pacing rate (70/min) with no requirement for drug infusion. The mean duration of ventricular pacing was 11 ± 1 min (range 5–14 min).

Coronary Angiography

The results of coronary angiographies are given in Table II. There were 13 patients with significant stenoses, 3 patients with single-vessel disease, 5 with double-vessel disease, and 5 with triple-vessel disease. In the three patients who had undergone coronary bypass, the grafts were assessed instead of the bypassed vessel and its territory. Twelve patients had no significant stenoses (normal angiograms in 10 and minor non-significant plaques in 2).

Results of Stress Echocardiography

Details of the stress tests are shown in Table II. The quality of images was good in 21 and moderate in 4 patients; nevertheless, the 16 segments could be assessed in these four patients, and the segments were correctly classified as 1 true positive and 3 true negative. The stress test was considered as positive in 11 and negative in 14 patients. Among the 11 positive tests, 3 ± 1 new altered segments were noted (range 2–6). The predicted significantly narrowed artery was left anterior or descending in five patients, left circumflex in four, and right coronary artery in four patients. In two patients, two vessels (left anterior descending and left circumflex) were predicted to be narrowed.

Stress echocardiography was true positive with respect to coronary angiography in 10 cases. There were 11 true negatives, 1 false positive, and 3 false negatives. Thus, sensitivity was 77%, specificity 90%, positive predictive value 91%, and negative predictive value 79%. The accuracy was 84% (21 of 25 patients correctly classified). The arteries predicted as being significantly narrowed had a significant angiographic lesion in all cases, and this was the most significant lesion shown by angiography (except in the false positive case), but in the patients with multivessel disease the number of diseased ves-

TABLE II Results of stress echocardiography and coronary angiography

Patient No.	Max rate (beats/min)	Arrest criterion	WMS index initial/final	Induced abnormality	No. of new altered segments	Predicted vessels	Angiographic diseased vessels
1	125	Angina	1.94/2.56	Yes	2, 3, 6, 8, 9, 12	LAD, Cx	LAD (80), Cx (70)
2	120	Angina	1.12/1.81	Yes	11, 12, 13, 14, 15, 16	LAD, Cx	LAD (70), Cx (90), RCA (70)
3	130	Angina	2.12/2.25	Yes	3, 9, 15	Cx	Cx (90), RCA (50)
4	125	Target rate	2.12/2.12	No	None	None	None
5	130	Chest pain	1.81/2.31	Yes	12, 13, 14, 16	LAD	LAD (80)
6	125	Target rate	1.25/1.25	No	None	None	None
7	100	Angina	1.81/2.31	Yes	6, 11	RCA	LAD (60), Cx (80), RCA (90)
8	120	Target rate	2.5/2.5	No	None	None	None
9	130	Chest pain	1/1	No	None	None	None
10	120	Target rate	1/1.06	No	None	None	None
11	120	Angina	1.25/1.81	Yes	5, 6, 11, 12	RCA	LAD (50), Cx (50), RCA (80)
12	120	Target rate	2.25/2.25	No	None	None	LAD (60), RCA (100)
13	120	Target rate	1/1	No	None	None	None
14	130	Discomfort	1.12/1.44	Yes	2, 7, 8	LAD	LAD (80)
15	125	Target rate	1/1.43	No	None	None	None
16	125	Target rate	2.06/2	No	None	None	None
17	120	Target rate	1/1	No	None	None	None
18	130	Angina	1.19/1.38	Yes	3, 4, 9, 10, 15	Cx	LAD (80), Cx (80), RCA (100)
19	135	Angina	1.12/1.25	Yes	5, 11	RCA	Cx (90), RCA (100)
20	125	Target rate	1/1	No	None	None	None
21	125	Angina	2.44/2.44	No	None	None	Cx (100), RCA (100)
22	140	Drop in BP	1.07/1.57	Yes	11, 12	LAD	None
23	130	Target rate	1.94/1.81	No	None	None	Cx (100)
24	125	Target rate	1.38/1.38	No	None	None	None
25	130	Angina	1.25/1.56	Yes	5, 11, 16	RCA	LAD (70), Cx (70), RCA (90)

Abbreviations: LAD = left anterior descending, Cx = circumflex, RCA = right coronary artery, (%) stenosis, WMS = wall motion score, BP = blood pressure.

sels was always underestimated except in the case of one patient with double-vessel disease (see Table II). Among the three patients with false negatives, it should be mentioned that all had a complete thrombosis of the circumflex artery and a previous myocardial infarction with an inferior akinetic plaque. One patient had only this lesion, another also had complete thrombosis of the right coronary, and the last patient with a triple-vessel disease had an occlusion of the right coronary with a moderate significant stenosis of the left anterior descending artery. Moreover, in these three patients, the presence of a coronary artery disease was previously known.

In the 20 patients without previous myocardial infarction, there were 8 true positives, 11 true negatives and 1 false positive. In this subgroup, sensitivity was 100%, specificity 92%, positive predictive value 88%, negative predictive value 100%, and the accuracy was 95%. In the 18 patients without previously demonstrated coronary artery disease, 6 true positives, 11 true negatives and 1 false positive were noted. In this subgroup, sensitivity was 100%, specificity 92%, positive predictive value 86%, negative predictive value 100%, and the accuracy was 94%.

Exercise tests were performed in 14 patients. Only one exercise test had been considered as positive on ECG criteria. Stress echocardiography allowed to classify 13 of these 14 patients correctly (a false positive stress echocardiogram).

Comparison of patients with positive and negative tests is presented in Table III. We noted significant differences only regarding age (66 vs. 74 years), hypercholesterolemia (7 vs. 2), arrest due to angina (8 vs. 1), any chest pain at the end of the test (9 vs. 2), mean drop in systolic blood pressure between maximal stress and initial stage (5 ± 17 vs. 26 ± 22 mmHg), mean drop in diastolic pressure (0 ± 15 vs. 10 ± 13 mmHg), and clear-cut stenoses on angiogram (10 vs. 3).

This new stress echocardiography method thus appears to be safe, feasible, quick, and accurate (overall accuracy 84%)

for the detection of significant coronary stenoses in patients with previously implanted pacemakers.

Discussion

Feasibility of the Method

This new method is convenient in patients with a pacemaker, and we observed no severe complications, in particular no arrhythmia. Patients usually experienced a moderate drop (except in one case) in both systolic and diastolic blood pressure, which is commonly observed with rapid ventricular pacing. A number of patients experienced moderate chest pain on pacing, which quickly disappeared on return to basal VVI mode. Patient tolerance was good and was better than with transesophageal pacing and transesophageal echocardiography.⁸⁻¹¹ The ability to stop the pacing at once and to return to baseline ventricular rhythm is an advantage for the slow reduction of tachycardia induced by dobutamine to obtain a shorter recovery period. The duration of the test appears to be shorter than that with a pharmacologic stress test. These advantages seem in agreement with the recent study of Lee *et al.*¹⁵ that compared transesophageal atrial pacing and dobutamine stress for stress echocardiography.

Experimental animal studies^{16, 17} have suggested that right ventricular pacing may decrease regional blood and alter left ventricular depolarization. Nevertheless, a study in humans¹³ comparing the effects of atrial, ventricular, and sequential atrioventricular pacing on coronary flow in the left anterior descending artery demonstrated that the ventricular pacing mode may lower resting coronary blood velocity but not maximal coronary blood flow in some patients. Thus, when the reference stage takes into account the ventricular paced wall motion, incremental ventricular pacing may be a useful meth-

TABLE III Comparison of patients with positive and negative stress tests

Characteristics	Positive tests n = 11	Negative tests n = 14	p Value
Age (years)	66 ± 8	74 ± 3	0.01
Male gender	10	11	NS
Hypercholesterolemia	7	2	0.02
Smokers	7	5	NS
Diabetes	3	2	NS
Previous MI	2	3	NS
Hypertension	9	9	NS
Angiographic significant stenoses	10	3	0.001
Maximal stimulation rate (beats/min)	126 ± 10	124 ± 3	NS
Arrest for angina	8	1	0.002
Arrest for chest pain	9	2	0.001
Mean drop in SBP (mmHg)	5 ± 17	26 ± 12	0.01
Mean drop in DBP (mmHg)	0 ± 15	10 ± 13	0.03
Initial wall motion score index	1.43 ± 0.39	1.57 ± 0.61	NS
Final wall motion score index	1.84 ± 0.45	1.59 ± 0.58	NS

Abbreviations: MI = myocardial infarction, SBP = systolic blood pressure, DBP = diastolic blood pressure, NS = not significant.

od for producing ischemic stress during echocardiography. In fact, ventricular pacing is feasible in the large majority of patients with pacemakers (except in those with an single-chamber atrial pacemaker) and is the only incremental pacing mode possible up to a high target rate in patients with single-chamber ventricular pacemakers or atrial fibrillation. This ventricular pacing allows a standardization of the test for a large population of patients with pacemakers when atrial or sequential pacing using pacemakers could previously be tested in only a part of patients.

Accuracy of This Method

Sensitivity (77%), specificity (90%), and accuracy (84%) of our method seemed in line with those recently reported in a large review of numerous studies of dobutamine stress echocardiography,¹⁸ that is, 80, 84, and 92%, respectively. These criteria also appeared to be in agreement with those of other usual stress echocardiographic methods using exercise or dipyridamole as stress agent.¹⁸

To our knowledge, only atrial pacing had been employed as pacing stress for echocardiographic examinations⁸⁻¹¹ in patients with moderate acceptance of either transesophageal pacing lead⁸ or transesophageal echocardiographic probe.⁹⁻¹¹ Overall, these studies reported an approximate 80% specificity, a 90% sensitivity, and a 90% accuracy, which are in line with our findings. Dobutamine stress echocardiography had been tested with promising results in a case of complete left bundle-branch block,¹⁴ in which ventricular depolarization resembled that obtained by right apex ventricular pacing using an implanted pacemaker. A sensitivity of 80%, a specificity of 87%, and an accuracy of 85% were reported in this case.

With respect to the location of the narrowed coronary arteries (except in the false positive case) it should be mentioned that the artery predicted by the test as narrowed always had a significant stenosis. Detection of the most significant stenosis was good, but the overall extent of the disease shown by angiography was underestimated. This underestimation of multi-vessel disease by stress echocardiography has been previously reported.¹⁸ Several factors contribute: limitations in stress protocols, premature cessation of stress test because of limiting ischemia, variations of anatomic distribution of coronary arteries, and comparison of a functional method with an angiographic standard. In terms of sensitivity, three false negative tests were observed in patients with large inferior akinetic plaques in the left ventricle resulting from previous inferior infarctions with a complete occlusion of the circumflex artery. A lower sensitivity for detection of circumflex stenoses is usually observed.¹⁸

Perspectives

This new simple method will provide a diagnostic tool for patients with pacemakers to detect coronary stenoses in those with no known coronary artery disease. This technique may be especially valuable for the exclusion of coronary artery disease in patients without a previous history of myocardial

infarction or known coronary disease. It can also be employed to assess the extent of myocardial ischemia in patients with known coronary artery disease and the functional significance of angiographically demonstrated lesions before and after therapeutical interventions. The VVI pacing mode is feasible with a large majority of pacemakers. Atrial pacing or atrioventricular sequential pacing using an implanted pacemaker should be interesting to test in particular groups of patients in whom it could be performed. When possible, this method should be compared with tomoscintigraphy and/or other types of pharmacologic stress echocardiography to determine its ability to detect myocardial ischemia as well as coronary stenoses more precisely. It should also be of interest to compare pacing via implanted pacemaker with other possible stress methods (pharmacologic or exercise tests). Its safety should allow its use in larger patient populations (i. e., those with various symptoms suggestive of a coronary artery disease, severe angina, postmyocardial infarction, etc.).

Limitations

Apart from the usual limitations of stress echocardiography (image quality, operator dependence), the main limitation is the presence of large akinetic regions secondary to a myocardial infarction, which reduces the ability to induce and detect new alterations in wall motion, but in this case the diagnosis of coronary artery disease has previously been established. This method thus appears more suited to patients with no previous large myocardial infarctions. The small number of patients of this first report is also a limitation, and further studies of larger patient populations will be required for a more complete assessment of the method and its reproducibility.

Conclusions

This new stress echocardiography method appears to be a convenient and safe way of detecting coronary stenoses in patients with pacemakers. It effectively transforms an implanted pacemaker into a useful and simple tool for stress echocardiography.

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