Effects of atrial pacing stress test on ultrasonic integrated backscatter cyclic variations in normal subjects and in patients with coronary artery disease

S. Iliceto*, L. Galiuto, P. Colonna*, V. F. Napoli and P. Rizzon

Institutes of Cardiology, University of Bari and *Cagliari, Italy

Aims To evaluate the effects of acute, atrial pacing-induced, reversible myocardial ischaemia on myocardial thickening and integrated backscatter cyclic variations in patients with or without coronary artery disease.

Methods and results Thirty-six patients with suspected coronary artery disease underwent transoesophageal echocardiography with simultaneous atrial pacing, and coronary angiography. In myocardial segments not related to a significantly narrowed coronary artery, both from patients with and without coronary artery disease, thickening and integrated backscatter cyclic variations were not reduced at peak pacing. In segments related to a significantly narrowed coronary artery, thickening decreased at peak pacing, was still reduced at pacing interruption and recovered at 2 min, while backscatter cyclic variations, blunted at peak pacing, immediately recovered after pacing interruption.

Conclusion During stress-induced myocardial ischaemia, backscatter cyclic variations are blunted and thickening reduced. Returning to baseline, pre-atrial pacing values occur more rapidly in backscatter cyclic variations than when thickening takes place. Evaluation of stress-induced alterations in backscatter cyclic variations may aid in the identification of ischaemia-induced regional left ventricular functional impairment and, hence, in coronary artery disease diagnosis.

Key Words: Integrated backscatter, transoesophageal echocardiography, stress-induced ischaemia, myocardial thickening.

Introduction

Ultrasonic tissue characterization is an innovative approach to the evaluation of the structural and functional state of the myocardium, providing quantitative indexes of its physical properties and pathophysiological changes1-3. Ultrasonic beams are refracted by scatterers smaller than their wave length and unprocessed radio frequency signals, re-directed back to the transmitting transducer, provide quantitative information about intramural architecture in terms of ultrasonic integrated backscatter4.

During contraction and relaxation of the myocardium, integrated backscatter has cardiac cycle-dependent variations with higher values in diastole and lower in systole. These cyclic variations of integrated backscatter are an expression of regional intramural myocardial contractile performance5-8 and are correlated, but not necessarily dependent, on inotropic state changes9. In experimental models of temporary coronary occlusion followed by reperfusion, integrated backscatter cyclic variations are promptly blunted by acute myocardial ischaemia and progressively return to baseline values during the post-ischaemic reperfusion phase10. However, despite this experimental evidence, little or no information is so far available in the clinical setting on the effect on integrated backscatter cyclic variations, and especially on their recovery phase, of acute, stress-induced, reversible myocardial ischaemia.

We hypothesized that acute myocardial ischaemia caused by a stress test capable of increasing oxygen demand could modify integrated backscatter cyclic variations. To verify this hypothesis this study investigated the effect of an atrial pacing stress test on cardiac-cycle
dependent variations of integrated backscatter and on myocardial thickening in patients with and without coronary artery disease. To this end, a group of patients without previous myocardial infarction was studied during simultaneous transoesophageal atrial pacing and imaging in both conventional echocardiography and densitometric mode.

**Materials and methods**

Thirty-six patients were enrolled in the study. They were undergoing stress transoesophageal echocardiography and coronary angiography for clinically indicated evaluation of chest pain, according to institutional guidelines. Thirty-one were male and five female; the mean age was 55.1 ± 12.3 years. Patients with previous myocardial infarction, previous cardiac surgery, left bundle branch block, valvular heart disease, mitral valve prolapse, cardiomyopathy or myocardial hypertrophy were excluded. In all patients coronary angiography was performed within 48 h of transoesophageal study during simultaneous atrial pacing. Cardioactive drugs were withheld for at least 72 h before transoesophageal echocardiography. All patients gave informed consent and the Institutional Ethical Committee approved the study protocol.

**Transoesophageal echocardiography at rest and during atrial pacing**

Transoesophageal examination was performed, after sedation with intravenously administered diazepam, using a 5 MHz omnilane transoesophageal probe connected to Hewlett Packard Sonos 1500 (Andover, U.S.A.) equipment; information on the electrocardiogram and blood pressure were monitored throughout the procedure and for 10–20 min after protocol cessation. After complete imaging of the heart and great vessels, the transoesophageal probe was advanced into the stomach and the transducer oriented in such a way as to obtain a clear and stable two-chamber view of the left ventricle. For the purpose of the present study, the transgastric view was selected since it allows excellent visualization of the anterior and inferior wall, perpendicular to the direction of the interrogating ultrasonic beam, and is thus ideal for both myocardial thickening and integrated backscatter data measurements.

Atrial pacing was performed by the transoesophageal approach using a special sheet designed by ARZCO (Arzco Medical System, Illinois, U.S.A.). This sheet has eight electrodes connected by wires to a transoesophageal atrial stimulator. It is designed in such a way as to be easily attached to a transoesophageal probe. The first electrode is located at the tip of the probe and the remaining seven are located at an equal distance of 5 mm. The stimulating sheet was connected to the ARZCO stimulator, which allows programmed atrial stimulation. Once the transoesophageal probe was positioned for optimal left ventricular imaging, several attempts were made to identify the electrode couple which permitted optimal and stable atrial capture. Usually this was achieved within 10 ms and an amplitude of 15–20 mA. Pacing was initially performed at a slow rate to ensure that the ventricle was not paced. The cycle length was then progressively decreased to 400 ms to select patients requiring premedication with atropine sulphate (0.02 mg kg⁻¹ intravenously) because of a low Wenckebach conduction point. Due to the premedication and sedation, the atrial pacing procedure was successful in all 36 patients and well tolerated in most cases. Continuous atrial pacing was performed according to a previously described protocol. Briefly, pacing was started at 110 beats min⁻¹ and increased every 3 min by 10 beats min⁻¹ until chest pain occurred or until a heart rate of 150 beats min⁻¹ was achieved, at which point pacing was continued for the entire acquisition time. We chose 150 beats min⁻¹ as an end point because this heart rate represents approximately 85 to 100% of the age-predicted heart rate of the majority of patients generally studied in our Institution. A 12-lead electrocardiogram at pacing interruption was considered positive for ischaemia if the ST segment was depressed at least 1 mm below the resting baseline level 0.08 s after the J point, with the ST segment slope 0 or greater.

**Ultrasonic tissue characterization data acquisition**

Both conventional and densitometric images were acquired using a two-dimensional ultrasonic tissue characterization prototype (Acoustic Densitometry system, Hewlett Packard), packaged in a Sonos 1500 machine, that permits real-time acquisition of myocardial integrated backscatter along each A-line in the field of view. A 5 MHz, 64-element phased-array transducer was used; signals from each transducer element were amplified, mixed to an intermediate frequency, phase shifted, delayed and summed with signals from all other elements. The summed intermediate frequency signal was then sent either to the standard video processing path or to a special integrated backscatter processor before scan conversion. The processor used employs digital hardware to produce a continuous signal that is proportional to the logarithm of integrated backscatter along each image line, with an integration time of 3-2 µs. The dynamic range of the integrated backscatter processor is approximately 30 dB. Integrated backscatter images were acquired in digital format and stored on an optical disk. Each digitized image contained 64 gray scale levels per pixel, yielding a resolution of 0.5 dB in integrated backscatter intensity per pixel. Pre-processing and post-processing gray scale curve settings were kept at identical levels for all patients. Pre-processing setting=1 and post-processing=0 were selected to...
ensure linearity of the backscatter measurements. Because the densitometric image remains under the influence of time gain compensation controls and transmit gain setting, the former was set as constant (140 dB) for both the anterior and the inferior wall, while the latter was adjusted to eliminate extraneous echoes from the ventricular cavity; these parameters were kept constant throughout the procedure. Compression and scan conversion settings do not affect ultrasonic tissue characterization data. 

Cardiac catheterization

Selective coronary angiography was performed in all 36 patients using the Seldinger technique. Significant coronary artery disease was defined as a visual estimation of luminal diameter narrowing of >50% in one or more major coronary vessels by two different observers unaware of the stress test results; if there was disagreement between the two observers, a third one was asked for final consensus.

Data analysis

Selection of patients and myocardial segments

Myocardial thickening and integrated backscatter cyclic variation analysis was performed, without knowledge of coronary angiography results, in all myocardial segments properly visualized on the long axis transgastric view; we discarded all segments in which the image quality was not sufficient to calculate the myocardial thickening and the integrated backscatter cyclic variations. According to the coronary angiography results, three groups of myocardial segments were identified: (1) myocardial segments supplied by normal coronary arteries in normal subjects, (2) myocardial segments supplied by coronary arteries without significant stenosis (narrowing <50%) in patients with coronary artery disease, (3) myocardial segments supplied by a significantly narrowed (≥50%) coronary artery in patients with coronary artery disease. We chose as a cut-off point, stenosis of 50% of the lumen according to most studies on validation of new stress tests. A myocardial segment was defined as being supplied by a significantly narrowed coronary artery if (a) it was anterior and the left anterior descending coronary artery was significantly narrowed or (b) it was inferior and both right and circumflex coronary arteries were significantly narrowed. On the other hand, a myocardial segment of a patient with coronary artery disease was defined as being supplied by a coronary artery without significant stenosis if (a) it was anterior and the left anterior descending coronary artery was not significantly narrowed or (b) it was inferior and both right and circumflex coronary arteries were not significantly narrowed.

Myocardial thickening

Myocardial thickening [(end-systolic thickness-end-diastolic thickness)/(end-diastolic thickness)x100] was measured only in those segments in which clear delineation of both endocardial and epicardial borders were obtainable in each of the four different moments of the atrial pacing protocol: baseline (cine loop acquired immediately before atrial pacing start), peak pacing (acquired 3 min after pacing at 150 beats min⁻¹), post-pacing (5 s after atrial pacing interruption), recovery (2 min after atrial pacing interruption). End-diastole was defined as the frame corresponding to the R wave of the electrocardiogram, and end-systole as that corresponding to the smallest left ventricular area. Cine loop reviewing was helpful in further improving the identification of endocardial borders and of end-diastolic and end-systolic frame selection. Myocardial thickness evaluation was performed on an 'Image Vue' computer workstation (Nova Microsonics, U.S.A.) equipped with specific software which permits the reviewing of echocardiographic images recorded on an optical disk. End-diastolic and end-systolic wall thickness were measured by means of software calipers at the central point of each segment. The percentage of wall thickening at each measurement point was then calculated for at least three consecutive cardiac cycles; values obtained were averaged and the final value used for analysis.

Ultrasonic tissue characterization

Ultrasonic integrated backscatter data were analysed in the same myocardial segments selected for thickening evaluation as well as in the same four moments of the atrial pacing protocol (baseline, at peak-pacing, 5 s and 2 min after pacing interruption).

Within a specific segment, an elliptical region of interest was placed in the subendo-midmyocardial portion of the left ventricular wall thickness, taking care to exclude the endocardial and epicardial reflection. During the integrated backscatter measurement in order to increase the signal-to-noise ratio, the region of interest was set as large as possible, at least 31 x 31 pixels. The selected region of interest was placed constantly in the same myocardial segment, by moving it to each new frame following the endocardial inward and outward motion of the left ventricular wall during the cardiac cycle. The mean integrated backscatter value within each region of interest was simultaneously displayed frame by frame on a time-intensity graph and expressed in decibels. Integrated backscatter cyclic variations were calculated, for each cardiac cycle, by the difference between end-diastolic peak to end-systolic nadir of integrated backscatter values, and then averaged for three consecutive cycles.

Reproducibility studies

In order to calculate intra- and inter-observer variability of both integrated backscatter cyclic variations and myocardial thickening, 30 myocardial segments,
randomly selected among patients with and without coronary artery disease, were independently analysed by two trained observers, and again 15 days later by one of the two. In five normal subjects, two consecutive rest transgastric two-chamber views were acquired in integrated backscatter mode 10 min apart. Segments from these images were analysed by the same observer to assess longitudinal reproducibility.

There were no significant differences between the data of the three repeated measurements of integrated backscatter cyclic variations. The mean absolute difference between observations was 1.3 ± 0.9 dB (inter-observer variability), and 1.6 ± 1.3 dB (inter-observer variability). The mean absolute difference for longitudinal measurements was 0.9 ± 1.3 dB with no significant difference between observations. Repeated measurements of myocardial thickening showed no significant differences. Intra-observer variability was 10.6 ± 10.4%, inter-observer variability 16.2 ± 14.8% and longitudinal reproducibility 2.6 ± 2.5%. All data are expressed as mean absolute difference between observations.

Statistical analysis

Data are expressed as mean ± 1 standard deviation. Within the same group of segments, repeated measures of analysis of variance (ANOVA), implemented with the Student t-test with Bonferroni’s correction, was used to determine the statistical significance of differences between protocol steps. Comparison between groups was obtained using the Student’s t-test for unpaired data.

Intra- and inter-observer variability, as well as longitudinal reproducibility of both integrated backscatter cyclic variations and myocardial thickening, were estimated by calculating the mean absolute differences between observations. The statistical difference between observations was assessed using repeated measures ANOVA with the Student t-test with Bonferroni’s correction (intra- and inter-observer variability) and with the paired t-test (longitudinal).16

Results

Of the 36 patients considered in this study, 10 had normal coronary arteries at coronary angiography; none of these patients developed electrocardiographic signs of myocardial ischaemia during atrial pacing. The remaining 26 patients had coronary artery disease (nine had significant stenosis of the left anterior descending, three of both the right and circumflex coronary artery, 14 of all three vessels); nine patients developed electrocardiographic signs of ischaemia during atrial pacing. In the 10 patients with normal coronary arteries, 23 myocardial segments could be evaluated: 12 were anterior and 11 inferior. In the 26 patients with coronary artery disease, 61 segments could be evaluated: 45 were in a territory unequivocally supplied by a significantly narrowed coronary artery (29 were anterior and 16 inferior), 16 were in a territory unequivocally supplied by a coronary artery without significant narrowing (6 were anterior and 10 inferior).

In the group of patients without coronary artery disease, the heart rate was 70.3 ± 7.9 beats·min⁻¹ at rest, 146 ± 3.9 at peak atrial pacing, 96.5 ± 6.9 after atrial pacing interruption and 85.3 ± 7.5 at 2 min recovery. In patients with coronary artery disease, the heart rate was 70.8 ± 9.5 beats·min⁻¹ at baseline, 142.8 ± 9 at peak atrial pacing, 98.8 ± 8.5 at post-atrivial pacing, 89.8 ± 6.9 at recovery.

Effects of atrial pacing stress test on myocardial thickening

In the group with normal segments, myocardial thickening was 44 ± 16% at rest, 37.9 ± 16.2% at peak atrial pacing (P=ns vs rest), slightly and significantly increased immediately after atrial pacing interruption (48.2 ± 27%; P<0.05 vs peak atrial pacing, P=ns vs rest) and returned to values not significantly different from baseline (45.2 ± 12%) at recovery.

A similar trend was observed in myocardial segments of coronary artery disease patients supplied by a coronary artery without a significant stenosis: myocardial thickening was 43.7 ± 14% at rest, 42.5 ± 11.4% at peak atrial pacing (P=ns vs rest), slightly but not significantly increased (46.2 ± 13%) immediately after atrial pacing interruption and returned to values not different from baseline (43.8 ± 12.2%) at recovery.

In the group of segments supplied by a significantly narrowed coronary artery, myocardial thickening significantly decreased from baseline to peak atrial pacing (from 41.4 ± 18.9% to 28.8 ± 16.1%, P<0.001), was still impaired 5 s after atrial pacing interruption (34 ± 17.8%, P<0.05 vs rest, P=ns vs peak atrial pacing) and returned to the baseline pre-atrivial pacing value at 2 min recovery (40.7 ± 12.9%, P=ns vs baseline, P<0.002 vs peak atrial pacing and atrial pacing interruption). Myocardial thickening values in the three groups of myocardial segments are schematically summarized in Table 1.

Effect of atrial pacing stress test on integrated backscatter cyclic variations

In the group with normal myocardial segments there were no significant differences in the magnitude of integrated backscatter cyclic variations between the four protocol moments. An example of the effect of an atrial pacing stress test on integrated backscatter cyclic variations in normal myocardium from a patient without coronary artery disease is presented in Fig. 1.

At each pacing protocol step, comparison of mean values of integrated backscatter cyclic variations

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Table 1  Integrated backscatter and myocardial thickening before, during and after atrial pacing

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Myocardial S</th>
<th>n</th>
<th>Baseline</th>
<th>Peak atrial pacing</th>
<th>Post atrial pacing</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Th (%)</td>
<td>Normal S</td>
<td>23</td>
<td>44 ± 16</td>
<td>37.9 ± 16.2</td>
<td>48.2 ± 27.4</td>
<td>45.2 ± 12.9</td>
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<td></td>
<td>CAD S supplied by CA without st</td>
<td>16</td>
<td>43.7 ± 14</td>
<td>42.5 ± 11.4</td>
<td>46.2 ± 13.6</td>
<td>43.8 ± 12.2</td>
</tr>
<tr>
<td></td>
<td>CAD S supplied by CA with st</td>
<td>45</td>
<td>41.4 ± 18.9</td>
<td>28.8 ± 16.1*¹</td>
<td>34.3 ± 17.8*¹</td>
<td>40.3 ± 12.9*²</td>
</tr>
<tr>
<td>IBScv (dB)</td>
<td>Normal S</td>
<td>23</td>
<td>7.4 ± 2.2</td>
<td>7.7 ± 1.8</td>
<td>7.8 ± 1.7</td>
<td>7.6 ± 1.7</td>
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<tr>
<td></td>
<td>CAD S supplied by CA without st</td>
<td>16</td>
<td>7.7 ± 1.5</td>
<td>7.1 ± 2</td>
<td>7.2 ± 2.2</td>
<td>7.5 ± 1.8</td>
</tr>
<tr>
<td></td>
<td>CAD S supplied by CA with st</td>
<td>45</td>
<td>7.4 ± 1.9</td>
<td>5.6 ± 2.1*³</td>
<td>6.9 ± 2.4*³</td>
<td>6.9 ± 1.5</td>
</tr>
</tbody>
</table>

n = number of myocardial segments; Peak atrial pacing = continuous atrial pacing at 150 beats . min⁻¹; Post atrial pacing = 5 s after atrial pacing interruption; Recovery = 2 min after atrial pacing interruption; S = segments; CAD = coronary artery disease; Th%, myocardial thickening; CA = coronary artery; st = significant coronary stenosis (≥50% narrowing); IBScv, integrated backscatter cyclic variations.

*P<0.05 vs normal segments and normal segments of CAD patients in the same protocol conditions; †P<0.001 vs normal segments and <0.05 vs normal segments of CAD patients in the same protocol conditions.

Data are expressed as mean ± standard deviation.

between the anterior and inferior wall showed no statistically significant differences (respectively, 7.3 ± 1.4 dB vs 8.1 ± 2.6 dB at rest, P=ns; 8.3 ± 1.8 dB vs 7.3 ± 1.9 dB at peak atrial pacing, P=ns; 8.2 ± 1.8 dB vs 7.1 ± 1.5 dB after atrial pacing interruption, P=ns; 7.8 ± 1.5 dB vs 7.4 ± 1.9 dB at recovery, P=ns).

In myocardial segments of coronary artery disease patients, supplied by a coronary artery without a significant stenosis, the behaviour of integrated backscatter cyclic variation magnitude was similar to that observed in segments of normal subjects in the four protocol moments.

In the group with myocardial segments supplied by a significantly narrowed coronary artery, the mean magnitude of integrated backscatter cyclic variation significantly decreased from baseline to peak atrial pacing (from 7.4 ± 1.9 dB to 5.6 ± 2.1 dB, P<0.001 vs rest), promptly recovered immediately after atrial pacing interruption (6.9 ± 2.4 dB, P<0.001 vs peak atrial pacing, P=ns vs baseline), and did not change at 2 min recovery (6.9 ± 1.5 dB, P<0.001 vs peak atrial pacing, P=ns vs baseline and post atrial pacing). An example of the effect of an atrial pacing stress test on integrated backscatter cyclic variations in myocardium supplied by a significantly narrowed coronary artery is presented in Fig. 2. Therefore, in patients with coronary artery disease, recovery time of integrated backscatter cyclic variations was faster than that of myocardial thickening. In fact, in the immediate post-pacing period, while integrated backscatter cyclic variations had already recovered to pre-atrial pacing values, myocardial thickening was still impaired. Different behaviours of myocardial thickening and integrated backscatter cyclic variations, in segments supplied by coronary arteries with or without significant narrowing in coronary artery disease patients, throughout the atrial pacing stress test protocol are schematically represented in Table 1 and Fig. 3.

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Figure 1  Time-intensity graphs showing integrated backscatter cyclic variations (IBScv) curves at rest and at peak pacing obtained in a normal segment. Despite the increase in heart rate, the amplitude of integrated backscatter cyclic variations remains the same (13 dB at 78 beats . min⁻¹ and 10 dB at 149 beats . min⁻¹).
Integrated backscatter in myocardial ischaemia

The effects of atrial pacing on myocardial thickening in animals with or without coronary disease were observed in the experimental setting by Tomoike et al. They evaluated myocardial thickening before, during and after atrial pacing in myocardium supplied by a patent or significantly narrowed coronary artery. Similar to this experimental observation, in our patients without coronary artery disease, myocardial thickening slightly decreased during rapid atrial pacing, moderately, but significantly, increased in the first cycles after pacing interruption (possibly because of a transient increase in contractility caused by prolonged diastolic time following pacing interruption) and returned, immediately afterwards, to baseline pre-atrial pacing values. On the other hand, in myocardium supplied by a severely narrowed coronary artery, thickening importantly and significantly decreased during atrial pacing and gradually returned to baseline values in the post-atrial recovery period.

Integrated backscatter cyclic variations and myocardial ischaemia

Experimental studies have demonstrated that contraction and relaxation of normal myocardium are associated with a parallel, cyclical variation of integrated backscatter. The magnitude of integrated backscatter cyclic variations is correlated but not necessarily dependent on global and intramural differences in myocardial contraction.

Other experimental and clinical studies, performed during acute abolition of coronary blood flow (coronary occlusion, balloon inflation, acute myocardial infarction), have evaluated the effect of myocardial ischaemia on integrated backscatter cyclic variations. More recently Vitale et al. have shown similar behaviour during stress tests in patients, but did not investigate the recovery modalities or myocardial thickening.

Even if the models of myocardial ischaemia utilized to investigate acute changes of integrated backscatter cyclic variations in previous experimental and clinical studies (coronary occlusion, increased myocardial oxygen demand in the presence of a significant narrowing of a major epicardial coronary artery) are remarkably different from our atrial pacing stress test, the results of our study closely parallel those of previous ones. In the myocardium of patients without coronary artery disease, as well as in the myocardium supplied by non-stenotic coronary arteries in patients with coronary artery disease, atrial pacing did not affect integrated backscatter cyclic variations. However, in myocardium supplied by a significantly narrowed coronary artery, atrial pacing blunted integrated backscatter cyclic variations. Integrated backscatter cyclic variation recovery time has now been studied in experimental models. Interestingly, in all these studies recovery during perfusion mainly depended on occlusion duration and was much faster and more complete than...
Figure 3  Plots of changes in myocardial thickening (upper panel) and integrated backscatter cyclic variations (IBScv) (lower panel) in myocardial segments of patients with coronary artery disease, supplied by coronary arteries without (●) or with (▲) significant (≥50% narrowing) stenosis. In myocardium supplied by non-stenotic coronary arteries, neither myocardial thickening nor integrated backscatter cyclic variations changed significantly during the atrial pacing stress test protocol. However, in myocardium supplied by significantly narrowed coronary arteries, both myocardial thickening and integrated backscatter cyclic variations were significantly reduced at peak atrial pacing. While myocardial thickening was still impaired in the early phase of post-atrial pacing recovery (5 s after atrial pacing interruption) and recovered 20 s after atrial pacing interruption, integrated backscatter cyclic variations returned to pre-atrial pacing values soon after atrial pacing interruption. Data are expressed as mean ± SD. *P<0.005, **P<0.001.

Post-ischaemia recovery of integrated backscatter cyclic variations

We demonstrated, consistent with animal studies, that restoration of integrated backscatter cyclic variation to baseline pre-atrial pacing values occurred very rapidly (within few cardiac cycles after atrial pacing interruption), well before recovery of regional myocardial thickening.

However, this post-ischaemia recovery time observed in our study was much shorter than that observed in previous experiments. Such a difference is easily explained by the fact that the entity, duration and transmurality of atrial pacing-induced myocardial ischaemia is less pronounced than that of various conventional regional left ventricular functional parameters (myocardial thickening, systolic shortening, wall motion score index).
produced by coronary occlusion. Therefore, in this study, both post-ischaemic myocardial dysfunction and integrated backscatter cyclic variations (an expression of regional contractile activity) lasted for a much shorter period. Wickline et al. demonstrated that the longer coronary occlusion lasts, the longer the time needed for integrated backscatter cyclic variations to return to pre-occlusion values.

Following coronary occlusion and stress-induced transient acute myocardial ischaemia, recovery of integrated backscatter cyclic variations is faster than that of myocardial thickening. This underlines the fact that integrated backscatter cyclic variations are not only a simple effect of myocardial contraction, but may also be useful in the identification of post-ischaemic reversible myocardial dysfunction (‘stunned myocardium’). Such a potential has already been emphasized in previous experimental studies. The reason for the temporal dissociation in recovery time, after acute myocardial ischaemia, between ‘classical’ regional left ventricular functional contractility parameters and integrated backscatter cyclic variations is still unclear. It has been suggested that such a disparity could be due to intramural heterogeneity of myocardial contraction. Subendocardium mainly contributes to overall myocardial thickening and is more severely impaired during ischaemia than mid-subepicardium. Thus it is likely that during recovery, where overall thickening has not yet been restored because of subendocardium post-ischaemic functional impairment, mid-outter myocardium, where integrated backscatter cyclic variations are evaluated, has already regained its function.

**Limitation of the study**

In this study we only used those echocardiographic views that, during transgastric imaging, are perpendicular to the ultrasonic beam (anterior and inferior wall) in order to optimize integrated backscatter cyclic variation evaluations. Whether the result of this study can be extended to other echocardiographic views has to be further investigated.

The software we used for the integrated backscatter data analysis did not permit synchronization of the values obtained with the electrocardiographic R wave. For the end-diastolic value we used the peak of the integrated backscatter cyclic variation curve, but we could not calculate its time delay from the R wave.

We used transoesophageal echocardiography during atrial pacing to better visualize the left ventricular walls. The transoesophageal approach is less feasible and less tolerated than the transthoracic approach, but it provides echocardiographic images of such high quality that myocardial thickening, a particularly accurate regional left ventricular function parameter extensively used in experimental conditions, can be evaluated. In our study, thanks to transoesophageal imaging, it was possible to measure in basal, stress and recovery conditions, myocardial thickening. The results of this study, however, can be conceptually extrapolated to other stress test procedures as well as to transthoracic echocardiography. In this way wall motion score, instead of myocardial thickening, can be more easily assessed.

Analysis of integrated backscatter is still experimental. A future challenge will be to define an ischaemic integrated backscatter cyclic variation change cut-off point to calculate the sensitivity, specificity and accuracy of this technique. In our study, as in previous ones, the entity of the integrated backscatter cyclic variation change induced by ischaemia varied in different patients, depending on their pathophysiological conditions.

**Conclusions**

This study has shown that stress-induced myocardial ischaemia blunts integrated backscatter cyclic variations and that the return to pre-ischaemic values occurs more rapidly with integrated backscatter cyclic variations than with myocardial thickening. These findings highlight that it is possible to assess stress-induced alterations of integrated backscatter cyclic variations (a) when evaluating the effects of acute myocardial ischaemia on regional left ventricular function and, hence, in the diagnosis of coronary artery disease, (b) in the identification of post-ischaemic transient regional left ventricular dysfunction.

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**References**


