Left atrial spontaneous echo contrast in patients with permanent pacemakers

Tsung-Ming Lee, Sheng-Fang Su, Kuo-Liong Chien, Yueh-Juh Lin, Wen-Jone Chen, Ming-Fong Chen, Chiau-Suong Liau, Yuan-Teh Lee

Abstract
Objective—To determine the relations between left atrial appendage function, spontaneous echo contrast, and thromboembolism in patients with different modes of permanent pacemakers.

Patients and methods—88 patients with pacemaker implantation and 25 healthy controls in sinus rhythm had transoesophageal echocardiographic examination of the left atrial appendage. Left atrial size, appendage area, peak filling and emptying velocities of the atrial appendage, and the presence or absence of spontaneous echo contrast and thromboembolism were determined. The results in 63 patients with ventricular pacing (group 1, subdivided into subgroup 1A: 42 patients with sinus rhythm, and subgroup 1B: 21 patients with atrial fibrillation) were compared with those in 25 patients with synchronous pacing (group 2), and 25 normal control subjects (group 3).

Results—Patients with ventricular pacing had two distinct appendage flow patterns: well defined biphasic filling and emptying waves in subgroup 1A, and irregular very low filling and emptying waves in subgroup 1B. The ejection fraction of the left atrial appendage in subgroup 1A was significantly better than that in subgroup 1B (mean (SD) 40-6(12-0)% v 7-6(5-0)%, \( P < 0.0001 \)). The spontaneous echo contrast was observed in 90% of subgroup 1B patients but in only 19% in subgroup 1A (\( P < 0.05 \)) and was not found in groups 2 and 3 (\( P < 0.0001 \)). There was a trend for increased prevalence of spontaneous echo contrast in subgroup 1A v group 2 (\( P = 0.053 \)). Thrombi were detected in two cases, and cardiogenic embolism occurred in one case in subgroup 1B. All patients with spontaneous echo contrast had ventricular pacing. Multivariate analysis showed that atrial fibrillation was associated with occurrence of spontaneous echo contrast in patients with ventricular pacing (\( P = 0.005 \)).

Conclusions—The left atrial appendage ejection fraction was lower with ventricular pacing than with synchronous pacing. With ventricular pacing there was a trend towards increased prevalence of left atrial spontaneous echo contrast in patients in sinus rhythm, and a significantly increased prevalence in patients with atrial fibrillation.

Keywords: echocardiography; left atrial appendage; pacemaker; spontaneous echo contrast

It is well known that patients with ventricular pacing have an increased incidence of thromboembolism. In recent years synchronous pacing modes of pacemaker (AAI (R), DDD (R), VDD) have been developed to offer alternative options to VVI (R) mode. It is believed that normal anteroventricular conduction is not only physiologically relevant but also clinically important. In comparison with synchronous pacing, ventricular pacing has the disadvantage of the absence of—or random occurrence of—atrial contraction to ventricular filling; thus atrial fibrillation may be induced. Although the association of atrial fibrillation with thromboembolism is well established, the mechanism of thromboembolism in patients with ventricular pacing is still not clear.

Spontaneous echo contrast of the left atrium and the left atrial appendage can be demonstrated by transoesophageal echocardiography. The appearance of spontaneous atrial echo contrast is believed to be associated with left atrial appendage thrombus, with increased risks of thromboembolism. The purpose of our study was (1) to assess the effect of synchronous versus ventricular pacing on the function of the left atrial appendage; and (2) to investigate the correlation between the incidence of left atrial spontaneous echo contrast phenomenon and different pacing modes.

Methods

Patients
During a six month period, 92 patients with permanent pacemaker underwent transoesophageal echocardiographic examination. All patients were in sinus rhythm at the time of the pacemaker implantation. There was no pacemaker syndrome and no patients were taking oral anticoagulants. Patients with concomitant valvar disease were not included. Four patients were excluded because of the presence of persistent spontaneous rhythm at the time of echocardiographic study. Only paced beats were included for analysis at the time of echocardiographic study. The remaining 88 patients, with a mean age of 66-6 (SD 11-3) years (range 30 to 88; 50 men, 38 women), were prospectively studied. All
patients underwent detailed electrophysiologi-
cal study before pacemaker implantation. Indica-
tions for pacemaker implantation included sick sinus syndrome (n = 67) and complete atrioventricular block (n = 21). A VVI(R) pacemaker was implanted in 63 patients (ventricular group, group 1). The syn-
chronous group (group 2) consisted of 25 patients with pacemaker types AAI (R) (n = 13), VDD (n = 2), and DDD (R) (n = 10). Patients in group 1 were further divided into two subgroups on the basis of cardiac rhythm at the time of the transoesophageal echocardi-
ographic study: subgroup 1A, in sinus rhythm, n = 42; subgroup 1B, in atrial fibrillation, n = 21. The clinical characteristics of the patients are given in table 1. For comparison, an additional group was enrolled in the study: this control group (group 3) consisted of 25 normal subjects in sinus rhythm and no appar-
ent heart disease.

ECHOCARDIOGRAPHY

All patients were examined by transthoracic and transoesophageal echocardiography on the same day. M mode echocardiography was performed in all patients and left atrial size was determined. Transoesophageal echocardiographic examination was performed using a 5 MHz biplane (n = 87; 35 subgroup 1A, 17 subgroup 1B, 16 group 2, 19 group 3) or multi-
plane transducer (n = 26). Patients had fasted for six hours before transoesophageal echocardiography. Local pharyngeal anaesthesia with 8% lignocaine spray was the only pre-
medication. During echocardiography, a one lead electrocardiogram was recorded. Informed consent was obtained from all patients and normal control subjects. The study was approved by the institutional research ethics committee.

Left atrial appendage area and flow

Images of the left atrial appendage were obtained in the transverse and longitudinal planes and recorded on Super VHS videotapes for off-line analysis. The boundary of the base of the appendage was defined by a line drawn from the limbus of the left upper pulmonary vein to the exteriormost portion of the mitral annulus. Maximum and minimum left atrial appendage areas were determined by com-
puted planimetry along the endocardial border of the appendage (average of three consecutive values) (fig 1). The ejection fraction of the left atrial appendage was calculated as (maximum area − minimum area)/maximum area. Left atrial appendage velocity profiles were obtained by pulsed wave Doppler interrogation at the orifice of the appendage. The maxi-
mum forward positive flow velocity of Doppler left atrial appendage represented the peak emptying velocity (fig 2, a wave) and the maxi-
mum backward negative flow velocity repre-

Figure 1  Biplane longitudinal transoesophageal echocardiography in a VVI patient. The maximum (A) and minimum (B) areas of appendage were measured by tracing a line starting from the top of the limbus of the left upper pulmonary vein along the entire endocardial border to the exteriormost portion (arrowhead) of the mitral annulus. LA, left atrium.

Figure 2  Velocity profiles in VVI patients with preserved sinus activities (subgroup 1A), (A) with ventriculoatrial conduction and (B) without ventriculoatrial conduction. Both had an underlying disease of sick sinus syndrome. Both show left atrial appendage flow patterns. Regular and well defined embaying (a) waves regularly follow atrial electric activity (seen in A, but not seen in B). Filling (b) velocity waves follow the emptying wave. A respiratory trace is shown at the bottom.
Figure 3  Velocity profiles in a VVI patient with atrial fibrillation (subgroup 1B), an underlying disease of sick sinus syndrome. Left atrial appendage flow patterns show irregular low emptying and filling waves. A respiratory trace is shown at the bottom.

Figure 4  Velocity profiles in a patient with DDD pacemaker (group 2), an underlying disease of complete atrioventricular block. Left atrial appendage flow patterns show well defined emptying (a wave) after electrocardiographically antegrade P wave and filling (b wave) velocities following the a wave. A respiratory trace is shown at the bottom.

sent the peak filling velocity (fig 2, b wave). There were 25 patients in subgroup 1A with quadrifasic flows (c and d waves). Because of their smaller flow velocities, c and d waves did not affect the measurement of peak filling and emptying flow velocities. The ejection fraction of the left atrial appendage and the peak emptying and filling velocities were averaged with each RR interval over a minimum of five cardiac cycles for patients with atrial fibrillation, and over three cardiac cycles for those in sinus rhythm. Interobserver differences were resolved by consensus.

Spontaneous echo contrast and thrombus
Left atrial spontaneous echo contrast was diagnosed by the presence of dynamic smoke-like echoes within the atrial cavity, with a characteristic swirling motion distinct from white noise artefact.12 The gain was continuously adjusted to ensure the best possible visualisation and to avoid noise artefact. Spontaneous echo contrast was graded as previously described:12 grade 0 = no contrast; grade 1 = slight contrast localised in parts of the left atrium with a low density; grade 2 = heavy contrast with intense, swirling, smoke-like echoes in the whole atrium. Thrombi were defined as masses adherent to the wall of the left atrial appendage with different echogenic density. Particular attention was paid to differentiating these from pectinate muscles. The presence or absence of spontaneous echo contrast and thrombus was defined by the consensus of two experienced echocardiographers.

STATISTICS
Values are reported as mean (SD). A $\chi^2$ test was used to compare categorical variables. The continuous variables between groups were compared with Student’s $t$ test for two tailed unpaired observation. For comparison of multiple groups, analysis of variance was applied. For the identification of independent predictors of spontaneous echo contrast a multivariate regression analysis was used. Two tailed Fisher’s exact test was used for patient numbers less than five. A $P$ value $<0.05$ was considered statistically significant.

Results
Figures 2, 3, and 4 show typical findings of left atrial appendage flow in subgroups 1A and 1B and group 2.

BASELINE VARIABLES
The selection of pacing mode was not randomised but was dependent on patients’ age, physical activity, prognosis, and cost. The echo studies were performed at a mean time from implantation of 48 (52) months for subgroup 1A, 54 (47) months for subgroup 1B, and 12 (10) months for group 2. The average follow up time in subgroups 1A and 1B was much longer than in group 2. The patient age

| Table 1  | Characteristics of patients and left atrial appendage in different groups |
|-----------------|-----------------|-----------------|
|                | Group 1          | Group 2         | Control        |
|                | 1A ($n = 42$)    | 1B ($n = 21$)   | ($n = 25$)     |
| Age (years)    | 66.4 (10.9)*    | 72.4 (7.1)*     | 62.1 (12.9)    | 64.6 (7.9)    |
| Male/female    | 29/17           | 11/10           | 14/11          | 15/10         |
| SSS/CAVB       | 32/10           | 19/21           | 16/9           | —             |
| Set heart rate (beats/min) | 66.4 (4.8)* | 66.7 (4.8)* | 72.9 (5.2) | 62.3 (6.9)* |
| Follow up period | 48 (52)* | 54 (47)* | 12 (10) | — |
| Left atrial size (mm) | 36.5 (3.5)* | 46.3 (4.6)* | 34.2 (3.2) | 34.8 (4.2) |

<table>
<thead>
<tr>
<th>Left atrial appendage parameters</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum area (cm²)</td>
<td>5.4 (1-4)*</td>
<td>6.1 (1-4)*</td>
<td>4.7 (1-3)</td>
</tr>
<tr>
<td>Minimum area (cm²)</td>
<td>5.2 (1-2)*</td>
<td>5.6 (1-2)*</td>
<td>2.6 (1-2)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>40.6 (12.0)*</td>
<td>7.7 (5.0)*</td>
<td>48.2 (16.2)</td>
</tr>
<tr>
<td>Peak filling velocity (cm/s)</td>
<td>51.2 (19.6)*</td>
<td>10.8 (8-6)*</td>
<td>59.8 (17.6)</td>
</tr>
<tr>
<td>Peak emptying velocity (cm/s)</td>
<td>49.5 (17.8)*</td>
<td>11.4 (6-5)*</td>
<td>51.8 (18.3)</td>
</tr>
<tr>
<td>Spontaneous echo contrast</td>
<td>8 (19%)*</td>
<td>19 (90%)*</td>
<td>0</td>
</tr>
<tr>
<td>Thrombus</td>
<td>0</td>
<td>2 (9.5%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Values are number (%) of patients or mean (SD).

* $P < 0.05$ vs subgroup 1B; $\dagger P < 0.05$ vs group 2; $\ddagger P < 0.05$ vs group 2; $\ddagger\ddagger P < 0.05$ vs group 2.

CAVB, complete atrioventricular block; SSS, sick sinus syndrome.
in subgroup 1B was significantly higher than in subgroup 1A and group 2, at 72.4 (7.1)  
66.4 (10.9) and 62.1 (12.9) (both P < 0.05).  
The set heart rate of the pacemakers was  
significantly higher in group 2 than in sub-
groups 1A and 1B. The size of the left atrium was  
significantly greater in subgroup 1B than in sub-
groups 1A and groups 2 and 3, at 46.3 (4.6)  
v 36.5 (3.5), 34.2 (3.2), and 34.8 (4.2) mm (all  
P < 0.05) (table 1).

LEFT ATRIAL APPENDAGE  
In all patients in subgroup 1A, the left atrial  
appendage flow revealed an organised biphasic  
flow pattern with a peak filling and emptying  
velocity (fig 2). In contrast, all patients from  
subgroup 1B showed an irregular, very low  
peak filling and emptying velocity (fig 3).  
Table 1 compares the left atrial appendage  
transoesophageal echocardiography parameters  
in the three groups. The maximum  
appendage areas were significantly larger in  
subgroup 1B than in subgroup 1A and group  
2. More striking is the difference in the left  
atrial appendage ejection fraction, which was  
significantly reduced in subgroups 1A and 1B.  
There were almost no visible appendage con-
tractions in subgroup 1B. There were no  
significant differences of the ejection fraction  
of the left atrial appendage detected by biplane  
transoesophageal echocardiography compared  
with multiplane transoesophageal echocardi-
ography in subgroup 1A (41.2 (11.8) v 39.4  
(12.4) %, NS) (table 1).  
Two patterns of left atrial appendage flow  
were identified in group 1. In subgroup 1A  
and groups 2 and 3, Doppler image revealed a  
biphasic flow pattern with a peak filling and  
emptying velocity. The a wave occurred after  
the P wave and the b wave followed the a  
wave. In contrast, patients from subgroup 1B  
showed irregular, very low peak filling veloci-
ties (range 3 to 25 cm/s, mean 10.8 (8.6)  
cm/s) and peak emptying velocities (3 to 30  
cm/s, mean 11.4 (6.5) cm/s). The left atrial  
appendage peak filling and emptying velocities  
were significantly reduced in patients from  
subgroup 1B compared with patients from  
subgroups 1A, 2, and 3. There were no signifi-
cant differences in variable echocardiographic  
parameters between groups 2 and 3.

Table 2  Univariate analysis: clinical and echocardiographic factors related to left atrial  
spontaneous echo contrast (SEC) in pacemaker patients

<table>
<thead>
<tr>
<th>Predictor</th>
<th>SEC (+)</th>
<th>SEC (−)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.6 (11.5)</td>
<td>72.1 (7.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Male/female</td>
<td>36/25</td>
<td>14/13</td>
<td>NS</td>
</tr>
<tr>
<td>SSS/CAVB</td>
<td>43/18</td>
<td>24/3</td>
<td>NS</td>
</tr>
<tr>
<td>Ventricular/synchronous</td>
<td>36/25</td>
<td>27/0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atrial fibrillation percentage</td>
<td>2 (3%)</td>
<td>19 (70%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Set heart rate</td>
<td>69/0 (6.0)</td>
<td>66/3 (6.9)</td>
<td>0.049</td>
</tr>
<tr>
<td>Left atrial appendage area cm³</td>
<td>35.4 (4.2)</td>
<td>44.5 (3.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left atrial appendage parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum area (cm²)</td>
<td>5.2 (1.5)</td>
<td>5.9 (1.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Minimum area (cm²)</td>
<td>3.0 (1.2)</td>
<td>5.0 (1.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>42.6 (16.6)</td>
<td>15.5 (15.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peak filling velocity (cm/s)</td>
<td>53.2 (19.2)</td>
<td>20.6 (22.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peak emptying velocity (cm/s)</td>
<td>49.2 (18.2)</td>
<td>22.9 (23.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thrombus</td>
<td>0</td>
<td>2 (7.6%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are number (%) of patients or mean (SD).  
SSS, sick sinus syndrome; CAVB, complete atrioventricular block.

Table 3  Logistic regression model analysis of risk factors for development of spontaneous  
echo contrast in patients with ventricular pacing

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>21-7</td>
<td>2.53 to 187.21</td>
<td>0.005</td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>1-8</td>
<td>0.47 to 25.42</td>
<td>0.447</td>
</tr>
<tr>
<td>LA size</td>
<td>1-6</td>
<td>0.55 to 12.73</td>
<td>0.364</td>
</tr>
<tr>
<td>LAA peak emptying velocity</td>
<td>0-8</td>
<td>0.83 to 1.05</td>
<td>0.142</td>
</tr>
<tr>
<td>LAA ejection fraction</td>
<td>15-8</td>
<td>0.02 to 9874.31</td>
<td>0.372</td>
</tr>
</tbody>
</table>

Discussion  
Our study is the first study to show that  
patients with ventricular pacing have a high  
prevalence of impaired left atrial appendage  
function and the spontaneous echo contrast  
phenomenon in the left atrium, especially in  
the subgroup with concomitant atrial fibrilla-
tion. For patients with ventricular pacing and  
sinus rhythm, there is a tendency toward an  
increased prevalence of spontaneous echo

SPONTANEOUS ECHO CONTRAST AND  
THROMBUS FORMATION  
The spontaneous echo contrast phenomenon  
was not observed in groups 2 and 3; however,  
it was present in 90% of subgroup 1B patients.  
The echo contrast was seen in eight patients  
(19%) of subgroup 1A. In subgroup 1B, left  
atrial spontaneous echo contrast was graded as  
slight in 12 patients (63%) and heavy in seven  
(36%). In subgroup 1A, all left atrial sponta-
neous echo contrast was graded as slight.  
There was a trend of an increased prevalence  
of spontaneous echo contrast in subgroup 1A  
compared with in group 2, although this was  
not statistically significant (P = 0.053).  
However, the statistic power of the study was  
0.45 for α = 0.05. Two patients from sub-
group 1B showed a left atrial appendage  
thrombus; one experienced ischaemic stroke.  
The frequency of atrial fibrillation was higher  
(P < 0.0001) in patients with echo contrast  
than in those without echo contrast (table 2),  
as were the minimum and maximum atrial  
appendage areas (P < 0.001 and P = 0.02,  
respectively). The ejection fraction of the  
atrial appendage was lower in patients with echo  
contrast than in patients without (42.6 (14.6)  
v 15.5 (15.3), P < 0.0001). The peak filling  
and emptying velocities for all patients with  
echo contrast were lower than for patients  
without echo contrast (both P < 0.0001).  
Although univariate analysis showed that  
older age, ventricular pacing, atrial fibrillation,  
left atrial size, and maximum/minimum areas  
and peak filling/emptying velocities of the left  
atrial appendage were significantly related to  
ocurrence of spontaneous echo contrast (table 2),  
multivariate analysis identified atrial fibrillation  
as the variable associated with a signifi-
cantly increased risk of left atrial sponta-
neous echo contrast in patients with  
ventricular pacing (table 3). The value of −2  
log L (likelihood ratio test) compared with  
the full model was 3.00, df = 1 (P = NS). All  
patients with spontaneous echo contrast had  
ventricular pacing. Ventricular pacing was an  
independent determinant in the univariate  
analysis of spontaneous echo contrast.
contrast, but this was not statistically significant (P = 0.053) because of the small number of patients in this subgroup (power = 0.45).

LEFT ATRIAL APPENDAGE

Left atrial appendage velocities and flow patterns vary according to rhythm. In sinus rhythm, biphasic or quadrophasic clearly defined emptying and filling flows associated with appendage contraction and relaxation were observed. The a wave, representing forward flow towards the left atrial cavity, was associated with left atrial appendage contraction and began from the initial deflection of the P wave on the electrocardiogram. The b wave, representing retrograde flow toward the left atrial appendage, was associated with re-expansion of the left atrial appendage and began immediately after the a wave. Some patients with sinus rhythm had quadrophasic flow patterns in the left atrial appendage. The c and d waves are passive flows. The c wave, coinciding in timing with early mitral inflow, was associated with a pressure gradient between the left atrial appendage and the left ventricle on opening of the mitral valve. The d wave, occurring just after the c wave but before appendage contraction, indicated left atrial appendage filling during the diastolic period of mitral inflow. Because the c and d waves were significantly lower in velocity, they did not affect measurement of peak filling and emptying velocities.

In atrial fibrillation, a disorganised flow pattern and reduced velocities of emptying and filling flows are seen. Muggé et al11 meticulously divided patients with non-rheumatic atrial fibrillation into two subgroups on the basis of left atrial appendage function. One group had a high flow profile with high peak filling and emptying velocities of the left atrial appendage; the other had a low flow profile with very low peak filling and emptying velocities. Their results show that the incidence of spontaneous echo contrast was significantly increased in patients with low left atrial appendage flow than in those with high flow. Porte et al12 found that left atrial appendage contractile function was a predictor of spontaneous echo contrast. Because the appendage patterns were of the low flow profile type with impaired contractile function in our subgroup 1B, it was expected that there would be a high incidence of spontaneous echo contrast. Our results are consistent with previous studies13-17 that patients with low flow profiles of the left atrial appendage have a high incidence of spontaneous echo contrast.

SPONTANEOUS ECHO CONTRAST AND THROMBUS FORMATION

The left atrial spontaneous echo contrast phenomenon was significantly more frequent in the ventricular group with atrial fibrillation. One study showed that patients with left atrial spontaneous echo contrast are 27 times more likely to have had a previous stroke or peripheral embolism than those without echo contrast.18 Daniel et al21 found that in patients with mitral valve disease, left atrial echo contrast was an independent predictor of left atrial thrombus and cardiogenic embolism. However, only one patient developed cerebral embolism in our study, although there was a higher prevalence of spontaneous echo contrast in the ventricular group. Because only surviving patients were examined and the loss of some patients with severe stroke cannot be ruled out, the real incidence of thromboembolism is probably higher than shown by our study.

MULTIVARIATE PREDICTORS OF SPONTANEOUS ECHO CONTRAST

In the non-fibrillation, atrial fibrillation was significantly associated with left atrial spontaneous echo contrast in patients with ventricular pacing. The left atrial size, underlying sick sinus syndrome, and left atrial appendage parameters were not predictors of spontaneous echo contrast in patients with ventricular pacing. These results agree with previous observations11, that atrial fibrillation is associated with an increased risk of developing spontaneous echo contrast. However, the relation between ventricular pacing and spontaneous echo contrast has not previously been reported. Our results showed that there was a prevalence of spontaneous echo contrast in patients with ventricular pacing: 19% in patients with preserved atrial activity and 90% in patients with atrial fibrillation. One explanation for the high prevalence of spontaneous echo contrast is that ventricular pacing results in a dilated left atrium21 and relatively reduced cardiac output.22 Conditions favouring stasis of left atrial blood, including left atrial enlargement and low cardiac output, were associated with left atrial spontaneous echo contrast.

Therefore ventricular pacing, even with sinus rhythm, was associated with a trend towards the occurrence of spontaneous echo contrast.

CLINICAL IMPLICATIONS

The effect of ventricular pacing and atrial fibrillation on left atrial appendage function and left atrial spontaneous echo contrast suggests a hidden benefit of synchronous pacing. Left atrial spontaneous echo contrast is a phenomenon that usually appears in regions of blood stasis including an enlarged left atrium, as in this study; however, the mechanism of this phenomenon remains unclear. The pathogenesis of spontaneous echo contrast is complex and includes not only the velocity or shear rate of local blood flow but also factors such as abnormalities of blood components. Siegel et al23 suggested that rouleaux formation of erythrocytes and increased level of serum fibrinogen may be responsible. However, Erbel et al24 found increased platelet aggregation in all their patients. Mahony et al25 reported a patient with left ventricular spontaneous echo contrast despite heparin treatment, in whom platelet aggregates were detected in the peripheral blood. Complete spontaneous echo contrast resolution was noted after five days of antiplatelet treatment. Sasaki et al26 significantly reduced the incidence of stroke by using anticoagulants in patients with ventricular
Left atrial spontaneous echo contrast in patients with permanent pacemakers

Thus further studies are warranted comparing the therapeutic value of anticoagulant and antiplatelet drugs in paced patients with spontaneous echo contrast.

STUDY LIMITATIONS

This study has limitations. First, it was not randomised. The selection of pacemaker modes depended on patient age, the preference of primary cardiologists, and the cost. Second, the number of patients with ventricular pacing and sinus rhythm was small, which precluded any definite conclusion about the relation between ventricular pacing and spontaneous echo contrast. Third, estimation of the ejection fraction of the left atrial appendage can be influenced by movement of the transoesophageal probe, which will affect the echo plane in which the atrial appendage is evaluated and may cause overestimation or underestimation of the appendage ejection fraction. However, this did not seem to be a problem because this variable was averaged over a minimum of five cardiac cycles in patients with atrial fibrillation and over three cardiac cycles in those in sinus rhythm. Fourth, the rarity of thromboembolic events in this series of patients precluded a definite correlation between systemic embolism and the proposed mechanism involved in thromboembolism in patients with ventricular pacing. Fifth, the presence or absence of spontaneous echo contrast is subjective. However, interpretations were by two experienced cardiologists and any differences were resolved by consensus, so we feel there was little likelihood of misinterpretation. Finally, although some basic clinical variables were not considered in the multivariate analysis, this will not affect the conclusions because all variables with a P value < 0.05 in univariate analysis were considered. Values of $X^2$ for covariates compared with the full model were used to check the differences of $-2 \log$ of various models and to select the optimum model for interpretation.

CONCLUSIONS

Patients with ventricular pacing had a decreased ejection fraction of the left atrial appendage compared with patients with synchronous pacing. With ventricular pacing, there was a trend towards increased prevalence of left atrial spontaneous echo contrast in patients in sinus rhythm, and a significantly high prevalence in patients with atrial fibrillation.

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