Clinical and Echocardiographic Characteristics of Patients With Left Atrial Thrombus and Sinus Rhythm
Experience in 20,643 Consecutive Transesophageal Echocardiographic Examinations

Yoram Agmon, MD; Bijoy K. Khandheria, MD; Federico Gentile, MD; James B. Seward, MD

Background—Left atrial (LA) thrombus is infrequently detected in the presence of sinus rhythm (SR) and, in these cases, is usually associated with additional cardiac pathologies. We sought to determine the clinical and echocardiographic characteristics of patients with LA thrombus and SR to define a high-risk group of patients prone to this uncommon clinical presentation.

Methods and Results—The institution’s echocardiographic laboratory database was searched to identify patients with LA thrombus, diagnosed by transesophageal echocardiography (TEE), who were in SR during the TEE examination. Of 20,643 consecutive TEE examinations performed during an 11-year period, LA thrombus was detected in 314 patients in 380 TEE examinations. Of these, SR was present in 20 patients (age 69 ± 13 years; 40% men) in 23 examinations (0.1% of all TEE examinations; 6.1% of TEE examinations with LA thrombus). High-risk structural heart disease (severe left ventricular dysfunction or significant left-sided valve disease [predominantly mitral valve disease]), previous documented episodes of atrial fibrillation, or both (structural heart disease and previous atrial fibrillation) were present in 10, 4, and 5 of the 20 patients, respectively. Only 1 patient with LA thrombus and SR did not have high-risk features.

Conclusions—LA thrombus is very infrequently detected in the presence of SR. Patients with LA thrombus and SR constitute a high-risk group characterized by specific structural cardiac abnormalities or previous atrial fibrillation, abnormalities that are potentially detectable before TEE. (Circulation. 2002;105:27-31.)

Key Words: heart atrium ▪ thrombosis ▪ echocardiography

Thrombus within the left atrium (LA) is well visualized with transesophageal echocardiography (TEE),1 and its diagnosis may have major therapeutic implications. LA thrombus is usually detected in association with atrial arrhythmias but is uncommon in the presence of sinus rhythm (SR).2,3 Thus, the yield of TEE in detecting LA thrombus in unselected patients with SR appears to be low.4,5

The objectives of our study were to determine the clinical and echocardiographic characteristics of patients with echocardiographically detected LA thrombus who were in SR during the echocardiographic examination. Using a large echocardiographic laboratory database, we sought to characterize a high-risk group of patients with SR in whom TEE may be indicated to detect LA thrombus in the appropriate clinical setting.

Methods
The echocardiography laboratory database at Mayo Clinic was searched to identify all patients with LA (or LA appendage [LAA]) thrombus diagnosed by TEE between 1988 and 1998. From this group, we identified the patients who were in SR during the TEE examination, and the past medical histories and echocardiographic recordings of these patients were reviewed.

SR was determined by ECG monitoring during TEE and supported by Doppler echocardiographic evidence of regular LA mechanical activity (distinct mitral inflow atrial contraction [A] waves or LAA flow pattern typical of SR6) and/or 12-lead ECG performed within 24 hours of the TEE examination. The diagnosis of LA thrombus was confirmed by review of the echocardiographic recordings.7 In subjects with >1 TEE examination with LA thrombus and SR, the first qualifying examination was taken for the present analysis.

“High-risk” features for LA thrombus in patients with SR were defined a priori as follows:

1. Valve disease, mitral stenosis (at least moderate in severity),5,9 previous mitral valve surgery (valve replacement or repair),10 or severe aortic regurgitation;11
2. Left ventricular dysfunction: severe systolic dysfunction (ejection fraction <30%12) or severe diastolic dysfunction (morphological13 and hemodynamic14 features of restrictive cardiomyopathy: mitral inflow E to A velocity ratio >2, pulmonary venous systolic less than diastolic flow velocities, moderate or greater LA enlargement, and preserved left ventricular systolic function). Valvular disease and left ventric-
Table. The patients' 20 patients with LA thrombus and SR are presented in the section showing LA thrombus.

Between 1988 and 1998, 20,643 TEE examinations were performed at our institution. LA or LAA thrombi (or both) were detected in 314 patients in 380 TEE examinations. Of these, SR was found in 196 patients (6.1% of all TEE examinations; 6.1% of TEE examinations performed over an 11-year period). This frequency is similar to that recently reported2 but is apparently lower than the frequency in a more selected group of patients with acute neurological events.3 This low frequency is further supported by the infrequent finding of LA spontaneous echocardiographic contrast in patients with SR.15

2. Patients in whom LA thrombus is detected in SR are characterized by specific cardiac abnormalities, notably significant left ventricular dysfunction, valve disease (predominantly mitral valve disease), or previous episodes of AF. These features define a higher-risk group of patients in SR who are at risk for LA thrombus formation, in whom the yield of TEE for detecting LA thrombus is expected to be higher than in unselected patients with SR.

The risk of LA thrombus is low even in this potentially higher-risk” group in SR (an overall small number of subjects with LA thrombus and SR detected in our TEE database, which includes a large number of patients with high-risk features). Nevertheless, the therapeutic implications of this finding may be substantial, specifically in subjects without additional indications for anticoagulant therapy; therefore, high-risk patients should be referred for TEE to detect LA thrombus in the appropriate clinical setting (ie, after an embolic event). Our results also demonstrate that the probability of detecting LA thrombus in patients without high-risk features is negligible, thereby questioning the need for TEE for detection of LA thrombus in these patients.

LA Thrombus and SR
Several structural and functional cardiac abnormalities are associated with significant LA stasis, which may lead to LA thrombus formation even in the presence of SR.

Valve Disease
Hemodynamically significant mitral stenosis,8,9 mitral prosthesis,10 or severe aortic regurgitation,11 which were common in our study population (45% of our patients), are associated with LA stasis. Mitral regurgitation may decrease LA stasis and protect against LA thrombus formation, and although recently described,16 aortic stenosis (or aortic prosthesis) usually does not result in significant LA stasis unless accompanied by left ventricular dysfunction. Therefore, these latter valve lesions were not predefined as high risk in our analysis.
Left Ventricular Dysfunction

Significant left ventricular systolic\textsuperscript{12,17} and/or diastolic dysfunction,\textsuperscript{3} which were common in our study population (35% of our patients), predispose to LA thrombus formation via their secondary effect on LA hemodynamics.\textsuperscript{18} Notably, patients with cardiac amyloidosis constitute a specific high-risk group in whom LA thrombus may occur in SR as a result of restrictive ventricular physiology as well as amyloid infiltration within the atrial myocardium,\textsuperscript{19} both contributing to atrial dysfunction. The early post--myocardial infarction period has also been recognized as a high-risk state for LA thrombus in patients with SR, specifically in those with large anterior myocardial infarctions.\textsuperscript{20}

Overall, structural heart disease was very common in our patients, most commonly mitral valve disease or left ventricular dysfunction, which occurred (alone or in addition to a history of AF) in 75% of the patients.

Paroxysmal AF

Previous AF is a high-risk marker for recurrent AF. Transient paroxysms of AF may result in atrial dysfunction during the arrhythmia and after conversion to SR (the phenomenon of atrial stunning\textsuperscript{6}), thus predisposing to LA thrombus formation.\textsuperscript{21} Subsequently, LA thrombus may be detected in the presence of SR, with or without clear clinical recognition of the preceding atrial arrhythmia. In our study, previous episodes of AF were documented in 4 of the 5 patients without structural heart disease, suggesting that transient AF may have been the cause of LA thrombus in the patients lacking additional apparent risk.

Clinical and Echocardiographic Characteristics of 20 Patients With LA Thrombus and Sinus Rhythm*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>69±13 (25–84)</td>
</tr>
<tr>
<td>Male</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>Indication for TEE</td>
<td></td>
</tr>
<tr>
<td>Source of embolism (8 cerebral and 2 peripheral ischemic events)</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Prosthetic valve evaluation (3 mitral and 1 aortic prostheses)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Native valve evaluation (1 mitral stenosis, 1 mitral regurgitation)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Thrombus location</td>
<td></td>
</tr>
<tr>
<td>LA</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>LAA</td>
<td>15 (75%)</td>
</tr>
<tr>
<td>LA and LAA</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17 (85%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>History of congestive heart failure</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>Anticoagulation†</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>Severe left ventricular dysfunction</td>
<td></td>
</tr>
<tr>
<td>Systolic dysfunction (ejection fraction &lt;30%)‡</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Diastolic dysfunction (restrictive cardiomyopathy§)‡</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Significant valve disease</td>
<td></td>
</tr>
<tr>
<td>Mitral valve prosthesis¶‡</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Post mitral valve repair (annuloplasty)¶‡</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Mitral stenosis (≥ moderate severity)¶‡</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Mitral regurgitation (severe)#</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Aortic regurgitation (severe)¶‡</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Aortic prosthesis**</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Previous documented AF‡</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>Recent AF episode (&lt;30 days before index echocardiographic examination)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Recent cardioversion (&lt;30 d)</td>
<td>2 (10%)</td>
</tr>
</tbody>
</table>

*Continuous data are presented as mean±SD (range in parenthesis); categorical data are presented as number of patients (percentage in parenthesis).
†Anticoagulation at the time of the index echocardiographic examination.
‡Predefined high-risk features for LA thrombus in SR.
§See definition in Methods section.
¶No evidence of systemic amyloidosis in this patient.
¶¶Mechanical prostheses in 4 and bioprosthesis in 1 patient.
#Severe left ventricular dysfunction in addition to severe mitral regurgitation in this patient.
**Bioprostheses in both patients.
Factors. Five of the 15 patients with structural heart disease had had previous episodes of AF, suggesting that transient AF may have contributed to LA thrombus formation in this group of patients as well. Our findings also suggest that unrecognized episodes of AF in patients without previously documented AF are an extremely rare cause of LA thrombus, possibly occurring in only 1 patient in our large echocardiographic database (the single patient without evident high-risk features).

Role of TEE in Detecting Cardiac Sources of Embolism

TEE is commonly performed in search of cardiac sources of embolism. Although multiple sources are frequently demonstrated echocardiographically, the therapeutic implications of many of these findings are not well defined. This is the result of the high prevalence of potential sources of embolism in the general population, the frequent demonstration of multiple sources in individual patients, and the lack of well-established efficacious treatment for some putative sources of embolism (eg, patent foramen ovale, aortic atheroma). In contrast to many potential sources of embolism, LA thrombus is a treatable source of embolism, and its detection may clearly affect patient management.

A previous cost-effectiveness analysis suggested that routine TEE is cost-effective in patients with recent ischemic stroke who are in SR, even assuming that LA thrombus is the only treatable source of embolism detected echocardiographically. That conclusion was not supported by a clinical study analyzing the diagnostic role of TEE in 824 consecutive patients with embolic events undergoing both transthoracic echocardiography and TEE. In that study, LA thrombus was not detected in any of the patients with SR and a normal transthoracic echocardiographic examination. Conversely, transthoracic echocardiography and/or cardiac rhythm were abnormal in all patients with LA thrombus, therefore questioning the role of routine TEE for diagnosis of LA thrombus in unselected patients. In another study of 770 patients referred for TEE for multiple indications (most commonly after embolic events), LA thrombus was significantly more common in patients with specific risk factors for thrombus formation (AF, LA dilatation, left ventricular dysfunction, mitral stenosis, or mitral prosthesis). Nevertheless, LA thrombus was also detected in a small number of patients without apparent risk factors. As appropriately discussed by the authors, some of these patients may have had previous episodes of AF predisposing to LA thrombus, but because only findings during echocardiography were analyzed, the role of paroxysmal AF as a risk factor for LA thrombus formation was not assessed in that study. In a recently published study of patients with acute (≤24 hours) ischemic neurological events, LA thrombus was detected in 6 of 583 patients with SR (3 patients had mitral stenosis and the other 3 had aortic stenosis, coronary artery disease, and cardiomyopathy). This unique group of patients with SR was characterized by dilated left atria and decreased LAA function, as observed in patients with LA thrombus and AF, emphasizing the role of LA dysfunction as the cause of LA thrombus formation in subjects with SR. Although AF was not detected during intermediate-term (6 months) follow-up of these patients, the authors do not provide data on cardiac rhythm before the index TEE (ie, data on previous episodes of AF).

In our study, structural heart disease and/or previous AF were uniformly present in subjects with SR and LA thrombus, thereby extending these previous observations to a very large group of patients undergoing TEE in a heterogeneous clinical practice setting, the largest series of consecutive TEE examinations published to date.

Study Limitations and Future Directions

The main limitations of our study are its retrospective design and the selected nature of patients referred to a tertiary medical center. Nevertheless, the size of our echocardiographic database strengthens our conclusions, which need to be confirmed prospectively in other patient populations. Documentation of AF may vary significantly between different medical settings. Therefore, additional clinical and echocardiographic markers of high risk of AF (eg, age, hypertension, congestive heart failure, LA enlargement, and left ventricular diastolic dysfunction) need to be examined prospectively as potential predictors of LA thrombus in patients undergoing TEE in SR.

To fully define the role of TEE in evaluating cardiac sources of embolism, the adequate therapeutic approach to specific sources should be established and the diagnostic yield of clinical evaluation, transthoracic echocardiography, and TEE should be examined, as currently examined for LA thrombus. This information should enable us to focus the TEE examination on high-risk patients with treatable sources of embolism and allow better utilization of medical resources.

References


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