Systemic Lupus Erythematosus Valve Disease by Transesophageal Echocardiography and the Role of Antiphospholipid Antibodies

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The valve disease associated with systemic lupus erythematosus has been categorized as 1) masses or vegetations (Libman-Sacks endocarditis), 2) leaflet thickening, 3) valve regurgitation and, infrequently, 4) valve stenosis (1,2). The true prevalence and distribution of types of lupus-associated valve disease are uncertain. The prevalence of valve abnormalities as assessed in prior transthoracic echocardiographic studies (1-5) ranges from 0% to 79%. Because of limitations in the image quality of these studies, these estimates may be low. Postmortem studies (6-9) generally yield higher estimates (range 13% to 100%).

Transesophageal Doppler echocardiography produces high resolution images of the cardiac valves and is superior to transthoracic echocardiography in the detection of valve abnormalities (10,11). Therefore, it should yield more accurate information about the true prevalence and type of valve abnormalities in patients with lupus erythematosus than that obtained with previously utilized methods.

The pathogenesis of lupus-associated valve disease is unknown. Recent reports (4,12,13) suggest that the antiphospholipid antibodies, which include anticardiolipin antibodies, lupus anticoagulant antibody and false positive Venereal Disease Research Laboratory (VDRL) test may cause valve injury. These antibodies are IgG, IgM or IgA immunoglobulins directed against negatively charged phospholipids present in the membrane of endothelial cells. They have been found in patients with lupus erythematosus, patients with the antiphospholipid syndrome and infrequently in normal subjects (14,15). Patients with antiphospholipid syndrome are those with positive antiphospholipid antibodies and arterial or venous thrombotic events, thrombocytopenia or frequent miscarriages who do not meet criteria for systemic lupus erythematosus. Valve abnormalities similar to those associated with lupus erythematosus have been described in this syndrome (4,16,17).

The purpose of this study is twofold: 1) to better characterize the valve abnormalities in patients with systemic lupus erythematosus by using transesophageal echocardiography, and 2) to determine whether there is a specific association...
between antiphospholipid antibodies and lupus-associated valve disease.

Methods

Study patients. This research protocol was approved by the Human Research Committee of the University of New Mexico and all subjects signed informed consent. The study group consisted of 54 patients with systemic lupus erythematosus, 10 patients with antiphospholipid syndrome and 35 age- and gender-matched normal subjects. The diagnosis of systemic lupus erythematosus was made according to the criteria of the American Rheumatologic Association (18). The patients with this diagnosis were unselected, representing about 80% of outpatients <60 years of age followed up at the Rheumatology-Immunology Division at two affiliated hospitals. Twenty-one patients with lupus erythematosus >60 years of age were excluded on the basis of age because degenerative valve thickening, calcification and regurgitation are frequent in this age group (19,20). We also excluded three other patients with lupus erythematosus: two patients who had a history of rheumatic fever and one patient who was an intravenous drug abuser.

The diagnosis of antiphospholipid syndrome was based on the presence of one or more antiphospholipid antibodies and 1) evidence of the associated clinical syndrome of arterial or venous thrombosis, or 2) a history of miscarriages but no criteria for systemic lupus erythematosus, or 3) both. Four of these patients were defined as having primary antiphospholipid syndrome and six patients as having a secondary syndrome. These patients also were unselected and represented 10 of 13 patients diagnosed with this condition over the last 5 years by the rheumatology and hematology-oncology divisions. All study subjects underwent rheumatologic and serologic testing to confirm diagnoses. All subjects studied were outpatients in stable condition. Four patients (7%) with lupus erythematosus had a history of a heart murmur. The normal subjects had no evidence of medical illness by history or physical examination and had negative antiphospholipid antibodies.

Antiphospholipid antibody profile. Serum for determination of antiphospholipid antibodies (IgG and IgM) was drawn in all subjects including the control group at the time of transesophageal Doppler echocardiography. The antiphospholipid antibodies were measured in a reference laboratory by an enzyme-linked immunosorbent assay (ELISA) and expressed in IU defined by standard sera (21). The IgG and IgM antiphospholipid antibodies were considered present when >8 and >10 IU, respectively, were detected.

Patients tested positive with lupus anticoagulant antibody or false positive VDRL were included in the groups with antiphospholipid antibody.

Doppler echocardiography. All subjects underwent monoplane or biplane transesophageal color Doppler echocardiography with use of a Hewlett-Packard 77020 A/AC/AR with a 5 MHz transducer. Echocardiographic studies were copied in random order and interpreted by an experienced observer unaware of all clinical data. In addition to standardized transesophageal echocardiographic views (10), careful scanning of the mitral and aortic valves was performed in multiple planes to define anatomy and the presence and severity of valve regurgitation or stenosis, or both.

To assess mitral leaflet thickness, M-mode echocardiograms were recorded at the leaflet base, mid and tip in the four-chamber view during systole. Similar M-mode recordings were made of the noncoronary cusps and right coronary cusp of the aortic valve in the long-axis view. M-mode echocardiograms of the left and right coronary cusps also were obtained in the short-axis view. Imaging of the tricuspid valve was performed in a manner analogous to that of the mitral valve. The pulmonary valve was not included in the present study because of its limited and variable visualization by transesophageal echocardiography.

Left ventricular size, wall motion and function and the appearance of the pericardium were assessed.

Criteria for echocardiographic interpretation. Valve abnormalities were classified into three principal categories: thickening of leaflets with or without calcification, valve masses and valve regurgitation or stenosis, or both.

Valve thickening. Mitral leaflet thickness on transesophageal two-dimensional echocardiographic images was measured in 10 randomly selected control subjects and found to be 1 ± 1 mm at the base and midportions, and 2 ± 1 mm at the tip. Aortic cusp thickness in the same control subjects was found to be 1 ± 1 mm. Abnormal leaflet thickening was considered present when at least two leaflets showed a thickness ≥3 mm (for the mitral valve) and ≥2 mm (for the aortic valve) or when noted in one leaflet if an associated mass or regurgitation of the respective valve, or both, was noted. Calcification associated with thickening was considered present when acoustic shadowing was demonstrated from a region of high reflectance.

Valve masses. A mass was defined as an abnormal localized echodensity with well defined borders either as part of or adjacent to valve leaflets, the subvalvular apparatus, great vessels or on the atrial or ventricular walls. The size of the mass on the two-dimensional image was determined by planimetry and expressed in cm².

Regurgitation. Grading of regurgitation severity was based on the size and duration of the Doppler color flow jet. Regurgitation was trivial if the jet extended into the receiving chamber for <1 cm and lasted <100 ms. It was mild if the jet extended only 1 to 2 cm and persisted throughout the regurgitant period. It was moderate if the jet was >2 cm and occupied up to 50% of the atrial or left ventricular outflow tract area (for mitral and aortic regurgitation), or if the halftime was <400 ms (for aortic regurgitation). It was severe if the jet was >2 cm and occupied >75% of atrial or left ventricular outflow tract area or if halftime was <200 ms (for aortic regurgitation). Trivial lesions were considered absent for the purpose of analysis.
Table 1. Patient Groups by Clinical Diagnosis

<table>
<thead>
<tr>
<th>Group</th>
<th>Total patients</th>
<th>Female</th>
<th>Age (yr)</th>
<th>Disease duration (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I (SLE + AB)</td>
<td>22</td>
<td>21; 95</td>
<td>37 ± 13</td>
<td>9.3 ± 9.3</td>
</tr>
<tr>
<td>Group II (SLE - AB)</td>
<td>32</td>
<td>28; 88</td>
<td>40 ± 10</td>
<td>36 ± 10</td>
</tr>
<tr>
<td>Group III (APS)</td>
<td>10</td>
<td>4; 40</td>
<td>42 ± 10</td>
<td>17 to 57</td>
</tr>
<tr>
<td>Group IV (normal)</td>
<td>35</td>
<td>27; 77</td>
<td>30 to 58</td>
<td>17 to 57</td>
</tr>
</tbody>
</table>

Statistical analysis. The frequency of each type of valve abnormality was compared between groups by the chi-square test. The two sample t test (for two groups) and analysis of variance (for more than two groups) were used to compare the means of continuous variables. A p value < 0.05 was considered significant.

Results

Study group. The study patients were classified into four groups by clinical diagnoses (Table 1). Groups differed only by predominance of female gender in group I, II or IV versus group III (p < 0.02).

Antibody profile. The patient groups with antibodies (groups I and III) showed a similar frequency of anticardiolipin and lupus anticoagulant antibodies. False positive VDRL was more frequent in group I (p < 0.03) (Table 2).

Most patients with one type of antibody had other antibody types detected. All patients with lupus anticoagulant antibodies had at least one additional antibody type present. Groups I and III had a similar mean concentration of the IgG and IgM anticardiolipin antibodies (Table 3).

Valve abnormalities on transesophageal echocardiography. The frequency of valve abnormalities in groups I to IV is presented in Table 4. Valve abnormalities of at least one type were very common in patients with lupus erythematosus (74%) regardless of the presence or absence of antiphospholipid antibodies. More than one valve abnormality was present in 50% of patients in group I and in 38% of patients in group II. Patients in these two groups had a significantly higher frequency of valve abnormalities than did those in group III or IV, (group I or II vs. group III or IV, p < 0.02; group I vs. group II or III vs. group IV, p = NS).

Valve thickening. Valve leaflet thickening was a common finding in patients with lupus erythematosus regardless of the presence of antiphospholipid antibodies. In contrast, this abnormality was uncommon in patients with the antiphospholipid syndrome (1 [10%) of 10) or in normal subjects (3 [9%] of 35) (group I or II vs. group III or IV, p < 0.03; group I vs. group II or III vs. group IV, p = NS).

In group I, nine patients had mitral, seven had aortic and one had mitral chordal thickening. In group II, 11 patients had mitral, 9 had aortic, 2 had mitral chordal and 1 had tricuspid valve thickening. In both groups, the anterior and posterior leaflets of the mitral valve and each of the three aortic valve cusps were similarly affected. Diffuse leaflet thickening (aortic in 9, mitral in 12) was observed in 20 patients with lupus erythematosus (Fig. 1 and 2). Localized thickening (aortic in 8, mitral in 7) was seen in 13 patients with lupus erythematosus and was limited to the leaflet base in six valves, mid and tip portion in five valves and to the tip in four valves (Fig. 3). Most patients with lupus erythematosus (70%) had more than one leaflet and nine patients (35%) had more than one valve affected. Nineteen patients with lupus erythematosus (73%) with valve thickening had associated valve regurgitation, 13 (50%) had a mass and 12 (46%) had both. The extent and location of valve thickening

Table 2. Frequency and Distribution of Antiphospholipid Antibodies in Groups I (SLE + AB) and III (APS)

<table>
<thead>
<tr>
<th>Antibody Type</th>
<th>Group I (SLE + AB)</th>
<th>Group III (APS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticardiolipin</td>
<td>IgG</td>
<td>IgM</td>
</tr>
<tr>
<td>17</td>
<td>77</td>
<td>9</td>
</tr>
</tbody>
</table>

*Group I vs. group III, p < 0.03. VDRL = Venereal Disease Research Laboratory test; other abbreviations as in Table 1.

Table 3. Concentration of IgG or IgM Anticardiolipin Antibodies in Groups I and III

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Group I (SLE + AB)</th>
<th>Group III (APS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG (IU)</td>
<td>59 ± 61</td>
<td>65 ± 35</td>
</tr>
<tr>
<td>IgM (IU)</td>
<td>34 ± 24</td>
<td>40 ± 22</td>
</tr>
</tbody>
</table>

All values are expressed as mean value ± 1 SD. Abbreviations as in Table 1.
Table 4. Frequency of Valve Abnormalities on Transesophageal Echocardiography

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Patients</th>
<th>Valve Abnormalities</th>
<th>Regurgitation</th>
<th>Thickening</th>
<th>Masses</th>
<th>Any Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (SLE + AB)</td>
<td>22</td>
<td>14</td>
<td>64</td>
<td>50</td>
<td>9</td>
<td>77</td>
</tr>
<tr>
<td>II (SLE - AB)</td>
<td>32</td>
<td>19</td>
<td>59</td>
<td>15</td>
<td>8</td>
<td>72</td>
</tr>
<tr>
<td>III (APS)</td>
<td>10</td>
<td>1</td>
<td>10</td>
<td>10</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>IV (normal)</td>
<td>35</td>
<td>7</td>
<td>20</td>
<td>9</td>
<td>0</td>
<td>23</td>
</tr>
</tbody>
</table>

Group I vs. group II or III vs. group IV, p = NS for all abnormalities; group I or II vs. group III, p < 0.03 for regurgitation, thickening or any abnormality; group I or II vs. group IV, p < 0.002 for all abnormalities. Abbreviations as in Table 1.

were similar in groups I and II. Only three patients (12%) with leaflet thickening had associated calcification. Mitral anulus thickening or calcification was not noted.

Valve masses. Seventeen (31%) of all patients with lupus erythematosus had a valve mass, nine (41%) in group I and eight (25%) in group II. Only one patient in group III had a valve mass (group I vs. group III, p < 0.08; group I or II vs. group IV, p < 0.002). In group I, 12 masses were seen: 7 on the aortic valve, 3 on the mitral valve and 2 on the mitral chordae. In group II, 11 masses were detected: 5 on the aortic valve, 3 on the mitral valve, 2 on the mitral chordae and 1 on the tricuspid valve. In both groups, the valve masses were equally distributed among the valve leaflets.

Two thirds (12 of 18) of aortic and mitral valve masses were located on the basal portion of the leaflets, and one third were located on the mid and distal leaflets. Five of six mitral valve masses were located on the atrial side of the valve (Fig. 2 and 3). Eight of 12 aortic valve masses were on the aortic vessel side (Fig. 4 and 5). Most patients (71%) with lupus erythematosus who had a valve mass had associated thickening of the respective valve leaflets and 88% had associated thickening or regurgitation of the respective valve. No masses were seen on the aortic, ventricular or atrial walls.

Valve masses were of variable size (0.2 to 0.85 cm²) and...
Figure 3. Mitral valve thickening and a mass in a patient with systemic lupus erythematosus with antiphospholipid antibody. This transesophageal four-chamber view shows thickening of the mid and tip portions of the anterior (aml) and posterior (pml) mitral leaflets. There is an irregular mass (arrow) on the atrial side of the posterior mitral valve leaflet. Moderate mitral regurgitation was present. Abbreviations as in Figures 1 and 2.

Figure 4. Aortic valve mass in a patient with systemic lupus erythematosus with negative antiphospholipid antibody. This transesophageal longitudinal view shows a mass (arrow) of irregular borders and irregular echogenicity located at the base of the noncoronary cusp (ncc) and anteromedial aortic root wall. No aortic regurgitation was detected. Abbreviations as in Figures 1 and 2.

Figure 5. Aortic cusp mass lesions in a patient with systemic lupus erythematosus with negative antiphospholipid antibody. This transesophageal longitudinal view of the left ventricular (LV) outflow tract shows a small mass (arrow) on the right coronary cusp (rcc) and another mass (arrowhead) at the base of the noncoronary cusp (ncc). No aortic regurgitation was detected. RA = right atrium; other abbreviations as in Figure 1.

Valve regurgitation. Valve regurgitation was a frequent abnormality (61%) in patients with lupus erythematosus. Fourteen (42%) of all patients with lupus erythematosus-associated valve regurgitation had moderate or severe regurgitant lesions. Three patients with lupus erythematosus-associated severe mitral or aortic regurgitation had respective mild mitral or aortic stenosis. The frequency and severity of regurgitation in each valve was similar in patients with lupus erythematosus with or without antibody (Table 5). Patients in group I or II had significantly more frequent and more severe lesions compared with patients in group III or IV (p < 0.005). In group I 27% and in group II 25% of all patients had moderate or severe lesions, and an equal number of patients in each group had more than one regurgitant valve. No patient in group III or IV had more than single or mild lesions.

Other cardiac findings. Eleven patients with lupus erythematosus (20%) (six in group I and five in group II) had segmental or global left ventricular systolic dysfunction. In 3 of the 11, severe left ventricular systolic dysfunction was associated with severe valve disease; the other 8 had left ventricular dysfunction without significant valve disease. Four of the 11 patients underwent coronary angiography, and 3 of the 4 were found to have coronary artery disease. One patient had a sinus of Valsalva aneurysm associated with severe aortic regurgitation and mild aortic stenosis. Only two patients had pericardial effusion.
Table 5. Valve Regurgitation Distribution and Severity in Groups I (SLE + AB) and II (SLE - AB)

<table>
<thead>
<tr>
<th></th>
<th>Mitral Regurgitation</th>
<th>Aortic Regurgitation</th>
<th>Tricuspid Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
<td>Group II</td>
<td>No.</td>
</tr>
<tr>
<td>Mild</td>
<td>7</td>
<td>64</td>
<td>10</td>
</tr>
<tr>
<td>Moderate</td>
<td>3</td>
<td>27</td>
<td>4</td>
</tr>
<tr>
<td>Severe</td>
<td>1</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>15</td>
<td>3</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

Discussion

Major findings. There are four major findings in this study. 1) Valve disease is present in the majority of patients with systemic lupus erythematosus. 2) Patients with lupus erythematosus have a similar frequency and severity of valve disease regardless of the presence or absence of antiphospholipid antibodies. 3) Antiphospholipid antibodies in the absence of lupus erythematosus were not associated with valve disease. 4) The leaflet thickening and associated masses observed by transesophageal echocardiography in patients with lupus erythematosus have an appearance that may be unique to this disease.

Comparison with previous studies. The results of this study differ from those of recent studies. We observed a relative lack of valve disease in patients with the primary or secondary antiphospholipid syndrome (10%). Nihoyannopoulos et al. (4) reported a much higher incidence (67%) of valve disease in patients with either syndrome and Brenner et al. (22) reported valve abnormalities in 32% of patients with the primary antiphospholipid syndrome. These differences may be related to the small size of the groups studied in combination with other selection factors. Our subjects were neither suspected of having heart disease nor referred for echocardiography. A difference in valve disease prevalence in the primary and secondary syndromes may warrant consideration. In our study, an equal number of patients with antiphospholipid syndrome had a primary or a secondary syndrome. The duration of the disease also may influence the frequency of valve disease.

The reported prevalence of lupus erythematosus-associated valve disease varies widely depending on the study methods used and patients studied. Bahl et al. (5) recently reported the virtual absence of valve disease in patients with a diagnosis of lupus erythematosus of <1 year's duration. Galve et al. (1) reported an 18% prevalence of abnormal valve morphology in patients with chronic lupus erythematosus. Nihoyannopoulos et al. (4) found an overall 28% prevalence of valve disease (40% in those with antiphospholip antibodies and 14% in those without antibodies) in patients with lupus erythematosus. Enomoto et al. (3) reported a 79% prevalence of valve regurgitation in patients with lupus erythematosus. Pathologic studies generally yield an estimate of >50% for the prevalence of valve involvement in patients with lupus erythematosus. By contrast, the present data showed a prevalence of 77% in patients with lupus erythematosus with antibodies and of 72% in those without antibodies.

Several factors probably contribute to the variable results of available studies. It is likely that transthoracic echocardiographic studies underestimate the true prevalence. Also, studies of patients older than 60 years may overestimate the presence of valve disease because of degenerative disease. In addition, studies including patients referred for suspected valve disease or with more severe lupus erythematosus may overestimate the frequency of valve disease.

The mean duration of lupus erythematosus in this study of 9.2 ± 8.4 years (range 0.2 to 35) may have contributed to the high prevalence of valve disease. However, overestimation of valve disease probably was reduced by excluding subjects over age 60 years. Our subjects were not referred because of suspected valve disease (only 4 of 54 were aware of having a heart murmur) or because of severe lupus erythematosus. The prevalence of lupus-associated valve disease in this study is generally representative of an outpatient population, although skewing of our study group toward more severe lupus erythematosus cannot be excluded.

Pathogenesis of systemic lupus-associated valve disease. Our results do not support the hypothesis that antiphospholip antibodies are a key pathogenic factor for valve disease in patients with lupus erythematosus (4). Neither the presence nor the concentration of IgG or IgM anticardiolipin antibodies, nor the presence of lupus anticoagulant antibody nor a false positive VDRL was associated with more frequent or more severe valve disease. In addition, careful review of our data failed to show any difference in the appearance of leaflet thickening or associated masses between patients with lupus erythematosus with or without antibodies.

These data suggest caution in attributing valve disease to the simple presence of antiphospholipid antibodies. The participation of such antibodies in this process is possible, but their presence does not seem to be required, and these data suggest that other factors may be important as well.

Comparison with rheumatic valve disease. Important differences were found in this study between the valve abnor-
malities of lupus erythematosus-associated valve disease and those of rheumatic valve disease. In patients with lupus erythematosus, valve leaflet thickening was generally diffuse rather than localized to the leaflet tips, as is typical for rheumatic disease. When localized leaflet thickening was noted in patients with lupus erythematosus, the leaflet midportion or base was usually involved. Only minimal involvement of the mitral subvalvular apparatus was observed in our patients with lupus erythematosus. This involvement took the form of small masses attached to normal-appearing chordae, without the chordal thickening, fusion and calcification characteristic of rheumatic disease. Valve masses in lupus erythematosus were frequently located near the base of leaflets, and calcification was not a prominent feature. In contrast, mass lesions associated with rheumatic disease are usually located near leaflet tips and are heavily calcified. In both diseases the aortic and mitral valves tend to be involved, and regurgitation usually predominates although stenosis has been reported (23, 24). Regurgitant lesions were the rule in our study as in several others (3,12,28).

Comparison with postmortem studies of lupus-associated valve disease. The findings of this study differ from those of the early pathologic studies of lupus-associated valve disease by Libman and Sacks (6), Klemperer (7) and Brigden (8). These investigators described frequent tricuspid involvement that was not confirmed by more recent pathologic and echocardiographic studies or in our study (1–4,25,26). They also observed aortic valve masses primarily on the ventricular side of the valve, whereas we observed these lesions usually on the vessel side. Similarly, they reported mitral lesions to be near the leaflet tips on either the ventricular or the atrial surface, whereas the mitral masses in our study were primarily at the leaflet base on the atrial surface. Finally, we did not observe the endocardial (“pocket”) lesions previously reported by these investigators.

Some of these differences may be related to certain limitations of transesophageal echocardiography. The monoplane transesophageal technique allows only a limited number of imaging planes for the detection of ventricular endocardial lesions or abnormalities of the tricuspid valve. Nevertheless, we think that the differences between the early and recent studies may reflect the effects of current therapy for lupus erythematosus on the development of valve disease.

Lupus-associated valve disease versus infective endocarditis. Lupus-associated valve masses differ from infection-associated masses by their location, appearance and mobility. Lupus-associated valve masses are predominantly located near the leaflet base, whereas infection-associated masses are almost always located at the leaflet’s line of closure. Lupus-associated valve masses are of heterogeneous echodensity and usually show central regions with high reflectance suggesting connective tissue or even calcific density; vegetations caused by acute infective endocarditis usually demonstrate a homogeneous soft tissue density. As observed by transesophageal echocardiography, the lupus-associated valve masses move exactly parallel to the motion of the related leaflet, whereas infection-associated vegetations show vibratory or rotatory motion at least partly independent from the motion of the valve.

Limitations of the study. The small number of patients in our study with antiphospholipid syndrome may cause error in estimation of the prevalence of valve disease in these patients. Similarly, the small number of patients with antiphospholipid syndrome in other series limits the validity of the reported association between valve disease and antibodies. Conversely, the large number of our patients with lupus erythematosus with and without antibodies makes a strong association between antiphospholipid antibodies and valve disease unlikely, although we do not have the statistical power to rule out an association.

The lack of pathologic confirmation of transesophageal echocardiographic findings in our study limits the assessment of the accuracy of this technique. Systemic lupus erythematosus is a complex and protean disease, and factors such as the duration of active disease, the status of other immunologic markers and the duration of steroid, cytotoxic or antithrombotic drug therapy all may have a major impact on the development of valve disease. The relation of these important factors to either valve disease or antiphospholipid antibodies was not analyzed in this study. In addition, longitudinal, controlled studies would be useful to fully define the role of antiphospholipid antibodies in lupus-associated valve disease. It is possible that antiphospholipid antibodies over a long time or at high concentrations, or both, contribute to valve involvement in this disease.

Clinical implications of lupus-associated valve disease. The discovery of valve disease in a patient with lupus erythematosus has several important implications. The most feared consequence of valve involvement is progression to severe valve dysfunction and the need for valve replacement (27,28). Two patients in our study underwent aortic valve replacement because of symptomatic severe aortic regurgitation. However, lupus-associated valve disease may present with other important clinical sequelae before signs or symptoms of severe valve dysfunction develop. For example, valve lesions may serve as a substrate for systemic thromboembolism (29,30). Six patients in our study with valve disease had previously documented transient ischemic attacks or strokes. Although the etiologic role of the valve abnormalities is not proved in these patients, valve involvement was not suspected in any of these patients before the neurologic event occurred. The additional valve data obtainable by transesophageal echocardiography suggests that this diagnostic study may be indicated in patients with systemic lupus erythematosus with transient or permanent focal cerebrovascular dysfunction to detect a valvular or other cardiac substrate for thromboembolism. Infective endocarditis is another potential complication that has been reported clinically and pathologically (26,30,31). Finally, valve disease may be an important indicator of the degree of activity or severity, or both, of systemic lupus erythematosus.
Conclusions. This study has shown with transesophageal echocardiography that patients with systemic lupus erythematosus have a similar prevalence and severity of valve disease whether or not they have antiphospholipid antibodies. These data do not support the hypothesis that antiphospholipid antibodies are a primary pathogenetic factor in lupus-associated valve disease. Finally, the characteristic appearance of leaflet thickening and associated masses may be unique to lupus-associated valve disease.

We gratefully thank Dorothy Pattack, PhD for her expert statistical contribution.

References


