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Anti-phospholipid Antibodies and Heart Valve Disease in Systemic Lupus Erythematosus

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Abstract

Purpose—Evaluation of antiphospholipid antibodies (aPL) and correlation with heart valve abnormalities among SLE patients.

Methods—Nested case-control study was conducted with 70 SLE patients selected from a longitudinal database based on levels of aPL and presence or absence of valve disease by echocardiogram.

Results—Valvular abnormalities observed were regurgitation (52), other (14), artificial valves (4), stenosis (2), thickening (2), and no Libman-Sacks endocarditis (0). The mitral valve was the most commonly affected (30 abnormalities), followed by the tricuspid (20 abnormalities).

Multivariate logistic regression for those with and without an aPL value ≥ 20 units/mL, adjusted for disease duration and age, showed significant differences for any valve abnormality (OR=3.1, CI 95% 1.0–8.9, $p=0.041$) and individually for the tricuspid valve (OR=3.3, CI 95% 1.0–11.1, $p=0.052$) but not for the mitral valve (OR=2.1, CI 95% 0.68–6.45, $p=0.195$). Levels of aPL ≥ 20 units/mL showed no association with aortic ($p=0.253$), pulmonic ($p=1.000$), tricuspid ($p=0.127$), or mitral ($p=0.249$) valve abnormalities.

Conclusion—Levels of aPL correlate with certain valvular abnormalities among SLE patients.

Key terms

Antiphospholipid antibodies; Antiphospholipid Syndrome; Systemic Lupus Erythematosus; Heart Valve Diseases

Introduction

Elevated levels of antiphospholipid (aPL) antibodies can be seen among patients with SLE, and are often associated with clinical hypercoagulability. Antiphospholipid Syndrome (APS), whether primary or secondary in the setting of SLE, often presents as arterial/venous

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thrombosis and pregnancy loss. Thrombocytopenia is present in about 20% of APS cases, ranging from 50 to 140,000 platelets/mm³ [1]. The formation of beta 2 glycoprotein I (B₂GPI)/aPL immune complexes can deposit and damage valvular surfaces, predisposing to hemodynamic dysfunction and thromboembolic events. Thus, it can be speculated that heart valve disease may be a predictive factor for APS-related complications.

The aPL antibodies of interest are the lupus anticoagulant (LA), anticardiolipin (aCL), and anti-beta 2 glycoprotein I antibodies. These are found elevated in about 1–6% of the general population [2]. These antibodies are directed against negatively charged phospholipids and plasma proteins, particularly the B₂GPI. This protein has been shown to form complexes with anionic phospholipids resulting in inhibitory functions in coagulation pathways.

Autoimmune-mediated and inflammatory cardiovascular damage is one of the common causes of mortality in SLE [3]. It is currently well recognized that patients can have clinically significant cardiac valve disease, typically aortic insufficiency, leading to prosthetic valve replacement. The classic cardiac lesion of SLE is Libman-Sacks Endocarditis, which manifests as an atypical endocarditis with 1–4 mm verrucous vegetations present on either side of the mitral and aortic valves. Studies by Ziporen et al. and Eiken et al. found aPL immune complexes, complement fragments, fibrin, and platelets in valvular vegetations among SLE patients in Libman-Sacks endocarditis valve specimen studies [4,5]. The prevailing theory behind SLE-related valvular disease is that antiphospholipid antibodies contribute to damage via inflammatory and thrombotic-mediated pathways. Specifically, aPL immune complexes interact with different cells inducing a pro-inflammatory/coagulatory environment.

Previous studies examining the role of aPL in SLE heart valve disease were limited by small sample sizes and by inconsistent cutoffs used for defining elevated aPL levels. Our study sets out to determine the association of heart valve abnormalities with aPL levels among well characterized SLE patients followed in a longitudinal registry to address these questions.

Patients and Methods

Study Design

This research was carried out with the approval of the Institutional Review Board at the Medical University of South Carolina (MUSC). This study was conducted by reviewing data collected within the longitudinal SLE Database at MUSC. This was a retrospective observational nested case control study investigating the presence of cardiac valve abnormalities by echocardiogram in relation to aPL levels. All SLE patients that had an echocardiogram and aPL levels from the database were included in the study.

Study Population

Eligible patients were: 1) age 10 years and above, 2) classified as having “definite” SLE, meeting at least 4 of the 11 revised 1997 American College of Rheumatology (ACR) classification criteria [6,7], 3) able and willing to give informed consent, 4) available echocardiogram report, and 5) available aPL levels. About 75% of SLE patients within the

database are African American, with the majority of them being Gullah African American. This is a unique population from the Sea Islands of South Carolina and Georgia with lower European admixture and greater genetic homogeneity compared to other African American populations, as previously described [8].

Variables

Study subjects were split into aPL negative (levels <20 units/mL), aPL low positive (levels between 20–40 units/mL) and aPL high positive (levels ≥ 40) groups based on the following antibodies: anticardiolipin (aCL) IgM, IgG as well as anti- B₂GPI IgM, IgG [9].

Echocardiogram reports were assessed for: valvular thickening, Libman-Sacks endocarditis, stenosis, regurgitation, and artificial valve placement. Non-hemodynamic valvular abnormalities such as calcifications and sclerosis were categorized together as “Other Findings.” Childhood onset SLE (cSLE) was defined as being diagnosed with SLE < 18 years of age.

Statistical Analyses

An a priori sample size calculation was conducted, using a power of 0.8 and Type I error probability of 0.05. Based on prior literature, we calculated a required sample size of 70 subjects required for our study, assuming the true probability of any valve disease among aPL positive patients is 0.3.

Prior to conducting the formal hypothesis tests, descriptive statistics were generated and differences at baseline were tested. In order to assess differences in proportions, Pearson’s chi-squared tests or Fisher’s exact tests were performed, as appropriate. Single variable regression models were performed to examine abnormalities in any valve as well as individual valves in relation to race, gender, age of SLE onset, SLE duration and age at visit, and thrombocytopenia. Multivariate logistic regression models, adjusted for disease duration and age, were performed to assess associations between aPL levels and valve abnormalities. Significance was set at an alpha of 0.05. All statistical analyses were performed using Stata v14.

Results

Data were collected from SLE patients with known diagnosis dates; demographics and clinical measures are presented in Table 1. The study population consisted primarily of African American (69%) females (93%). Mean age at the time of the study visit was 34.0 years (sd= 16.7). The mean age at SLE diagnosis was 27.2 years (sd= 15.6) with average disease duration of 6.8 years (sd= 7.3). No significant difference was seen between the negative and positive aPL groups in regards to age, gender, disease duration, age at diagnosis, and ethnicity as seen in Table 1.

The most common echocardiogram findings among the SLE patients in our study were valvular abnormalities (61% of patients). The second was pericardial effusion (39% of patients) and third was diastolic dysfunction (29% of patients). Only one patient had an ejection fraction less than 40%. There was no significant difference in pericardial effusion prevalence in relationship to aPL status (p-value = 0.337). There was also no significant

difference found in terms of diastolic dysfunction prevalence in relationship to aPL status (p-value = 0.662).

Among the 70 patients, the mitral valve had the highest number of abnormalities (30), followed by the tricuspid (20), aortic (15), and pulmonic (9). Eight patients had more than one valve abnormality present. The most common valve abnormality overall was regurgitation, with 52 cases. Valve regurgitation was evident on echocardiogram in: 19 tricuspid, 18 mitral, 8 pulmonic, and 7 aortic valves. There were 14 non-hemodynamically significant “other findings” (6 mitral and 6 aortic valves) and 3 patients with mechanical/artificial valve replacements. Two occurrences of stenosis and thickening each were also found. Libman Sacks endocarditis was not found in this cohort, including a chart review of the 3 patients with valve replacements. Details are shown in Table 1.

Pearson Chi-Squared analysis and Fisher’s Exact test were conducted to compare valve abnormalities between aPL negative or positive groups of patients. No significant association was found between aPL group and valve abnormalities for the tricuspid (p-value= 0.127), mitral (p-value= 0.249), aortic (p-value= 0.253), or pulmonic (p-value= 1.000). Echocardiograms were not able to visualize a certain valve in a few cases, explaining why some valve groups had less than 70 patients, per Table 1.

Using single variable regression models, shown in Table 2, significant associations were seen between abnormalities in any valve and aPL levels ≥ 20 units/mL (OR= 3.3, CI 95%= 1.1–7.8, p-value= 0.035) and visit age ≥ 40 years (OR= 5.2, CI 95%= 1.4–18.9, p-value= 0.012). However, there was not a significant association between aPL titers ≥ 40 and abnormalities in any valve (OR= 2.6, CI 95%= 0.8–8.1, p-value= 0.098). Regression models for the tricuspid valve showed no correlation in aPL titers ≥ 20 (OR= 3.1, CI 95%= 0.9–9.9, p-value= 0.062) and titers ≥ 40 (OR= 2.3, CI 95%= 0.8–7.0, p-value= 0.133), even though there was a trend toward significance. Regression models for the mitral valve showed no correlation in aPL titers ≥ 20 (OR= 2.1, CI 95%= 0.7–6.5, p-value= 0.195) and titers ≥ 40 (OR= 1.5, CI 95%= 0.5–4.6, p-value= 0.460), but were significant for disease duration (OR= 3.2, CI 95%= 1.1–9.4, p-value= 0.038). There was no significant association between abnormalities in any cardiac valve, tricuspid, and mitral valve in regards to race, gender, age at diagnosis, or platelet levels.

Multivariate logistic regression models, adjusted for both disease duration and age, showed a significant association between aPL titers ≥ 20 and an abnormality in any valve (OR= 3.1, CI 95%= 1.0–8.9, p-value= 0.041) and tricuspid valve (OR= 3.3, CI 95%= 1.0–11.1, p-value= 0.052). There was no association in multivariable regression models of the mitral valve (OR= 2.1, CI 95%= 0.7–6.5, p-value= 0.195). All regression models are shown in Table 2.

Medication use history among the patients in our study reflected common medications used for the treatment of SLE, but were not significantly different based on aPL status. Patients with aPL levels ≥ 20 were more commonly taking hydroxychloroquine (93.3% vs. 84.6%), azathioprine (46.7% vs. 16.7%), rituximab (30.8% vs. 8.3%), cyclophosphamide (28.6% vs. 16.7%), and were less commonly taking mycophenolate (46.75% vs. 61.5%). However, none

of these differences in medication use were statistically significant, albeit limited by small sample size (only 30 of the 70 patients had complete medication use records).

Discussion

Among this population of patients with SLE, 61% were found to have HVD by echocardiogram. Higher levels of aPLs were associated with an increased presence of HVD. Consistent with previous literature, patients that had aPL levels ≥ 20 units/mL also had a higher prevalence of HVD. Also, as expected, age of the patient at their study visit was a significant predictor of the presence of HVD. Importantly, the association between aPL level and HVD remained significant even when controlling for patient age. An association was also seen between SLE disease duration and mitral valve abnormalities. These findings suggest that aPLs are risk factors in the development of HVD among SLE patients. Therefore, we suggest these “at risk” patients be screened via echocardiogram for HVD to reduce potential complications.

Although it has been reported that approximately 30–38% of patients with SLE will have cardiac vegetations, most of which are asymptomatic but still put them at risk of endocarditis, we did not find evidence of these in our study population [10, 11]. A systemic review by Zuily et. al examined 23 studies finding 508 HVD cases among 1656 SLE patients. Compared to aPLs negative patients, the presence of aPLs lead to an overall pooled odds ratios for HVD and Libman-Sacks endocarditis in aPL-positive patients of 3.13 (CI 95% = 2.31–4.24) and 3.51 (CI 95% = 1.93–6.38), respectively [12]. This study also supported our findings with 21 studies showing regurgitation of the total 23 studies. It should be noted that this same systemic review showed some contrary results to ours including other common abnormalities such as thickening (17 studies), stenosis (10 studies), and Libman-Sacks Endocarditis (16 studies) of the total 23 studies assessed. Additionally, the mitral valve was found to be the most common site of abnormalities (19 studies). The second was the aortic valve (17 studies) and third was the tricuspid (10 studies). Our cohort showed the mitral valve being most commonly affected, but the tricuspid valve being second.

Our analysis showed only a significant association between aPL titers and HVD, not Libman-Sacks endocarditis. Our cohort showed regurgitation, 52 total cases, to be the most common valve abnormality affecting the mitral (18 cases) and tricuspid (19 cases) valves most commonly. Interestingly, our cohort showed only two cases of valve thickening and 2 cases of valve stenosis. Despite known association between high aPL titers and Libman Sacks Endocarditis from the literature, we found no cases in our cohort. Reasons for fewer cases may be due to increased adherence to quality of care guidelines recommending hydroxychloroquine and aspirin for patients with APS.

A Serbian cohort described by Djokovic et al. elucidated some new relationships [13]. This study found that the most common cardiac manifestation in the primary APS group (n=260) was unstable angina pectoris and in the secondary APS group with SLE (n=114) was valvular manifestations. In fact, it was found that the frequency of Libman-Sacks endocarditis was much higher in secondary APS (35% of group) versus primary APS (24%

of group) (OR= 4.36, CI= 2.433–7.770, p-value= 0.0001). Further aPL subtype analysis showed a significant association between aCL IgG and the presence of Libman-Sacks endocarditis (OR= 2.04, CI= 1.161–3.584, p-value= 0.009), valve thickening and dysfunction (OR= 3.09, CI= 1.050–9.067, p-value= 0.030), and overall cardiac manifestations (OR= 1.62, CI= 1.024–2.567, p-value= 0.026). LA positivity was significantly associated with the presence of myocardial infarction (P = 0.010, OR 3.96, CI 0.523–2.072). This study shed some light on the differences in cardiovascular manifestations between primary/secondary APS and aPL subtypes. In addition, this study found a strong correlation between aPL and Libman-Sacks endocarditis, an interesting contrast to our cohort.

In addition, a 2011 study by Plazak et al. showed that IgG aPLs correlated with perfusion defects in the myocardium and increased right ventricular systolic pressure. However, it also showed that valvular and pericardial thickening were more likely related to laboratory markers of acute inflammation [14]. Another systemic review by Mattos et al. consisting of a total of 1,593 SLE patients studies showed a significant association between aPL and HVD as well as Libman-Sacks endocarditis among 13 and 9 of the 20 studies assessed, respectively [15]. Furthermore, a 2016 study by Mohammed et al. also showed correlation between anticardiolipin antibodies, lupus anticoagulant, and anti- β 2 glycoprotein antibodies and mitral valve regurgitation (p values 0.044, 0.006, and 0.023) [16]. These findings support our aPLs and HVD claim, yet also show contrast to our Libman-Sacks endocarditis findings.

It is important to emphasize that our study showed not only a statistically significant association between aPLs and HVD among SLE patients, but provides the groundwork for other prospective studies to gauge the clinical significance of these valvular lesions. For example, a prospective cohort study by Perez-Villa et al., consisting of 61 SLE patients matched with 40 controls, found that valvular lesion prevalence increased from 39% to 73% during the 10-year follow up. Seven patients (12%) developed severe regurgitation, which was significantly related to anticardiolipin IgG antibodies (p-value= 0.001). The combined incidence of stroke, peripheral embolism, need for valve surgery, and death was 86% in patients with severe valvular regurgitation, compared with 25% in those without (p-value= 0.003). Of particular importance is that 5 out of these 7 patients required valve replacement surgery with a mechanical valve, which in turn further increased the risk of thromboembolic events [17]. Interestingly, our study had four patients that also underwent valve replacement surgery. Three of those cases had severe regurgitation thought to be due to SLE, and the fourth case was due to rheumatic heart disease. A 2015 paper studied the combined risk of thrombosis in patients with artificial valves and anticardiolipin antibodies concluding that inappropriate anticoagulation played the major role in thrombotic complications, while anticardiolipin IgM and IgG only played a minor role [18]. Another study showed that patients with HVD such as regurgitation, thickening, vegetations and LA had 2–3 increased risk of cerebrovascular accidents (all p-value <0.04) [19]. There is compelling evidence to suggest that aPL-mediated heart valve disease leads to significant clinical complications.

Our study had limitations, including those due to the cross-sectional study design limiting our ability to look at duration of aPL positivity prior to development of HVD. We also were

limited by the type of imaging available. It has been well documented that transesophageal echocardiograms produce higher resolution images of valves and is the superior technique for assessing valvular damage [20, 21]. The majority of our patients underwent transthoracic echocardiograms; therefore, it is possible that the more frequent use of transthoracic echocardiography in our study may have resulted in missed cases of HVD.

Although we looked at aPL positivity in general, rather than the role each specific subtype, literature review suggests the most predictive HVD risk factors include both the LA and aCL IgG, having a pooled odds ratio of 5.88 and 5.63, respectively [12]. Literature of HVD and anti-B2GPI antibodies specifically is limited. An interesting point is that SLE patients are at a sixfold increased risk of venous thromboembolism with high titers of LA compared to only a twofold increased risk with high titers of aCL when compared to their negative aPL counterparts [22].

In conclusion, the prevailing pathophysiologic theory is that aPL immune complexes deposit upon valvular surfaces resulting in direct valvular damage via a thrombotic and/or inflammatory mechanism and can predispose patients to clinically significant valve disease and thromboembolic events. Our findings in a cohort of patients with SLE support those mechanisms, finding that the high levels of aPL antibodies, especially 40 units/mL, are significantly associated with heart valve disease. Future directions should include completing prospective cohort studies to assess the clinical impact of valvular lesions. Such information can then better inform our HVD risk factor prediction and our screening recommendations in the care of patients with SLE.

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References

1. Petri, Michelle. Primer on the Rheumatic Diseases. 13. New York City: Springer; 2008. Antiphospholipid Syndrome; p. 339-42. Print
2. Petri, M. Epidemiology of the Antiphospholipid Syndrome. In: Asherson, RA, Cervera, R, Piette, J-C., Shoenfeld, Y., editors. The antiphospholipid syndrome. Boca Raton, FL: CRC Press; 1996. p. 13-28.
3. McMahon M, et al. A panel of biomarkers is associated with increased risk of the presence and progression of atherosclerosis in women with systemic lupus erythematosus. *Arthritis Rheum.* 2014; 66:130-139.
4. Ziporen L, Goldberg I, Arad M, Hojnik M, Ordi-Ros J, Afek A, Blank M, Sandbank Y, Vilardell-Tarres M, de Torres I, Weinberger A, Asherson RA, Kopolovic Y, Shoenfeld Y. Libman-Sacks endocarditis in the antiphospholipid syndrome: immunopathologic findings in deformed heart valves. *Lupus.* 1996; 5:196-205. [PubMed: 8803890]
5. Eiken, Patrick W., Edwards, William D., Tazelaar, Henry D., Mcbane, Robert D., Zehr, Kenton J. Surgical Pathology of Nonbacterial Thrombotic Endocarditis in 30 Patients, 1985-2000. *Mayo Clinic Proceedings.* 2001; 76(12):1204-212. Web. [PubMed: 11761501]
6. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfeld NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum.* 1982; 25:1271-7. [PubMed: 7138600]

7. Hochberg MC. for the Diagnostic and Therapeutic Criteria Committee of the American College of Rheumatology. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus [letter]. *Arthritis Rheum.* 1997; 40:1725.
8. Kamen DL, Barron M, Parker TM, Shaftman SR, Bruner GR, Aberle T, James JA, Scofield RH, Harley JB, Gilkeson GS. Autoantibody prevalence and lupus characteristics in a unique African American population. *Arthritis Rheum.* 2008; 58(5):1237–1247. [PubMed: 18438839]
9. Lockshin MD, Kim M, Laskin CA, et al. Prediction of adverse pregnancy outcome by the presence of lupus anticoagulant, but not anticardiolipin antibody, in patients with antiphospholipid antibodies. *Arthritis Rheum.* 2012; 64:2311–8. [PubMed: 22275304]
10. Luce EB, Presti CF, Montemayor I, Crawford MH. Detecting cardiac valvular pathology in patients with systemic lupus erythematosus. *Spec Care Dentist.* 1992; 12(5):193–197. [PubMed: 1308315]
11. Gabrielli F, Alcini E, Di Prima MA, Mazzacurati G, Masala C. Cardiac valve involvement in systemic lupus erythematosus and primary antiphospholipid syndrome: lack of correlation with antiphospholipid antibodies. *Int J Cardiol.* 1995; 51(2):117–126. [PubMed: 8522406]
12. Zuily S, Regnault V, Selton-Suty C, Eschwege V, Bruntz J-F, Bode-Dotto E, De Maistre E, Dotto P, Perret-Guillaume C, Lecompte T, Wahl D. Increased Risk for Heart Valve Disease Associated With Antiphospholipid Antibodies in Patients With Systemic Lupus Erythematosus: Meta-Analysis of Echocardiographic Studies. *Circulation.* 2011; 124(2):215–24. Web. [PubMed: 21690492]
13. Djokovic, Aleksandra, Stojanovich, Ljudmila, Kontic, Milica, Stanisavljevic, Natasa, Radovanovic, Slavica, Marisavljevic, Dragomir. Association between Cardiac Manifestations and Antiphospholipid Antibody Type and Level in a Cohort of Serbian Patients with Primary and Secondary Antiphospholipid Syndrome. *Israel Medical Association Journal.* 2014; 16(3):162–67. Print. [PubMed: 24761704]
14. Plazak W, Gryga K, Milewski M. Association of heart structure and function abnormalities with laboratory findings in patients with systemic lupus erythematosus. *Lupus.* 2011; 20:936–944. [PubMed: 21636627]
15. Mattos, Priscila, Santiago, Mittermayer B. Association of Antiphospholipid Antibodies with Valvulopathy in Systemic Lupus Erythematosus: A Systematic Review. *Clin Rheumatol Clinical Rheumatology.* 2011; 30(2):165–71. Web. [PubMed: 21207090]
16. Mohammed AG, Alghamdi AA, ALjahlan MA, Al-Homood IA. Echocardiographic findings in asymptomatic systemic lupus erythematosus patients. *Clin Rheumatol.* 2016; doi: 10.1007/s10067-016-3486-4
17. Perez-Villa, Felix, Font, Josep, Azqueta, Manel, Espinosa, Gerard, Pare, Carles, Cervera, Ricard, Reverter, Joan C., Ingelmo, Miguel, Sanz, Gines. Severe Valvular Regurgitation and Antiphospholipid Antibodies in Systemic Lupus Erythematosus: A Prospective, Long-term, Followup Study. *Arthritis Rheum Arthritis & Rheumatism.* 2005; 53(3):460–67. Web. [PubMed: 15934103]
18. Aykan AÇ, Gökdeniz T, Kalçık M, Astarçio lu MA, Gündüz S, Karakoyun S, Gürsoy MO, O uz AE, Ertürk E, Çakal B, Bayram Z, Özkan M. Role of Anticardiolipin Antibodies in the Pathogenesis of Prosthetic Valve Thrombosis. *Herz.* 2015; 40(3):528–33. [PubMed: 24441396]
19. Roldan CA, Gelgand E, Qualls C, Sibitt W. Valvular heart disease as a cause of cerebrovascular disease in patients with systemic lupus erythematosus. *Am J Cardiol.* 2005; 95:1441–7. [PubMed: 15950567]
20. Shively BK, Gurule FT, Roldan CA, Leggett JH, Schiller NB. Diagnostic value of transesophageal compared with transthoracic echocardiography in infective endocarditis. *J Am Coll Cardiol.* 1991; 18(2):391–397. [PubMed: 1856406]
21. Seward JB, Khandheria BK, Oh JK, Abel MD, Hughes RW Jr, Edwards WD, et al. Transesophageal echocardiography: technique, anatomic correlations, implementation, and clinical applications. *Mayo Clin Proc.* 1988; 63(7):649–680. [PubMed: 3290590]
22. Wahl DG, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk for venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus: a meta-analysis. *Lupus.* 1997; 6:467–473. [PubMed: 9229367]

Significance and Innovations

- This study explored whether high titers of antiphospholipid antibodies are risk biomarkers for cardiac valve disease among patients with SLE.
- Cardiac valve disease mediated by aPL in SLE patients most commonly presents as mitral and tricuspid regurgitation.
- Libman Sacks endocarditis was not associated with aPLs in this study population.
- While current evidence suggests aPL-mediated valve disease predisposes to significant complications, additional prospective cohort studies are needed to characterize the clinical relevance of aPL-mediated valvular damage.

Table 1

Demographics and Valve Abnormality Types/Prevalence

P-Values for single valve data were calculated via Pearson Chi-Squared and Fisher's Exact Analysis (if $N < 5$).

Demographics		All Patients N = 70	High aPL Patients (40 units/mL) n = 24		
Age –Mean (StdDev)		34.0 (16.7)	36.9 (19.0)		
Age at SLE Dx –Mean (StdDev)		27.2 (15.6)	29.7 (19.8)		
SLE Disease Duration –Mean (StdDev)		6.8 (7.3)	7.2 (6.8)		
African American– N(%)		48 (68.6)	12 (50)		
Female – N(%)		65 (92.9)	23 (95.8)		
Type of Valvular Abnormality	Tricuspid	Mitral	Aortic	Pulmonic	Any Valve
Stenosis – N	0	1	1	0	2
Regurgitation – N	19	18	7	8	52
Libman-Sacks Endocarditis –N	0	0	0	0	0
Thickening – N	0	2	0	0	2
Artificial Valve – N	0	3	1	0	4
Other – N	1	6	6	1	14
Total Abnormality for valve type – N	20	30	15	9	74

Single Valve Analysis		Normal – N	Abnormality – N	Total – N	P-Value
Tricuspid Valve					
aPL < 40 units/mL	36	10	46		
aPL 40 units/mL	14	9	23		
Total	50	19	69		0.127
Mitral Valve					
aPL < 40 units/mL	33	13	46		
aPL 40 units/mL	14	9	23		
Total	47	22	69		0.249
Aortic Valve					
aPL < 40 units/mL	34	5	39		
aPL 40 units/mL	23	7	30		
Total	57	12	69		0.253
Pulmonic Valve					

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Single Valve Analysis	Normal – N	Abnormality – N	Total – N	P-Value
aPL < 40 units/mL	34	5	39	
aPL ≥ 40 units/mL	22	3	25	
Total	56	8	64	1.000

Table 2**Regression Models**

Single and Multi Variable Regression Models for sample data.

		Odds-Ratio	CI 95%	P-Value
Single Variable Regression, Abnormality in Any Valve				
aPL	20	3.3	1.1–7.8	0.035
aPL	40	2.6	0.8–8.1	0.098
African American		0.7	0.2–2.2	0.577
Female		0.6	0.1–4.2	0.641
Childhood Onset SLE		0.4	0.1–1.2	0.108
Visit Age	40 Years	5.2	1.4–18.9	0.012
Disease Duration	10 years	1.2	0.4–3.9	0.763
Platelets		1.0	1.0–1.0	0.235
Single Variable Regression, Tricuspid Valve Abnormality				
aPL	20	3.1	0.9–9.9	0.062
aPL	40	2.3	0.8–7.0	0.133
African American		1.0	0.3–3.1	0.987
Female		1.5	0.2–14.6	0.711
Childhood Onset SLE		0.6	0.2–1.9	0.382
Visit Age	40 Years	1.6	0.5–4.7	0.402
Disease Duration	10 years	1.7	0.6–5.3	0.352
Platelets		1.0	1.0–1.0	0.936
Single Variable Regression, Mitral Valve Abnormality				
aPL	20	2.0	0.69–5.9	0.202
aPL	40	1.8	0.6–5.3	0.282
African American		0.5	0.2–1.6	0.250
Female		0.3	0.04–1.8	0.176
Childhood Onset SLE		0.7	0.2–1.9	0.433
Visit Age	40 Years	2.4	0.9–6.9	0.095
Disease Duration	10 years	3.2	1.1–9.4	0.038
Platelets		1.0	1.0–1.0	0.197
Multivariate Logistic Regression, adjusted for disease duration and age.				
Abnormality in Any of the Valves				
aPL	20	3.1	1.0–8.9	0.041
Abnormality in Tricuspid Valve				
aPL	20	3.3	1.0–11.1	0.052
Abnormality in Mitral Valve				
aPL	20	2.1	0.7–6.5	0.195