Legends of Video Clips of Figures 1A and Supplemental Figures 1-5.

Legend of video clip 1A: 55 year old female with SLE and acute transient ischemic attack. This TEE view demonstrates a moderate size, elongated, sessile, and heterogeneously echoreflectant Libman-Sacks vegetation (arrow) on the atrial side of the posterior mitral leaflet.

Legend of supplemental video clip 1A: **18 year old female with SLE and acute homonymous hemianopsia, confusional state, and cognitive dysfunction.** This TEE four chamber view demonstrates a large (area of 1.3 cm2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetation (arrow) on the atrial side and mid to distal portions of the anterior mitral leaflet.

Legend of supplemental video clip 2A,B,E,F: 29 year old male with SLE and acute stroke and cognitive dysfunction. **A.** This two-dimensional (2-D) TEE view demonstrates large (area of 1.5 cm^2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations on the atrial side and distal portions of the anterior and posterior mitral leaflets associated with leaflets' thickening and decreased mobility. **B.** This real time 3-dimensional (RT3-D) TEE let atrial view (LA view) of the mitral valve demonstrates large, severely protruding with irregular surface, and roll-like shape vegetations on the atrial side and tip of the entire anterior and posterior mitral leaflets with associated decreased mobility and incomplete coaptation of the leaflets. **E, F**. After 3 months of immunosupressives and clopidogrel, the anterior

and posterior mitral leaflets vegetations (arrows) significantly decreased in size by 2-D (**E**) and RT-3D TEE (**F**) to a vegetation area of only 0.22 $cm^{2.}$ LA = left ventricle, LV = left ventricle on 2E, LA view (left atrial view), AV = aortic valve on 2F.

Legend of supplemental video clips 3A,D,F: 21 year old female with SLE with acute transient ischemic attack and previous stroke. **A**. This close-up 2D-TEE view demonstrates moderate size (area 0.85 cm^2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations on the LA side and distal portions of the anterior and posterior mitral leaflets associated with leaflets' thickening and decreased mobility. **D.** After 3 months of anticoagulation, repeat imaging demonstrated resolution of the anterior mitral valve vegetation and significant reduction in size of the posterior mitral leaflet vegetation. **F.** Associated with non-compliance with anticoagulation, the patient had a recurrent TIA and repeat imaging demonstrated recurrence of a moderate size posterior mitral leaflet vegetation.

Legend of supplemental video clips 4A: 38-year old female with SLE and acute stroke. **A.** This four-chamber TEE view demonstrates multiple small (total area of 0.46 cm^2), sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations on the LA side and mid to distal portions of the anterior and posterior mitral leaflets.

Legend of supplemental video clips 5A,D,E,F: 50 year old female with SLE with an acute transient ischemic attack, progressive memory loss, past stroke and seizure disorder. **A.** This four chamber 2D-TEE view demonstrates moderate size (area of 0.85 cm^2), oval shape, sessile, and predominantly soft tissue echoreflectant Libman-Sacks vegetations on the atrial side and distal portions of the anterior and posterior mitral leaflets with associated decreased leaflets' mobility. **D.** After 6 weeks of non-compliance with anticoagulation the patient had a recurrent TIA and her repeat TEE demonstrated persistent but smaller (area 0.58 cm^2) mitral valve vegetations and a new small (0.05 cm^2) aortic valve vegetation (not shown). **E**. After 5 months of therapeutic anticoagulation and aspirin, repeat TEE demonstrated significantly smaller (area 0.13 cm^2) and homogeneously hyperreflectant (healed) mitral valve vegetations. **F**. This corresponding RT3D-TEE LA view of the mitral valve demonstrates multiple homogeneously hyperreflectant nodular vegetations on the atrial side and leaflet tips of the anterior and posterior mitral leaflets consistent with healead vegetations. Decreased mobility of the posterior mitral leaflet without commissural fusion was also noted.

Supplemental Figure Legend

Supplemental Figure 1. 18 year old female with SLE and acute homonymous hemianopsia, confusional state, and cognitive dysfunction. A. This TEE four chamber view demonstrates a large (area of 1.3 cm^2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetation (arrow) on the atrial side and mid to distal portions of the anterior mitral leaflet (aml) (*see video clip supplemental 1A*). **B**. Transcranial Doppler of the right middle cerebral artery demonstrates 1 of 4 microemboli within the spectral Doppler (upper arrow) and within the vessel (lower arrow). **C**. Diffuse weighted imaging of the brain demonstrates bilateral acute parietal infarcts (arrows). **D**. This T2 FLAIR image demonstrates large periventricular and multiple smaller white matter lesions (arrows). Also, cortical edema is seen in the parietal lobe related to an acute infarct (horizontal arrow). She had a total of 115 focal brain lesions and a lesion load of 13.71 cm^3. Her global neurocognitive score was -3.21 and consistent with moderate neurocognitive dysfunction. She had a recurrent transient ischemic attack 1 week after her initial event and repeat imaging showed mitral valve vegetations, cerebromicroembolism, and new ischemic lesions in the right frontal lobe. After stabilization with immunosupressives and anticoagulants for 9 weeks, repeat imaging showed resolution of the mitral valve vegetation **(E),** resolution of cerebromicroembolism, decrease of brain lesions to 83 (**F)** and lesion load to 7.72 cm^3**,** and significant improvement in her global neurocognitive score to -1.3, consistent with mild neurocognitive dysfunction. LA = left atrium, LV = left ventricle, pml = posterior mitral leaflet.

Supplemental Figure 2. 29 year old male with SLE and acute stroke and cognitive dysfunction. A. This two-dimensional (2-D) TEE view demonstrates large (area of 1.5 cm^2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations on the atrial side and distal portions of the anterior (aml) and posterior (pml) mitral leaflets (arrows) associated with leaflets' thickening and decreased mobility (*see video clip supplemental 2A*). **B.** This real time 3-dimensional (RT3-D) TEE let atrial (LA) view of the mitral valve demonstrates large, severely protruding with irregular surface, and roll-like shape vegetations on the atrial side and tip of the entire anterior (downward pointing arrows) and posterior (upward pointing arrows) mitral leaflets with associated decreased mobility and incomplete coaptation of the leaflets (*see video clip supplemental 2B)*. **C**. Associated severe mitral regurgitation is demonstrated by RT3D-TEE color Doppler. **D.** Transcranial Doppler of the middle cerebral artery demonstrates 1 of 2 microembolic events (arrows). On MRI 8 small white matter lesions were demonstrated. On neurocognitive testing he demonstrated a global neurocognitive score of -9.12 consistent with severe neurocognitive dysfunction. Nineteen weeks later due to discontinuation of warfarin because a bleeding complication, patient had a recurrent TIA and repeat evaluations demonstrated persistent valve vegetations, 3 microemboli, a new cerebral infarct and 10 white matter lesions, and unchanged global neurocognitive of -8.9. **E, F**. After 3 months of immunosupressives and clopidogrel, the anterior and posterior mitral leaflets vegetations (arrows) significantly decreased in size by 2-D (**E**) and RT-3D TEE (**F**) to a vegetation area of only 0.22 cm^2 (*see video clips supplemental 2E and 2F*). Also, cerebromicroembolism resolved, brain lesions decreased to 7, and his global neurocognitive score improved to –6.9.

Supplemental Figure 3. 21 year old female with SLE with acute transient ischemic attack and previous stroke. A. This close-up 2D-TEE view demonstrates moderate size (area 0.85

cm^2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations (arrows) on the LA side and distal portions of the anterior (aml) and posterior (pml) mitral leaflets associated with leaflets' thickening and decreased mobility (*see video clip supplemental 3A*). **B**. Transcranial Doppler of the left middle cerebral artery demonstrates 1 of 4 microemboli (arrows). **C.** On MRI 2 of 4 old cerebral infarcts (arrowheads) and several of a total of 54 white matter lesions (arrows) and a lesion load of 7.05 cm^3 were demonstrated. She had a global neurocognitive score of -6.12, consistent with severe neurocognitive dysfunction. After 3 months of anticoagulation, repeat imaging demonstrated resolution of the anterior mitral valve vegetation and significant reduction in size (arrow) of the posterior mitral leaflet vegetation (**D**, *see video clip supplemental 3D***)**, reduction of cerebromicroembolism to 2 events, decrease in white matter lesions size (arrows in **E**) and lesion count to 41, and improvement in her global neurocognitive score to -4.48. **F.** Associated with non-compliance with anticoagulation, the patient had a recurrent TIA and repeat imaging demonstrated recurrence of a moderate size posterior mitral leaflet vegetation (arrow) (*see video clip supplemental 3F)*, 9 cerebromicroemboli, increase in the brain lesion count to 61, and persistent severe neurocognitive dysfunction.

Supplemental Figure 4. 38-year old female with SLE and acute stroke. **A.** This four-chamber TEE view demonstrates multiple small (total area of 0.46 cm^2), sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations on the LA side and mid to distal portions of the anterior (aml) and posterior (pml) mitral leaflets (arrows) (*see video clip supplemental 4A)*. **B**. Transcranial Doppler of the right middle cerebral artery demonstrates 1 of 2 microemboli (arrows). **C**. This FLAIR brain MRI shows multiple areas of increased signal intensity in the distribution of the right middle cerebral artery (arrows). She had a total of 10 brain lesions and her lesion load was 13.5 cm3. **D**. This diffuse weighted imaging of the brain demonstrates multiple areas of restricted diffusion corresponding to the areas of increased signal intensity in the FLAIR images in **C** consistent with acute cerebral infarcts (arrows). Her global neurocognitive score was -4.68 consistent with severe neurocognitive dysfunction. She had a recurrent TIA and repeat MRI showed recurrent or persistent mitral valve vegetations and new small infarcts within the right caudate head and putamen. After stabilization with anticoagulants for 6 weeks, repeat imaging showed resolution of mitral valve vegetations (**E**), resolution of cerebromicroembolism, and smaller residual cerebral infarcts (arrows in **F**), decreased lesion load, and improved neurocognitive dysfunction score to -3.49. Abbreviations as in previous Figures.

Supplemental Figure 5. 50 year old female with SLE with an acute transient ischemic attack, progressive memory loss, past stroke and seizure disorder.
A. This four chamber 2D-TEE view demonstrates moderate size (area of 0.85 cm^2), oval shape, sessile, and predominantly soft tissue echoreflectant Libman-Sacks vegetations (arrows) on the atrial side and distal portions of the anterior (aml) and posterior (pml) mitral leaflets with associated decreased leaflets' mobility (*see video clip supplemental 5A*). **B**. Transcranial Doppler of the middle cerebral artery demonstrates 1 of 2 microemboli (arrows). **C.** MRI of the brain demonstrates 1 of 3 cerebral infarcts (arrowhead) and several of 10 small periventricular and deep white matter abnormalities (arrows) for a lesion load of 1.2 cm^3. Her global neurocognitive z-score was -3.29, consistent with moderate neurocognitive dysfunction. **D.** After 6 weeks of non-compliance with anticoagulation the patient had a recurrent TIA and her repeat TEE

demonstrated persistent but smaller (area 0.58 cm^2) mitral valve vegetations (arrows) (*see video clip supplemental 5D*) and a new small (0.05 cm^2) aortic valve vegetation (not shown). She also had 3 cerebromicroemboli, her brain lesion load increased to 1.6 cm^3 and her global neurocognitive score worsened to -3.49**. E**. After 5 months of therapeutic anticoagulation and aspirin, repeat TEE demonstrated significantly smaller (area 0.13 cm^2) and homogeneously hyperreflectant (healed) mitral valve vegetations (*see video clip supplemental 5E*). **F**. This corresponding RT3D-TEE LA view of the mitral valve demonstrates multiple homogeneously hyperreflectant nodular vegetations (arrows) on the atrial side and leaflet tips of the anterior and posterior mitral leaflets consistent with healead vegetations (*see video clip supplemental 5F*). Decreased mobility of the posterior mitral leaflet without commissural fusion was also noted. She had no cerebromicroemboli and although the number of brain lesions and lesion load increased to 23 and 1.7 cm^3, respectively, her neurocognitive score improved to -2.99.

Supplemental Table 1. Clinical, Therapy, and Laboratory Data in Patients with NPSLE and SLE without NPSLE			
Characteristic	**Acute NPSLE (N = 30)**	**SLE (N = 46)**	
Variable	**mean ± SD, median (IQR), or n (%)**	**mean ± SD, median (IQR), or n (%)**	**P value**
Duration of SLE (years)	7.98 ± 6.95	7.83 ± 6.56	0.92
Age at diagnosis of SLE (years)	30.53 ± 12.493	27.50 ± 12.12	0.30
Non-Neuro-SLEDAI (U)	9.3 ± 6.81	6.96 ± 5.16	0.11
Non-Neuro-SLICC (U)	2.77 ± 1.85	2.11 ± 1.46	0.11
Vasculitis	3/28 (11%)	2/44 (5%)	0.37
Active renal disease	9 (30%)	7 (15%)	0.15
Prednisone therapy	16 (53%)	15 (33%)	0.10
Prednisone current dose (mg/d)	5.0 (0, 10)	0 (0, 5)	0.08*
Average prednisone (mg/d)	7.5 (3.0, 10)	5.0 (2.0, 10)	0.18*
Prednisone (years)	5.0 (1.0, 10)	5.5 (1.0, 10)	0.87*
Cyclophosphamide therapy	12 (40%)	15 (33%)	0.63
Cyclophosphamide (years)	0 (0, 1.0)	0 (0, 1.0)	0.38*
Total cyclophosphamide dose (grams)	0 (0, 13)	0 (0, 2.0)	0.36*
Mycophenalate, methotrexate, or rituximab therapy	5 (17%)	16 (35%)	0.12
Hydroxycloroquine or cloroquine therapy	20 (67%)	31 (67%)	1.00
Statin therapy	6 (20%)	1/45 (2.2)	0.01
Aspirin or warfarin	18(60%)	14 (30%)	0.02
dsDNA titer	6 (0, 34)	16 (0, 114)	0.20*
ANA titer	160 (80, 640)	480 (40, 1280)	0.66*
C3 (mg/dl)	91.9 ± 34.95	98.24 ± 35.78	0.45
C4 (mg/dl)	21.3 (11.3, 22.0)	16.1 (9.8, 21.9)	0.88*
CH50 (mg/dl)	78.29 ± 39.29	76.95 ± 42.59	0.89
Fibrinogen (mg/dl)	355.6 ± 81.83 (29)	340.8 ± 102.1 (44)	0.50
C-reactive protein (mg/dl)	0.6 (0.6, 1.1)	0.6 (0.4, 1.0)	0.28*
Erythrosedimentation rate (mm/hr)	30.87 ± 23.80	28.09 ± 25.41	0.63
Ribonucleoprotein antibody positive	8 (27%)	19 (41%)	0.23
Rheumatoid factor	0 (0, 17)	0 (0, 6)	0.54*
CCP antibody positive	5 (18%)	11 (25%)	0.57
Smith antibody positive	10 (33%)	20 (43%)	0.47
SSA antibody positive	17 (57%)	14 (30%)	0.03
SSB antibody positive	6 (20%)	9 (20%)	1.00
Any antiphospholipid antibody positive	21 (70%)	24 (52%)	0.15
Beta-2 glycoprotein I antibody positive	14 (33%)	5/42 (12%)	0.005
Lupus-like inhibitor positive	13 (43%)	12 (26%)	0.14

IgG, IgM, or IgA anticardiolipin positive	15 (50%)	18 (39%)	0.48
IgM anticardiolipin antibody (IU)	7.6 (1.5, 18)	6.3 (2.0, 12)	0.75*
IgG anticardiolipin antibody (IU)	8.2 (2.0, 30)	6.9 (2.9, 16.5)	0.51*
IgA anticardiolipin antibody (IU)	3.9 (1.2, 8.0)	2.5 (0.9, 5.5)	0.25*

*Wilcoxon test.
SLE = systemic lupus erythematosus, SLEDAI = SLE disease activity index, SLICC = Systemic Lupus International Collaborating Clinics, DNA = double stranded nuclear antibody, ANA = antinuclear antibody, SSA = Ro antibody, SSB = La antibody, U = units, IU = international units.

Supplemental Table 2. Clinical and Laboratory Data in NPSLE and SLE Patients and Controls				
Parameter	**Acute NPSLE (n = 30)**	**SLE (N = 46)**	**Controls (N= 26)**	**P Value**
	mean ± SD, median (IQR), or n (%)	**mean ± SD, median (IQR), or n (%)**	**mean ± SD, median (IQR), or n (%)**	
Age (years)	37.90 ± 12.27	35.5 ± 12.34	34 ± 11	0.39
Female gender	27 (90%)	42 (91%)	22 (85%)	1.00
Ethnicity/Race (Hispanic/non-Hispanic White)	17(57%)/6(20%)	31(67%)/12(26%)	13(50%)/8(31%)	0.21
Body mass index	27.20 ± 6.24	27.56 ± 5.15 (44)	27.05 ± 5.35	0.92
Education (grade)	13.20 ± 2.83*	13.40 ± 2.42*	15.93 ± 2.54	<0.001
Hypertension (>140/90 mmHg)	3/29 (10%)	5/43 (12%)	0	0.22
Systolic blood pressure (mmHg)	121.24 ± 16.49 (29)	121.53 ± 12.11	116 ± 7.75	0.20
Diastolic blood pressure (mmHg)	76.45 ± 9.33 (29)	75.0 ± 10.23	71.48 ± 8.66	0.16
Dyslipidemia or statin therapy	15/30 (50%)	19/45 (42%)	9/25 (36%)	0.62
Cholesterol (mg/dl)	191.73 ± 50.17	170.77 ± 40.57	192.9 ± 42.53	0.06
LDL cholesterol (mg/dl)	119.79 ± 41.82 (28)	100.59 ± 37.01	111.3 ± 31.62	0.12
HDL cholesterol (mg/dl)	47.68 ± 13.17 (28)	51.29 ± 17.27	50.38 ± 18.13	0.66
Triglycerides (mg/dl)	188.0 ± 95.46†	128.60 ± 55.70*	159.5 ± 96.26	0.01
Diabetes mellitus	1/29 (3.4%)	2/45 (4.4%)	0	0.79
Glucose (mg/dl)	93.80 ± 36.88	88.24 ± 15.97	82.81 ± 8.72	0.21
Smoking (currently)	16/30 (47%)	10 (22%)	6 (23%)	0.06
Atherogenic risk factors	22/30 (73%)	28 (61%)	14 (54%)	0.31
Postmenopausal	2 (7%)	3 (7%)	0	0.60
Hemoglobin (g/dl)	12.60 ± 2.03*†	13.44 ± 1.27	14.14 ± 1.41	0.002
White blood cell count (x10^3/mm3)	6.35 ± 2.88	6.0 ± 2.43	6.48 ± 1.60	0.67
Platelets (x10^3/mm3)	229.57 ± 89.40	248.61 ± 83.73	274.2 ± 41.10	0.11
Creatinine (mg/dl)	0.82 (0.74, 1.0)*	0.76 (0.63, 0.86)	0.70 (0.60, 0.82)	0.03‡
Urine protein (mg/dL)	26 (0, 50)*	0 (0, 20) (45)	0 (0, 0)	<0.001‡
Albumin (g/dL)	3.58 ± 0.71*†	4.0 ± 0.43 (45)	4.16 ± 0.39	<0.001
C3a (pg/mL)	1292 (945, 1941)	1372 (1036, 2233)	1366 (1198,	0.72‡

			1612)	
C5a (pg/mL)	26.65 ± 10.97	28.51 ± 10.58	27.23 ± 9.80	0.73
P-selectin (ng/dL)	43.67 ± 28.62	35.42 ± 17.42	37.84 ± 16.07	0.25
Peak thrombin generation (nmol/L)	281.52 ± 210.95 (29)*	341.37 ± 121.94 (44)*	435 ± 127	0.002
Thrombin-antithrombin complexes (ng/mL)	3.15 (2.2, 9.2)	3.3 (1.6, 5.3) (45)	2.8 (2.5, 5.0)	0.48‡
Quantitative D-dimer (mg/dL)	0.47 (0.24, 0.71) (29)*†	0.39 (0.23, 0.63) (43)	0.25 (0.11, 0.38)	0.04‡
Tissue plasminogen antigen (ng/mL)	11.56 ± 7.79*†	8.95 ± 3.07	7.91 ± 4.14	0.02
Plasminogen activator inhibitor-1 (U/mL)	4.7 (1.1, 9.5) (29)	5.0 (2.6, 11.8) (44)	6.7 (2.5, 12)	0.29‡
Total microparticles (U/mL)	3238 (2151, 3920)	3015 (1667, 3991)	2799 (1693, 3400)	0.44‡
Platelet derived microparticles (uL)	430 (113, 883)	340 (100, 625)	341 (213, 662)	0.44‡
Monocyte derived microparticles (uL)	132 (39, 752)	235 (100, 637)	280 (95, 700)	0.54‡
Endothelium derived microparticles (uL)	48 (20, 119)	51 (20, 143)	82 (40, 155)	0.32‡

*p<0.05 compared to controls by Fisher's post hoc least significant difference method.
†p<0.05 for acute NPSLE compared to SLE by Fisher's post hoc least significant difference method.
‡Kruskal-Wallis test.
LDL = low density lipoproteins, HDL = high density lipoproteins. Other abbreviations as in previous Tables.

Supplemental Table 3. Predictors of Acute NPSLE, Neurocognitive Dysfunction, Brain Lesions on MRI, and All 3 Outcomes Combined

	Univariate Analyses	**Multivariate Analyses**	
Variable	**OR (95% CI)**	**OR (95% CI)**	**P value***
	Acute NPSLE		
Valve vegetations	16.50 (4.81 – 56.61)	13.40 (3.31 – 54.35)	<0.001/<0.001
Valve thickening	12.19 (3.62 – 41.08)		<0.001
Valve regurgitation	8.2 (2.54 – 26.48)	5.10 (1.19 – 21.93)	<0.001/0.03
Vegetations and MES	3.8 (1.03 – 14.10)		0.04
Aortic or carotid plaque	3.14 (1.13 – 8.77)		0.03
Carotid IMT (per 100 microns)	1.85 (1.07 – 3.18)		0.03
Carotid plaque or intima-media	8.00 (1.57 – 40.91)		0.01

thickening			
Triglyceride levels (per 20 mg/dL)	1.24 (1.07 – 1.45)	1.27 (1.04 – 1.53)	0.005/0.02
Statin therapy	11.00 (1.25 – 96.75)		0.03
Smoking (currently)	3.15 (1.16 - 8.58)		0.02
SSA antibody positive	2.99 (1.15 – 7.78)		0.025
Aspirin or warfarin therapy	3.43 (1.31 – 8.98)		0.01
Beta 2-glycoprotein-1 antibody positive	5.66 (1.74 – 18.42)		0.004
	Global Neurocognitive Dysfunction		
Valve thickening	2.93 (1.11 – 7.79)		0.03
Valve regurgitation	5.22 (1.71 – 15.89)		0.004
Vegetations and cerebromicroembolism	10.0 (2.01 – 49.82)	8.01 (1.51 – 42.62)	0.005/0.01
Aortic IMT (per 100 microns)	1.22 (1.00 – 1.49)		0.046
Cerebromicroembolism	3.06 (1.28 – 7.34)		0.01
Age (per 10 years)	1.66 (1.11 – 2.49)		0.01
Hypertension	13.05 (1.51 – 112.93)		0.02
Smoking (currently)	3.15 (1.15 - 8.60)	3.79 (1.16 – 12.40)	0.025/0.03
tPA	1.12 (1.00 - 1.26)		0.04
Non-Neuro SLICC	1.40 (1.03 – 1.90)	1.50 (1.06 – 2.13)	0.03/0.02
Cholesterol (per 20 mg/dL)	1.27 (1.01 – 1.60)		0.04
Triglycerides level (per 20 mg/dL)	1.15 (1.01 – 1.31)		0.04
Proteinuria	1.01 (1.00 – 1.02)		0.04
Age at diagnosis of SLE (per 10 years)	1.81 (1.19 – 2.75)	2.08 (1.27 – 3.40)	0.005/0.004
	Focal Brain Lesions on MRI		
Valve vegetations	4.50 (1.70 – 11.93)	5.57 (1.72 – 18.01)	0.003/0.004
Valve thickening	4.43 (1.67 – 11.73)		0.003
Aortic or carotid plaque	2.99 (1.01 – 8.81)		0.048
Aortic IMT (per 100 microns)	1.28 (1.02 – 1.60)		0.04
Age (per 10 years)	2.01 (1.30 – 3.11)		0.002
Cholesterol level (per 20 mg/dL)	1.34 (1.06 – 1.70)		0.01
tPA level	1.14 (1.01 – 1.29)		0.04
Age at diagnosis of SLE (per 10 years)	1.73 (1.12 – 2.66)		0.01
P-selectin	1.14 (1.00 – 1.06)	1.04 (1.00 – 1.07)	0.04/0.02
Complement c4	1.09 (1.02 – 1.17)	1.12 (1.03 – 1.22)	0.01/0.009

	NPSLE, Cognitive Dysfunction, or Brain Lesions		
Valve vegetations	7.22 (2.44 – 21.39)	7.49 (2.49–22.5)	<0.001†
Valve thickening	5.38 (1.93 – 15.01)		0.001
Valve regurgitation	4.25 (1.12 – 16.17)		0.03
Cholesterol (per 20 mg/dL)	1.28 (1.01 – 1.63)		0.04
Triglycerides level (per 20 mg/dL)	1.26 (1.05 – 1.52)	1.28 (1.03 – 1.60)	0.02/0.03
LDL (per 10 mg/dL)	1.17 (1.02 – 1.35)		0.03
P-selectin	1.03 (1.0 – 1.07)	1.05 (1.01 – 1.09)	0.049/0.02
Complement c4	1.07 (1.00 – 1.15)	1.17 (1.04 – 1.32)	0.04/0.008
Age (per 10 years)	1.62 (1.06 – 2.47)		0.03

*First p values for univariate analysis; second p values for multivariate analysis adjusted for other variables in the "best" stepwise model.

† OR and p value adjusted for "best" of univariate predictors selected from all 3 components/outcomes in step wise model.

IMT = intima media thickness, tPA = tissue plasminogen antigen, LDL = low density lipoprotein. Other abbreviations as in previous Tables.

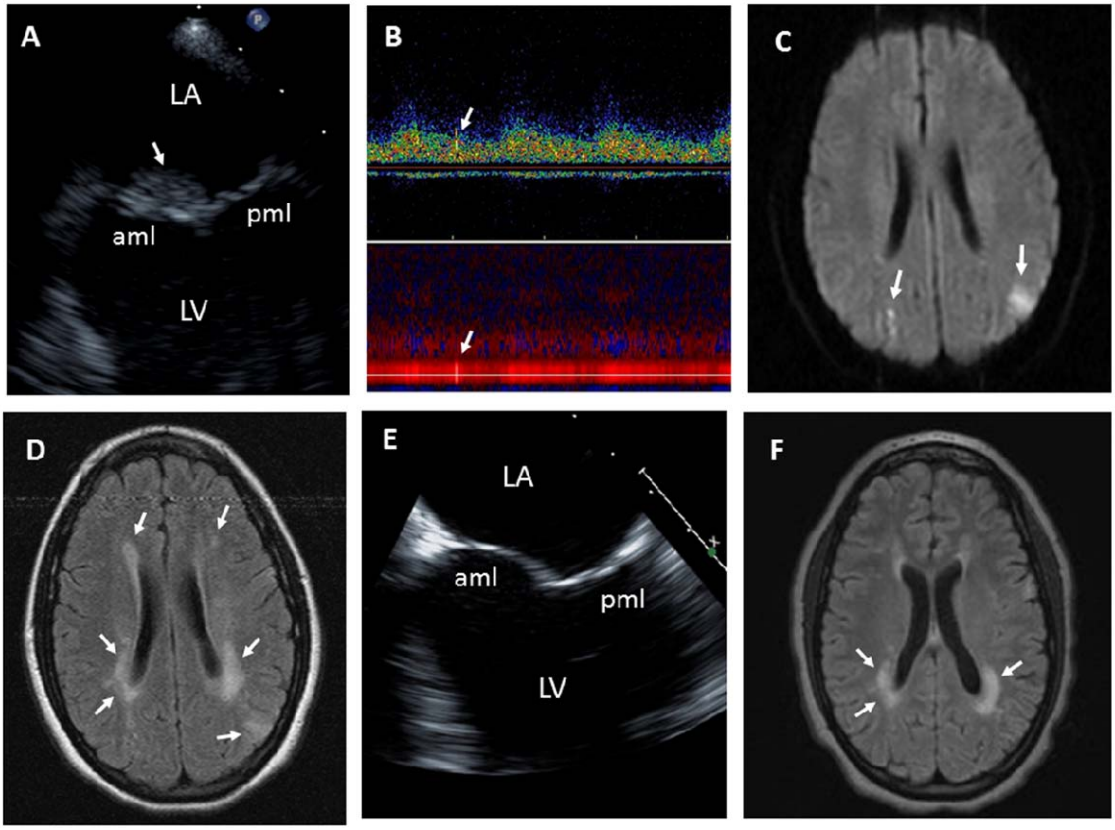
Supplemental Table 4. Effect of Libman-Sacks Vegetations and Cerebromicroembolism on Cerebral Blood Flow, NPSLE, Neurocognitive Dysfunction, Focal Brain Lesions, and Brain Lesion Load

	Patients with Vegetations and with cerebromicroembolism (N = 12)	Patients with no vegetations and no cerebromicroembolism (N = 32)	P value
	Brain Perfusion (ml/min/100 grams of tissue), mean ± SD		
Gray Matter	21.14 ± 5.77	28.69 ± 13.17	<0.001*
White Matter	12.37 ± 3.83	14.42 ± 4.58	0.001*
	NPSLE, n (%)		
Acute stroke/TIA	8 (67%)	1 (3%)	<0.001
Acute NPSLE	8 (67%)	4 (13%)	<0.001
	Neurocognitive z-scores, mean ± SD		
Attention	-3.29 ± 3.49	-0.85 ± 0.86	0.009†
Memory	-2.61 ± 1.07	-0.73 ± 1.0	<0.001†
Processing speed	-2.84 ± 1.90	-0.99 ± 1.21	0.003†
Executive function	-4.30 ± 3.98	-2.04 ± 2.7	0.05†
Motor function	-5.25 ± 7.82	-1.33 ± 1.06	0.006†

Global	-3.34 ± 2.44	-1.26 ± 0.97	0.002†‡
Global abnormal§	10 (83%)	10/31 (32%)	0.003
	Focal Brain Lesions, median (IQR), n (%)		
Brain lesions	9 (75%)	12 (38%)	0.03
Brain lesions (n)	11 (2.0, 54)	1.5 (0, 9.5)	0.05†
Cerebral infarcts	5 (42%)	0	<0.001
Cerebral infarcts (n)	0 (0, 4.0)	0	<0.001†
Old infarcts (n)	0 (0, 3.0)	0	<0.001†
Recent infarcts (n)	0 (0, 0)	0	0.02†
White matter lesions	9 (75%)	10 (31%)	0.02
White matter lesions (n)	9 (0, 52)	1.5 (0, 9.5)	0.02†
	White Matter Brain Lesion Load (cm^3), median (IQR)		
Left hemisphere	0.39 (0, 2.1)	0 (0, 0.11)	0.009†
Right hemisphere	0.43 (0.05 – 2.84)	0.02 (0, 0.07)	0.01†
Whole brain	1.14 (0.09 – 6.5)	0.03 (0, 0.21)	0.02†

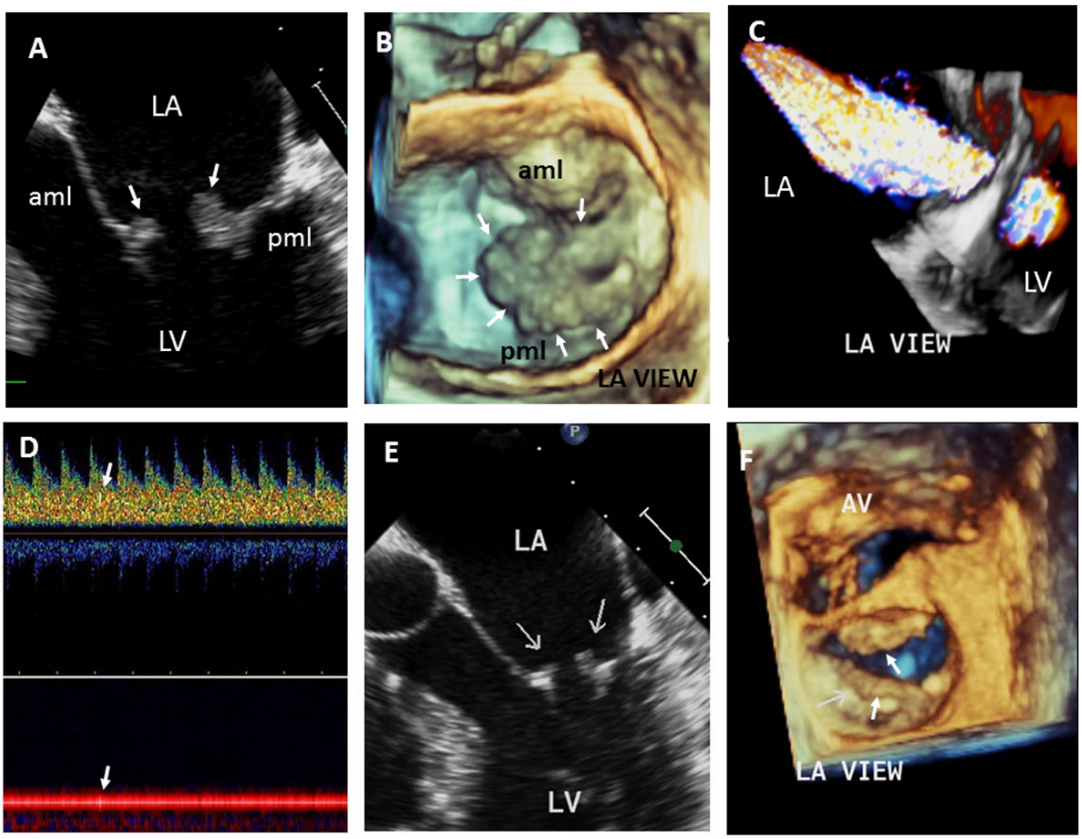
*RM ANOVA (across cerebral lobes), 11 patients with vegetations and microemboli and 24 with neither.
†Wilcoxon test.
‡p = 0.007 after simultaneously adjusting for age, depression index, pre-morbid intelligence, and education.
§Global abnormal defined as >1.5 SD below the mean total of controls
Other abbreviations as in previous Tables.

SUPPLEMENTAL FIGURES 1-5



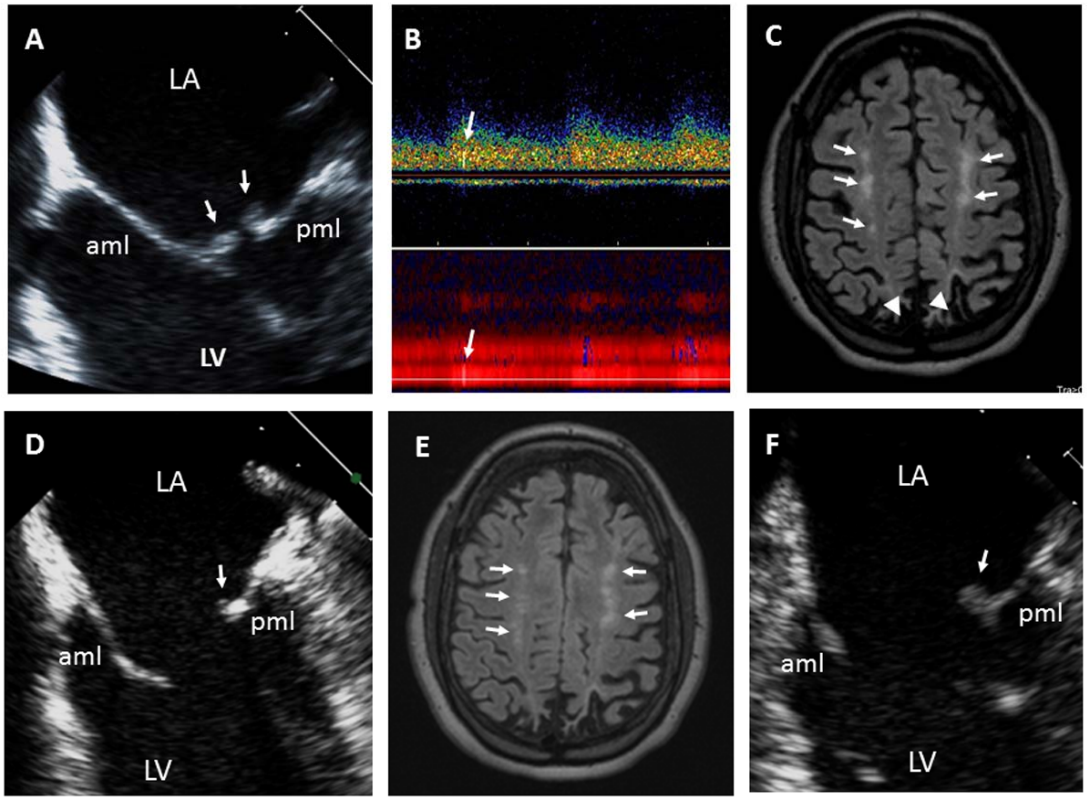
Supplemental Figure 1. 18 year old female with SLE and acute homonymous hemianopsia, confusional state, and cognitive dysfunction. A. This TEE four chamber view demonstrates a large (area of 1.3 cm^2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetation (arrow) on the atrial side and mid to distal portions of the anterior mitral leaflet (aml) (*see video clip supplemental 1A*). **B**. Transcranial Doppler of the right middle cerebral artery demonstrates 1 of 4 microemboli within the spectral Doppler (upper arrow) and within the vessel (lower arrow). **C**. Diffuse weighted imaging of the brain demonstrates bilateral acute parietal infarcts (arrows). **D**. This T2 FLAIR image demonstrates large periventricular and multiple smaller white matter lesions (arrows). Also, cortical edema

is seen in the parietal lobe related to an acute infarct (horizontal arrow). She had a total of 115 focal brain lesions and a lesion load of 13.71 cm^3. Her global neurocognitive score was -3.21 and consistent with moderate neurocognitive dysfunction. She had a recurrent transient ischemic attack 1 week after her initial event and repeat imaging showed mitral valve vegetations, cerebromicroembolism, and new ischemic lesions in the right frontal lobe. After stabilization with immunosupressives and anticoagulants for 9 weeks, repeat imaging showed resolution of the mitral valve vegetation **(E),** resolution of cerebromicroembolism, decrease of brain lesions to 83 (**F)** and lesion load to 7.72 cm^3**,** and significant improvement in her global neurocognitive score to -1.3, consistent with mild neurocognitive dysfunction. LA = left atrium, LV = left ventricle, pml = posterior mitral leaflet.



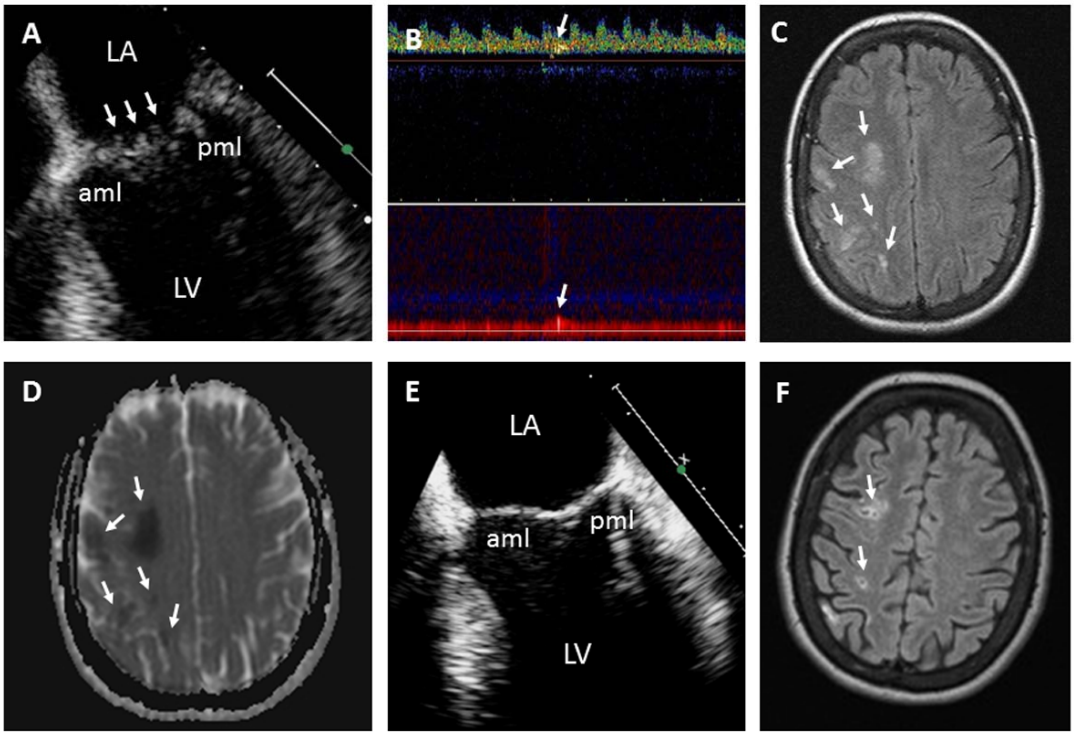
Supplemental Figure 2. 29 year old male with SLE and acute stroke and cognitive dysfunction. A. This two-dimensional (2-D) TEE view demonstrates large (area of 1.5 cm^2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations on the atrial side and distal portions of the anterior (aml) and posterior (pml) mitral leaflets (arrows) associated with leaflets' thickening and decreased mobility (*see video clip supplemental 2A*). **B.** This real time 3-dimensional (RT3-D) TEE let atrial (LA) view of the mitral valve demonstrates large, severely protruding with irregular surface, and roll-like shape vegetations on the atrial side and tip of the entire anterior (downward pointing arrows) and posterior (upward pointing arrows) mitral leaflets with associated decreased mobility and incomplete coaptation of the leaflets (*see video clip supplemental 2B)*. **C**. Associated severe mitral regurgitation is demonstrated by RT3D-

TEE color Doppler. **D.** Transcranial Doppler of the middle cerebral artery demonstrates 1 of 2 microembolic events (arrows). On MRI 8 small white matter lesions were demonstrated. On neurocognitive testing he demonstrated a global neurocognitive score of -9.12 consistent with severe neurocognitive dysfunction. Nineteen weeks later due to discontinuation of warfarin because a bleeding complication, patient had a recurrent TIA and repeat evaluations demonstrated persistent valve vegetations, 3 microemboli, a new cerebral infarct and 10 white matter lesions, and unchanged global neurocognitive of -8.9. **E, F**. After 3 months of immunosupressives and clopidogrel, the anterior and posterior mitral leaflets vegetations (arrows) significantly decreased in size by 2-D (**E**) and RT-3D TEE (**F**) to a vegetation area of only 0.22 cm^2 (*see video clips supplemental 2E and 2F*). Also, cerebromicroembolism resolved, brain lesions decreased to 7, and his global neurocognitive score improved to –6.9.



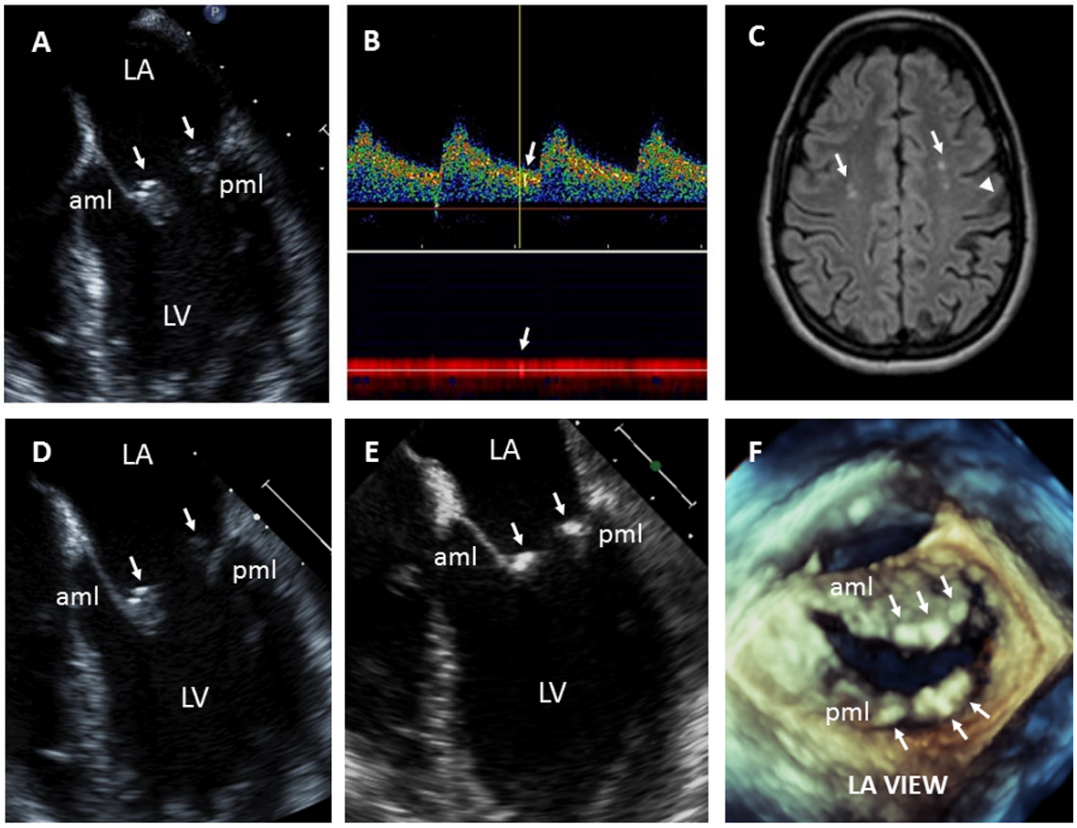
Supplemental Figure 3. 21 year old female with SLE with acute transient ischemic attack and previous stroke. **A**. This close-up 2D-TEE view demonstrates moderate size (area 0.85 cm^2), oval shape, sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations (arrows) on the LA side and distal portions of the anterior (aml) and posterior (pml) mitral leaflets associated with leaflets' thickening and decreased mobility (*see video clip supplemental 3A*). **B**. Transcranial Doppler of the left middle cerebral artery demonstrates 1 of 4 microemboli (arrows). **C.** On MRI 2 of 4 old cerebral infarcts (arrowheads) and several of a total of 54 white matter lesions (arrows) and a lesion load of 7.05 cm^3 were demonstrated. She had a global neurocognitive score of -6.12, consistent with severe neurocognitive dysfunction. After 3 months of anticoagulation, repeat imaging demonstrated resolution of the anterior mitral valve

vegetation and significant reduction in size (arrow) of the posterior mitral leaflet vegetation (**D**, *see video clip supplemental 3D***)**, reduction of cerebromicroembolism to 2 events, decrease in white matter lesions size (arrows in **E**) and lesion count to 41, and improvement in her global neurocognitive score to -4.48. **F.** Associated with non-compliance with anticoagulation, the patient had a recurrent TIA and repeat imaging demonstrated recurrence of a moderate size posterior mitral leaflet vegetation (arrow) (*see video clip supplemental 3F)*, 9 cerebromicroemboli, increase in the brain lesion count to 61, and persistent severe neurocognitive dysfunction.



Supplemental Figure 4. 38-year old female with SLE and acute stroke. **A.** This four-chamber TEE view demonstrates multiple small (total area of 0.46 cm^2), sessile, and homogeneously soft tissue echoreflectant Libman-Sacks vegetations on the LA side and mid to distal portions of the anterior (aml) and posterior (pml) mitral leaflets (arrows) (*see video clip supplemental 4A)*. **B**. Transcranial Doppler of the right middle cerebral artery demonstrates 1 of 2 microemboli (arrows). **C**. This FLAIR brain MRI shows multiple areas of increased signal intensity in the distribution of the right middle cerebral artery (arrows). She had a total of 10 brain lesions and her lesion load was 13.5 cm3. **D**. This diffuse weighted imaging of the brain demonstrates multiple areas of restricted diffusion corresponding to the areas of increased signal intensity in the FLAIR images in **C** consistent with acute cerebral infarcts (arrows). Her global neurocognitive score was -

4.68 consistent with severe neurocognitive dysfunction. She had a recurrent TIA and repeat MRI showed recurrent or persistent mitral valve vegetations and new small infarcts within the right caudate head and putamen. After stabilization with anticoagulants for 6 weeks, repeat imaging showed resolution of mitral valve vegetations (**E**), resolution of cerebromicroembolism, and smaller residual cerebral infarcts (arrows in **F**), decreased lesion load, and improved neurocognitive dysfunction score to -3.49. Abbreviations as in previous Figures.



Supplemental Figure 5. 50 year old female with SLE with an acute transient ischemic attack, progressive memory loss, past stroke and seizure disorder.

A. This four chamber 2D-TEE view demonstrates moderate size (area of 0.85 cm^2), oval shape, sessile, and predominantly soft tissue echoreflectant Libman-Sacks vegetations (arrows) on the atrial side and distal portions of the anterior (aml) and posterior (pml) mitral leaflets with associated decreased leaflets' mobility (*see video clip supplemental 5A*). **B**. Transcranial Doppler of the middle cerebral artery demonstrates 1 of 2 microemboli (arrows). **C.** MRI of the brain demonstrates 1 of 3 cerebral infarcts (arrowhead) and several of 10 small periventricular and deep white matter abnormalities (arrows) for a lesion load of 1.2 cm^3. Her global neurocognitive z-score was -3.29, consistent with moderate neurocognitive dysfunction. **D.** After 6 weeks of non-

compliance with anticoagulation the patient had a recurrent TIA and her repeat TEE demonstrated persistent but smaller (area 0.58 cm^2) mitral valve vegetations (arrows) (*see video clip supplemental 5D*) and a new small (0.05 cm^2) aortic valve vegetation (not shown). She also had 3 cerebromicroemboli, her brain lesion load increased to 1.6 cm^3 and her global neurocognitive score worsened to -3.49**. E**. After 5 months of therapeutic anticoagulation and aspirin, repeat TEE demonstrated significantly smaller (area 0.13 cm^2) and homogeneously hyperreflectant (healed) mitral valve vegetations (*see video clip supplemental 5E*). **F**. This corresponding RT3D-TEE LA view of the mitral valve demonstrates multiple homogeneously hyperreflectant nodular vegetations (arrows) on the atrial side and leaflet tips of the anterior and posterior mitral leaflets consistent with healead vegetations (*see video clip supplemental 5F*). Decreased mobility of the posterior mitral leaflet without commissural fusion was also noted. She had no cerebromicroemboli and although the number of brain lesions and lesion load increased to 23 and 1.7 cm^3, respectively, her neurocognitive score improved to -2.99.