Using 3T MRI To Characterize The Early Lesion Of Carotid Vessel Wall In Systemic Lupus Erythematosus Patients With Subclinical Atherosclerosis.

Wei Zhang[1], Jie Sun[2], Bin Zhou[1], Jianrong Xu[1], Daniel S Hippe[2], Thomas S Hatsukami[2], and Chun Yuan[2]

[1]*Department of Radiology, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, Shanghai, China,* [2]*Department of Radiology, University of Washington, Seattle, WA, United States*

Introduction: Atherosclerosis (AS) occurs prematurely in patients with Systemic Lupus Erythematosus(SLE) and is independent of traditional risk factors for cardiovascular disease. Subclinical AS can be documented in 30% to 40% of SLE patients[1]. It is important to detect AS lesions in the earliest stages of their development, which allows to implement appropriate preventive and therapeutic procedures. MR was widely used to analysis the plaque and its components but few reports focus on using MR to measure the earlier lesion in carotid artery before the plaque formation. In this study we try to use 3T MRI to detect early lesion in vessel wall and show the association with risk factors in female SLE patients with subclinical carotid AS.

Methods: *Patients:* A total of 47 female SLE patients (37.84±10.12 ys old) who met the ACR criteria for SLE were recruited for an MRI examination. Inclusion criteria were age 20 to 55 years old, more than 5 years disease duration. None of them had a history of cardiovascular disease. *Clinical variables of interest:* Demographic information were recorded and SLE-specific laboratory testing was performed. All the chemical analyses, antibodies, complements, cholesterols were assessed within 3 days before or after MR exam. Current medication and disease measurement (SLICC/SLEDAI/SLAM scores) were obtained. *MRI protocol:* Patients were scanned by a 3T scanner (Achieva, Philips, the Netherlands) and a multi-contrast MRI protocol was used for wall characters (TOF, T1, T2 and proton density). *Image analysis:* CASCADE[2] software was used to draw the inner and outer wall boundaries of the artery in images of each location(Figure 1). We only included CCA+Bulb as the final outcome measurement. For each artery, mean wall thickness (artery-MWT) and mean lumen area(artery-MLA) were recorded. *Statistical analysis:* A linear mixed model was used to assess the association between MWT/MLA and all the clinical parameters. The analysis was repeated after adjustment for age, SBP and cholesterol(TC).

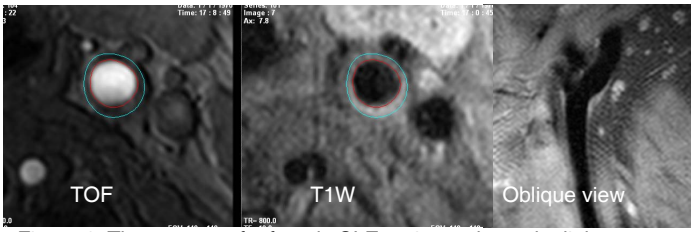

Figure 1: The contour of a female SLE patients showed a little thickening of the vessel wall, more obvious on oblique view.

Results: *Clinical characters:* SLE patients showed a pretty higher percentage of HBP(28%). Both ESR(31.74±24.76 mm/h) and CRP(9.65±11.76 mg/L) were higher than their normal range. 14% of lupus patients had CNS involvement and 24.7% had renal involvement. The MLA was 40.73±10.3 mm^2 and MWT was 0.75±0.05 mm. *Association with risk factors:* The SLE women with thicker wall tended to be older age, post-menopausal and had a higher systolic blood pressure(SBP), higher scores in SLEAM, SLEDAI and SLICC measurement. Among them age and HBP showed a strong association with wall thickness with p<0.001 and p=0.006 respectively (Table 1,2,3). Patients with more serious organ involvement, like CNS, kidney and hematology involvement, tended to have more thicker vessel wall. After adjusting for age, only kidney involvement contributed to the thickening of the vessel wall with p=0.034. While after adjusting for TC, variables that remained significantly associated with MWT included age (*P <0.001*), post menopause (p=0.047), elevated SBP (*P=0.008*), higher scores in SLAM (P<0.001), SLICC (*P*=0.026) and SLEDAI(P<0.001),and the organ involvement. Similarly, after adjusting for SBP, we found SLE, SLEDAI, CNS and hematology involvement were still in the model and contribute to the thickening of the vessel wall.

Discussion: This study in SLE patients with subclinical atherosclerosis demonstrated age(B=0.48, p<0.001) and SBP(B=0.28, p=0.01) were high risk factors in AS formation. We also found disease activity and organ involvement were among the most important factors and correlated with the wall thickening and enlarged lumen area. Large dose of prednisone did not show an obvious association with the wall thickening(B=0.27, p=0.06). We found a protective effect of current use of hydroxychloroquine(HCQ) on the thickening of the vessel wall even after adjusting of age and SBP(B=-0.317,p=0.049 and B=-0.558,p=0.001). C3, ESR and CPR associated with mean lumen area better than wall thickness in our study. Among all the antibodies only anti-U1RNP associated with mLA(B=0.78, p=0.02) even after adjusting for age and SBP(B=0.59, P=0.01 and B=0.71, p=0.04 respectively).

Conclusion: This represents one of the first attempts using MR to evaluate the subclinical atherosclerosis in female SLE patients. We found some traditional and disease related factors contribute to the SLE-AS formation. MR can provide more information in the early detecting of subclinical AS.

References: 1. Manzi S, et al. *Arthritis Rheum.*1999; 42:51–60; 2. Kerwin W, et al. *Top Magn Reson Imaging.* 2007; 18:371– 8.

N=47(93 arteries)	artery_mWT(mm)				artery_mLA(mm^2)			
	B	95% CI		p	B	95% CI)		p
Age, years	0.48	0.28	0.67	**<0.001**	0.43	0.23	0.64	**<0.001**
post menopausal	0.52	0.02	1.02	**0.04**	0.65	-0.09	1.40	0.09
SBP	0.28	0.08	0.48	**0.01**	0.28	-0.01	0.57	0.06
TC	0.06	-0.17	0.30	0.59	0.22	0.00	0.44	**0.05**
LDL	0.04	-0.19	0.26	0.76	0.24	0.03	0.46	**0.02**
ApoB	0.06	-0.15	0.26	0.60	0.31	0.09	0.53	**0.01**
SLAM	0.34	0.14	0.53	**<0.001**	0.19	-0.02	0.39	0.08
SLICC	0.26	0.04	0.49	**0.02**	0.31	0.07	0.54	**0.01**
SLEDAI	0.40	0.20	0.60	**<0.001**	0.32	0.12	0.53	**<0.001**
kidney involved	0.57	0.08	1.05	**0.02**	0.90	0.27	1.53	**0.01**
CNS involved	0.80	0.22	1.37	**0.01**	0.37	-0.25	0.99	0.24
Hematology involved	0.69	0.23	1.15	**<0.001**	0.83	0.41	1.24	**<0.001**
C3	-0.18	-0.40	0.04	0.11	-0.29	-0.56	-0.02	**0.03**
C1i	0.06	-0.14	0.26	0.58	0.21	0.00	0.42	**0.05**
ESR	-0.04	-0.25	0.17	0.70	0.36	0.06	0.65	**0.02**
anti_UIRNP	0.46	-0.28	1.20	0.22	0.78	0.13	1.43	**0.02**
Total_prednisone dose	0.27	-0.01	0.55	0.06	0.22	0.02	0.42	**0.03**

Table 1,2,3. Univariate linear regression analysis between artery morphology and clinical variables in female SLE patients(Table 1), with adjustment for age(Table 1) and TC(Table 2). All the continuous data were standardized.

N=47(93)	Adjusting for age							
	artery_mWT(mm)				artery_mLA(mm^2)			
	B	95% CI		p	B	95% CI		p
kidney involved	0.45	0.03	0.87	**0.03**	0.81	-0.24	1.37	**0.01**
Hematology involved	0.35	-0.06	0.77	0.10	0.56	0.12	1.00	**0.01**
C3	-0.17	-0.39	0.05	0.14	-0.28	-0.52	-0.04	**0.02**
CRP	-0.18	-0.36	-0.01	**0.04**	0.02	-0.21	0.25	0.87
GPI	-0.20	-0.60	0.20	0.33	-0.62	-1.12	-0.12	**0.01**
anti_UIRNP	0.24	-0.23	0.72	0.31	0.59	0.16	1.02	**0.01**
HCQ	-0.32	-0.63	0.00	**0.05**	-0.23	-0.75	0.28	0.38

N=47(93)	Adjusting for TC							
	artery_mWT(mm)				artery_mLA(mm^2)			
	B	95% CI		p	B	95% CI		p
age	0.48	0.28	0.68	**<0.001**	0.41	0.19	0.62	**<0.001**
post menopausal	0.51	0.01	1.00	**0.05**	0.60	-0.11	1.31	0.10
SBP	0.28	0.07	0.48	**0.01**	0.24	-0.03	0.52	0.08
SLAM	0.36	0.17	0.55	**<0.001**	0.12	-0.08	0.32	0.23
SLICC	0.29	0.04	0.55	**0.03**	0.26	0.02	0.49	**0.03**
SLEDAI	0.42	0.23	0.61	**<0.001**	0.28	0.09	0.48	**0.01**
kidney involved	0.68	0.18	1.19	**0.01**	0.88	0.15	1.60	**0.02**
CNS involvement	0.79	0.18	1.39	**0.01**	0.33	-0.32	0.97	0.32
Hematology involved	0.71	0.24	1.17	**0.00**	0.76	0.37	1.15	**<0.001**