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The Role of Cardiovascular Disease Risk Assessed by ASCVD Score in Primary Thrombosis Prophylaxis Strategy Among Antiphospholipid Antibody Carriers

Yu Zuo, M.D¹, Akriti Udupa, M.D¹, Jennifer Fan, M.D¹, Una E. Makris, M.D^{1,2}, David R. Karp, M.D,Ph.D¹, and Yu-Min Shen, M.D¹

¹University of Texas Southwestern Medical Center, Dallas, TX

²VA North Texas Health Care System, Dallas, TX.

Keywords

Antiphospholipid syndrome; antiphospholipid antibodies; thrombosis risk; CVD risks; ASCVD

Anti-phospholipid syndrome is an autoimmune pro-thrombotic condition that can have devastating effects on patients and their families¹. The presence of antiphospholipid antibodies (aPL) do not always lead to thromboembolic events.¹ Current consensus recommends maximizing control of cardiovascular disease (CVD) risk in aPL carriers². However, the exact role of quantified CVD risk in thrombogenesis among aPL carriers has not been evaluated. Atherosclerotic CVD 10-Year Risk Score (ASCVD) is a convenient tool designed to determine the absolute CVD risks among healthy individuals and to guide primary prevention^{3,4}. Our study aims to evaluate the role of quantified CVD risk in thrombosis risk stratification among ethnically diverse aPL positive carriers.

This study included a convenience sample of 147 patients with persistent high titer (≥ 99 percentiles) criteria aPL or positive lupus anticoagulant (LA) who attended University of Texas Southwestern Medical Center clinics from 2000–2017 (table 1). Persistent positive aPL is defined by having at least one positive test at ≥ 99th percentile cut-off values at two time points. 99th percentile cut-off values for aPL were established using 110 healthy controls. Cut-off values for anti-cardiolipin IgG/IgM are > 40 GPL/>40 MPL and for anti-β₂ Glycoprotein-I IgG/IgM are >16 GPL/>14 MPL. aPL testing was performed using FDA approved commercial kits. Lupus anticoagulant (LA) was tested by dilute Russell's viper venom time, partial thromboplastin time–LA and silica clotting time, with appropriate cut-offs established in the laboratory. ASCVD was calculated based on patient's age, sex, race, total cholesterol, HDL, most recently documented systolic blood pressure, hypertension treatment, diabetes status, and smoking status. Pearson Chi-squared analysis was used to

Corresponding author contact information: Yu-Min Shen, M.D., Division of Hematology and Oncology, University of Texas Southwestern Medical Center, Dallas, TX., 5323 Harry Hines Blvd., Dallas, TX. 75390-8852, Yu-Min.Shen@UTsouthwestern.edu.

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determine the association between increased ASCVD>7.5% or increased ASCVD>10% and various thromboembolic events. Non-parametric comparison of ASCVD as a continuous variable was performed among different groups using Mann-Whitney test.

Significantly higher 10-year CVD risk was seen among aPL patients with arterial thrombosis compared to asymptomatic carriers ($P=0.0063$). When comparing thrombotic APS patients to asymptomatic aPL positive carriers, 10-year CVD risk >7.5% ($OR=2.579$, 95% CI 1.063–6.595, $P=0.036$) and 10-year CVD risk >10% ($OR=2.902$, 95% CI 1.207–7.075, $P=0.017$) were significantly associated with arterial thrombosis but not venous thrombosis or any thrombosis. There were no significant CVD risk differences observed between aPL patients with venous thrombosis/or any thrombosis and asymptomatic carriers. 33.9% of aPL carriers who had a 10-year CVD risk >10% were on aspirin. 40.8% of aPL carriers who had a 10-year CVD risk >7.5% were on a statin.

Risk stratification of asymptomatic aPL carriers is challenging. The exact role of non-aPL thrombotic risks such as CVD risk in thrombotic APS pathogenesis is not fully understood⁵. We observed that aPL carriers with arterial thrombosis have significantly higher CVD risks compared to asymptomatic carriers. We demonstrated that a 10-year CVD risk >7.5% and >10% assessed by ASCVD score among aPL carriers is associated with arterial thrombosis but not venous thrombosis. The US Preventative Service Task Force (USPSTF) grants grade B recommendation for initiating a statin among individuals with ASCVD risk >7.5% and for initiating low dose aspirin among individuals with ASCVD risk >10%⁶. While a well-accepted APS specific risk stratification tool does not exist, general population CVD risk assessment models such as ASCVD may represent a convenient alternative tool to help determine CVD risks among aPL carriers to guide primary prophylaxis.

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Reference:

1. Giannakopoulos B, Krilis SA. The pathogenesis of the antiphospholipid syndrome. *N Engl J Med*. 2013;368(11):1033–1044. [PubMed: 23484830]
2. Erkan D, Lockshin MD. Antiphospholipid Syndrome : Current Research Highlights and Clinical Insights. Cham: Springer International Publishing Imprint: Springer; 2017.
3. Goff DC, Jr., Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(25 Pt B):2935–2959. [PubMed: 24239921]
4. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(25 Pt B):2889–2934. [PubMed: 24239923]
5. Barbhaiya M, Erkan D. Primary thrombosis prophylaxis in antiphospholipid antibody-positive patients: where do we stand? *Current rheumatology reports*. 2011;13(1):59–69. [PubMed: 21104348]

6. Bibbins-Domingo K, Force USPST. Aspirin Use for the Primary Prevention of Cardiovascular Disease and Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med.* 2016;164(12):836–845. [PubMed: 27064677]

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Figure 1.

Non-parametric comparison of 10-year CVD risk assessed by ASCVD score among different groups of aPL carriers. Box and whisker graph shows median, 25th and 75th percentile values, and CVD risk range. A-sx: asymptomatic. aPL: antiphospholipid antibodies

Table 1.

Demographic summary of 147 aPL positive carriers HTN: hypertension. HLD: hyperlipidemia. SLE dx: systemic lupus erythematosus diagnosis. aCL:

Characteristics	Arterial thrombosis aPL carriers (n=32*)	Venous Thrombosis aPL carriers (n=58)	A-sx aPLs Carriers (n=63)
Age, mean (S.D.)	60.8 (12.6)	52.7 (13.7)	55.9 (14.7)
Female	17 (53.1%)	32 (55.2%)	42 (66.7%)
African American	10 (31.3%)	17 (47.1%)	18 (28.6%)
Caucasian	18 (56.3%)	28 (48.2%)	38 (60.3%)
Hispanic	4 (12.5%)	13 (22.4%)	4 (6.3%)
Asian	0	0	3 (4.8%)
Smoking	18 (56.3%)	19 (32.8%)	13 (20.6%)
SLE dx	3 (9.4%)	11 (19.0%)	11 (17.5%)
Obstetric manifestation	0	4 ** (6.9%)	0
Hypertension	28 (87.5%)	33 (56.9%)	34 (54.0%)
Hyperlipidemia	11 (34.4%)	14 (24.1%)	14 (25.2%)
Diabetes	11 (34.4%)	13 (22.4%)	13 (27.0%)
aCL IgG/IgM	2 (6.3%)	5 (8.6%)	2 (3.2%)
aβ2GPI IgG/IgM	29 (90.6%)	38 (65.5%)	54 (85.7%)
LA	6 (18.8%)	24 (41.4%)	14 (22.2%)
Triple Positive	1 (3.1%)	2 (3.4%)	2 (3.2%)
10 years CVD risk, mean (S.D.)	20.4% (17.5)	9.3% (10.0)	12.2% (12.9)

Anti-cardiolipin. aβ2GPI: Anti-β2 Glycoprotein-I. LA: lupus anticoagulant. Triple positive: positive aCL, aβ2GPI, and LA.

* : Six patients had both arterial and venous thrombosis.

** :One patient had 1 × third trimester miscarriage and 1× first trimester miscarriage, two patients had intra-uterine growth retardations, one patient had 2 × first trimester miscarriages and 1× intra-uterine growth retardation.