

1 **Supplementary Table 1. Antibody profiles of patients with primary APS, secondary APS and SLE controls**

	APS (n=169)	SLE without APS (n=209)	PAPS (n=119)	SAPS (n=50)
ANA (n [%])	87 (51.8)	209 (100.0)	38 (32.2)	49 (98.0)
Low complement (n [%])	57 (34.1)	170 (81.3)	14 (12.0)	43 (86.0)
Coombs' test (n [%])	45 (28.3)	77 (44.0)	15 (13.6)	30 (60.0)
LAC (n [%])	147 (87.0)	40 (20.6)	99 (83.2)	48 (96.0)
aCL-IgG/M (n [%])	83 (49.1)	37 (18.1)	52 (43.7)	31 (62.0)
anti-β2GPI IgG/M (n [%])	108 (63.9)	43 (21.3)	80 (67.2)	28 (56.0)
Single aPL positivity (n [%])	69 (40.8)	37 (19.0)	52 (43.7)	17 (34.0)
Double aPL positivity (n [%])	31 (18.3)	13 (6.7)	22 (18.5)	9 (18.0)
Triple aPL positivity (n [%])	69 (40.8)	19 (9.7)	45 (37.8)	24 (48.0)
anti-β2GPI-DI IgG (n [%])	55 (32.5)	17 (8.1)	39 (32.8)	16 (32.0)

2 Abbreviations: ANA, antinuclear antibody; LAC, lupus anticoagulant; aPL, antiphospholipid antibodies.

3 Single, double, and triple refers to the positive numbers of the criteria aPLs, including aCL IgG/M, anti-β2GP1 IgG/M antibodies, and LAC.

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5 **Supplementary Table 2. Demographic characteristics of patients with primary APS and secondary APS**

	PAPS (n=119)	SAPS (n=50)
Demographic features		
Female (n [%])	75 (63.0)	42 (84.0)
Age at diagnosis (median, IQR)	34 (31, 42)	35 (30,40)
BMI (median, IQR)	24.1 (21.6, 26.2)	22.9 (21.4, 26.8)
Conventional risk factor		
Diabetes mellitus (n [%])	5 (4.2)	1 (2.0)
Arterial hypertension (n [%])	23 (19.3)	9 (18.0)

Smoking (n [%])	28 (23.5)	4 (8.0)
Coronary artery disease (n [%])	5 (4.2)	1 (2.0)
Thrombosis (n [%])	91 (76.5)	40 (80.0)
Venous thrombosis (n [%])	60 (50.4)	21 (42.0)
Arterial thrombosis (n [%])	41 (34.5)	15 (30.0)
Venous and arterial thrombosis (n [%])	13 (10.9)	6 (12.0)
Microvascular thrombosis (n [%])	14 (11.8)	19 (38.0)
Recurrent thrombosis before diagnosis (n [%])	78 (65.6)	36 (72.0)
Adverse pregnancy history (n [%])	48 (71.6, 67)	20 (66.7, 30)
Pre-eclampsia, eclampsia and placental dysfunction (n [%])	14 (20.9)	7 (23.3)
Early miscarriages ≥ 1 (n [%])	22 (32.8)	8 (26.7)
Fetal death (≥ 10 weeks) (n [%])	24 (35.8)	11 (36.7)
Extra-criteria manifestations (n [%])	46 (38.7)	40 (80.0)
Thrombocytopenia (n [%])	40 (33.6)	32 (64.0)
Autoimmune hemolytic anemia (n [%])	6 (5.0)	13 (26.0)
Valvular lesions (n [%])	0 (0.0)	12 (24.0)
APS nephropathy (n [%])	8 (6.7)	3 (6.0)
Non-vascular neurological manifestations (n [%])	5 (4.2)	10 (20.0)

6 Abbreviations: APS, antiphospholipid syndrome; BMI, body mass index; IQR, interquartile range. Only female patients with at least one conception were included in the analysis of adverse
7 pregnancy history.

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9 **Supplementary Table 3. Risk of extra-criteria manifestations in primary APS by univariable and multivariable logistic regression analysis**

	Univariable regression analysis		Multivariable regression model	
	OR (95%CI)	p	OR (95%CI)	p
Arterial hypertension	6.55 (2.34-18.29)	<0.001	9.64 (2.97, 31.27)	<0.001

Coombs' test positivity	3.94 (1.24-12.50)	0.020	5.79 (1.66-20.22)	0.006
anti-β2GPI-DI IgG positivity	4.22 (1.88-9.49)	0.001	2.98 (1.15-7.67)	0.024

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Supplementary Table 4. Antibody profiles of APS patients with events during the follow-up

ID	Diagnosis	Events	anti-β2GPI-DI IgG	LA	anti-β2GPI IgG	anti-β2GPI IgM	aCL-IgG	aCL-IgM	Treatment	
									Warfarin	Aspirin
1	PAPS	Venous thrombosis	NEG	POS	NEG	POS	NEG	NEG	Yes	Yes
2	PAPS	Venous thrombosis	POS	POS	POS	NEG	POS	NEG	Yes	Yes
3	PAPS	Venous thrombosis	NEG	POS	POS	NEG	POS	NEG	Yes	Yes
4	PAPS	Venous thrombosis	NEG	POS	NEG	NEG	NEG	NEG	Yes	No
5	PAPS	Venous thrombosis	POS	POS	POS	NEG	POS	NEG	Yes	Yes
6	PAPS	Venous thrombosis	POS	POS	POS	NEG	POS	NEG	Yes	Yes
7	PAPS	Venous thrombosis	POS	POS	POS	NEG	POS	NEG	Yes	Yes
8	SAPS	Venous thrombosis	NEG	POS	NEG	NEG	POS	NEG	Yes	No
9	PAPS	Arterial thrombosis	NEG	POS	NEG	NEG	NEG	NEG	Yes	Yes
10	PAPS	Arterial thrombosis	NEG	POS	NEG	NEG	NEG	NEG	Yes	Yes
11	PAPS	Arterial thrombosis	NEG	POS	POS	NEG	POS	NEG	Yes	Yes
12	PAPS	Arterial thrombosis	POS	POS	POS	NEG	POS	NEG	Yes	No
13	PAPS	APS nephropathy	POS	POS	POS	NEG	POS	NEG	Yes	Yes
14	PAPS	APS nephropathy, Valvular lesions	POS	POS	POS	POS	POS	NEG	Yes	Yes
15	PAPS	Non-vascular neurological manifestations	NEG	POS	NEG	NEG	NEG	NEG	No	No

16	SAPS	Non-vascular neurological manifestations	POS	POS	POS	NEG	POS	NEG	No	No
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Abbreviations: PAPS, primary APS; SAPS, secondary APS; POS, positive; NEG, negative.

Supplementary Table 5. Diagnostic performance of antiphospholipid antibodies for extra-criteria events in APS

	Sensitivity	Specificity	PLR	NLR	PPV	NPV	Accuracy	Youden Index	Odds ratio (95%CI)
LAC	95.35%	21.69%	1.22	0.21	55.78%	81.82%	59.17%	0.17	5.68 (1.83-17.60)
anti-β2GPI-DI IgG	44.19%	79.52%	2.16	0.70	69.09%	57.89%	61.54%	0.24	3.07 (1.55-6.08)
anti-β2GPI IgG/M	67.44%	39.76%	1.12	0.82	53.70%	54.10%	53.85%	0.07	1.37 (0.73-2.57)
anti-β2GPI IgG	55.81%	72.29%	2.01	0.61	67.61%	61.22%	63.91%	0.28	3.30 (1.73-6.26)
anti-β2GPI IgM	23.26%	67.47%	0.71	1.14	42.55%	45.90%	44.97%	-0.09	0.63 (0.32-1.24)
aCL IgG/M	63.95%	66.27%	1.90	0.54	66.27%	63.95%	65.09%	0.30	3.49 (1.85-6.56)
aCL IgG	63.95%	66.27%	1.90	0.54	66.27%	63.95%	65.09%	0.30	3.49 (1.85-6.56)
aCL IgM	4.65%	100.00%	NA	0.95	100.00%	50.30%	51.48%	NA	9.11 (0.48-171.89)
Single aPL positive	29.07%	46.99%	0.55	1.51	36.23%	39.00%	37.87%	-0.24	0.36 (0.19-0.69)
Isolated LAC	24.42%	67.47%	0.75	1.12	43.75%	46.28%	45.56%	-0.08	0.67 (0.34-1.31)
Isolated anti-β2GPI IgG/M	3.49%	79.52%	0.17	1.21	15.00%	44.30%	40.83%	-0.17	0.14 (0.04-0.50)
Isolated aCL IgG/M	1.16%	100.00%	NA	0.99	100.00%	49.40%	49.70%	NA	2.93 (0.12-72.95)
Double aPL positivity (n [%])	15.12%	78.31%	0.70	1.08	41.94%	47.10%	46.15%	-0.07	0.64 (0.29-1.41)
LAC-, anti-β2GPI IgG/M+, aCL IgG/M+	0.00%	98.80%	0.00	1.01	0.00	48.81%	48.52%	NA	0.32 (0.01-7.92)
LAC+, anti-β2GPI IgG/M-, aCL IgG/M+	6.98%	92.77%	0.97	1.00	50.00%	49.04%	49.11%	0.00	0.96 (0.30-3.11)
LAC+, anti-β2GPI IgG/M+, aCL IgG/M-	8.14%	86.75%	0.61	1.06	38.89%	47.68%	46.75%	-0.05	0.58 (0.21-1.58)
Triple aPL positive	55.81%	74.70%	2.21	0.59	69.57%	62.00%	65.09%	0.31	3.73 (1.94-7.16)
Triple positive IgG isotype	54.65%	74.70%	2.16	0.61	69.12%	61.39%	64.50%	0.29	3.56 (1.85-6.83)
Triple positive IgM isotype	4.65%	100.00%	NA	0.95	100.00%	50.30%	51.48%	NA	9.11 (0.48-171.89)

Abbreviations: LAC, lupus anticoagulant; PLR, positive likelihood ratio; NPV, negative likelihood ratio; PPV, positive predictive value; NPV, negative predictive value.