Platelet glycoprotein V autoantibodies and complement C3 are associated with thrombosis in systemic lupus erythematosus

Anders A. Bengtsson,[1] Elsa Grenmyr,[1] Andreas Jönsen,[1] Robin Kahn,[2] John W. Semple,[3-5] Leendert Porcelijn,[6] Rick Kapur[7] and Carl Petrus Linge[1]

[1]Department of Clinical Sciences Lund, Rheumatology, Lund University, Skåne University Hospital, Lund, Sweden; [2]Department of Clinical Sciences Lund, Wallenberg Center of Molecular Medicine and Section of Pediatrics, Lund University, Lund, Sweden; [3]Department of Laboratory Medicine, Division of Transfusion Medicine, Lund University, Lund, Sweden; [4]Clinical Immunology and Transfusion Medicine, Office of Medical Services, Region Skåne, Lund, Sweden; [5]Departments of Pharmacology, Medicine and Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada; [6]Department of Immunohematology Diagnostics, Sanquin Diagnostic Services, Amsterdam, the Netherlands and [7]Sanquin Blood Supply Foundation, Department Research, and Amsterdam UMC location University of Amsterdam, Landsteiner Laboratory, Amsterdam, the Netherlands

Correspondence: C. P. Linge
petrus.linge@med.lu.se

Received: October 22, 2025.
Accepted: February 18, 2026.
Early view: February 26, 2026.

https://doi.org/10.3324/haematol.2025.300094

Platelet glycoprotein V autoantibodies and complement C3 are associated with thrombosis in systemic lupus erythematosus.

Supplementary Methods

Stability of indirect MAIPA and long-term sample storage

MAIPA analyses were performed on serum samples stored at -80 °C for up to approximately 25-30 years. Previous work has demonstrated a strong correlation between indirect and direct MAIPA optical density values for platelet autoantibodies, including anti-GPV (1). In preliminary observations using samples stored at -20 °C, up to two freeze-thaw cycles did not affect indirect MAIPA results (Porcelijn, Kapur et al., unpublished observations). Although long-term storage at -20 °C may reduce detectability of platelet autoantibodies, this has not been formally assessed for samples stored at -80 °C. Any storage-related effects in the present study would therefore be expected to bias results toward underestimation rather than false-positive detection.

Reference

1. Porcelijn L, Schmidt DE, Oldert G, et al. Evolution and Utility of Antiplatelet Autoantibody Testing in Patients with Immune Thrombocytopenia. Transfusion medicine reviews. 2020;34(4):258-69.

Supplemental tables

Supplemental table S1. Distribution of SLEDAI-2K items during high (H) and low (L) disease activity states

SLEDAI-2K (points)	H (n)	H %	L (n)	L %
Seizure (8)	0	0%	0	0%
Psychosis (8)	0	0%	0	0%
Organic brain syndrome (8)	0	0%	0	0%
Visual disturbance (8)	1	1%	0	0%
Cranial nerve disorder (8)	0	0%	0	0%
Lupus headache (8)	0	0%	0	0%
CVA (8)	0	0%	0	0%
Vasculitis (8)	1	1%	0	0%
Arthritis (4)	31	35%	4	4%
Myositis (4)	0	0%	0	0%
Urinary Casts (4)	17	19%	1	1%
Hematuria (4)	33	37%	3	3%
Proteinuria (4)	39	44%	4	4%
Pyuria (4)	3	3%	0	0%
Rash (2)	31	35%	8	9%
Alopecia (2)	6	7%	2	2%
Oral/Nasal ulcer (2)	13	15%	2	2%
Pleuritis (2)	1	1%	0	0%
Pericarditis (2)	0	0%	0	0%
Low complement (2)	53	60%	34	38%
Anti-DNAab (2)	45	51%	20	22%
Fever (1)	6	7%	1	1%
Thrombocytopenia (1)	1	1%	1	1%
Leukopenia (1)	8	9%	4	4%

Table S2. Correlation between average SLEDAI-2K and anti-phospholipid antibodies

		SLEDAI-2K		
Spearman		**r**	**CI (95%)**	**p**
CL	IgG	**0.32**	**0.11 - 0.50**	**0.0023**
	IgM	0.01	-0.21 - 0.22	0.96
β2GP1	IgG	**0.31**	**0.11 - 0.49**	**0.0029**
	IgM	0.08	-0.14 - 0.29	0.45
PS/PT	IgG	**0.33**	**0.12 - 0.51**	**0.0018**
	IgM	-0.07	-0.28 - 0.15	0.53
AV	IgG	**0.28**	**0.074 - 0.47**	**0.0072**
	IgM	0.00	-0.21 - 0.22	0.97

Table S3. Thrombotic events and corresponding average antibody titers (anti-GP and aPL) measured by MAIPA and ELISA

Thrombotic events include deep vein thrombosis (DVT), pulmonary embolism (PE), myocardial infarction (MI), cerebrovascular insult (CVI), venous thrombosis (VT) and microthrombosis (MT). Anti-GP antibodies: GP IIb/IIIa, GPV, GPIb/IX. Anti-PL antibodies: anti-cardiolipin (CL), anti-β2-glycoprotein I (b2), anti-phosphatidylserine/prothrombin complex (PSPT), anti-annexin V (AV). Diagnostic methods: US = Ultrasound, MRI = Magnetic Resonance Imaging, CT = Computed Tomography. For the purpose of visual comparison between MAIPA and ELISA antibody titers, min-max normalization was applied to each antibody titer value (anti-GP and aPL) for each assay. All normalized values range between 0 to 1, where 0 represents the minimum observed value and 1 represents the maximum observed value. Shades of red indicate relative levels of anti-GP and shades of green aPL. *normalized values were used for graphical representation in figures and were not used in any statistical analyses.

Patient	Sex	Event (type)	Time to event (years)	Age at diagnosis	Age at baseline	GP IIb/IIIa*	GPV*	GP Ib/IX*	CL (IgG)*	CL (IgM)*	b2 (IgG)*	b2 (IgM)*	PSPT (IgG)*	PSPT (IgM)*	AV (IgG)*	AV (IgM)*	SLEDAI-2K H	SLEDAI-2K L	Thrombosis type	Detection method
1	M	MT	7	39	52	0.17	0.17	0.20	0.14	0.12	0.06	0.70	0.15	0.55	0.02	0.21	6	2	VT: Left, branch retinal v occlusion	Ocular exam and OCT
2	F	DVT	5	49	60	0.05	0.07	0.09	0.07	0.00	0.02	0.03	0.01	0.01	0.00	0.00	4	0	PE: decr perf right lung and left lower lobe	Ventilation/perfusion (V/Q) scan
3	F	CVI	7	46	48	0.00	0.01	0.02	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	2	0	CVI: Multiple vascular lesions	MRI
4	F	MI	2	50	71	0.03	0.07	0.07	0.02	0.01	0.01	0.02	0.02	0.01	0.01	0.01	4	0	MI: Right dominant coronary artery	Coronary angiography
5	F	DVT	2	32	48	0.12	0.27	0.27	0.20	0.00	0.12	0.02	0.09	0.01	0.04	0.00	19	2	DVT: lower extremity	US
6	F	CVI	0	55	55	0.03	0.12	0.28	0.01	0.06	0.02	0.25	0.01	0.06	0.00	0.06	8	0	CVI	CT and MRI
7	F	MI	3	28	37	0.04	1.00	0.71	0.02	0.00	0.17	0.02	0.01	0.00	0.00	0.01	12	2	MI: Thrombosis in LAD	Coronary angiography
8	F	MI	4	67	67	0.04	0.04	0.10	0.02	0.01	0.01	0.06	0.01	0.10	0.01	0.02	4	0	MI	Coronary angiography
9	F	DVT	0	45	45	0.27	0.03	0.05	0.01	0.01	0.00	0.07	0.13	0.89	0.00	0.02	8	0	DVT	US
10	F	MT	1	31	31	0.49	0.60	0.56	0.01	0.00	0.01	0.01	0.03	0.00	0.00	0.00	19	11	MT: fibrin thrombus	Kidney biopsy, histology
11	F	DVT	9	25	25	0.41	0.55	0.53	0.05	0.10	0.04	0.57	0.05	0.26	0.02	0.52	12	2	DVT: left v. fibularis	US
12	F	MI	7	24	35	0.06	0.27	0.15	0.09	0.01	0.03	0.04	0.05	0.04	0.01	0.02	8	2	MI: LAD occulsion	Coronary angiography
13	M	DVT	0	26	26	0.06	0.13	0.07	0.01	0.00	0.01	0.01	0.01	0.00	0.00	0.00	12	0	DVT: right v. femoralis	US and CT
14	F	DVT	0	16	19	0.19	0.11	0.20	0.01	0.06	0.01	0.31	0.01	0.08	0.00	0.05	5	2	DVT: left v. poplitea	US
15	F	MI	9	59	59	0.02	0.04	0.02	0.01	0.00	0.00	0.00	0.00	0.01	0.00	0.01	4	0	MI: LAD occlusion	Coronary angio
16	F	DVT	0	37	67	0.03	0.05	0.09	0.01	0.00	0.00	0.01	0.00	0.00	0.00	0.00	12	2	DVT: right lower extr	US
17	F	CVI	7	62	70	0.04	0.13	0.35	0.00	0.07	0.01	0.28	0.00	0.09	0.00	0.07	12	4	CVI: ischemic lesion frontal right	CT
18	F	PE	3	20	34	0.17	0.07	0.08	0.16	0.00	0.06	0.03	0.02	0.00	0.01	0.01	14	0	PE: right lung, lower lobe and left basal	Ventilation/perfusion (V/Q) scan
19	F	DVT	12	40	52	0.06	0.20	0.15	0.02	0.00	0.00	0.02	0.01	0.01	0.01	0.01	5	2	DVT	US
20	M	MI	5	46	46	0.03	0.02	0.01	0.04	0.06	0.03	0.27	0.09	0.09	0.01	0.08	8	0	MI	Coronary angiography
21	F	PE	0	50	57	0.06	0.06	0.09	0.03	0.00	0.01	0.00	0.01	0.01	0.01	0.00	7	0	PE	Ventilation/perfusion (V/Q) scan
22	M	MI	2	54	56	0.05	0.11	0.11	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	2	0	MI: LAD occlusion	Cor Angiography
23	M	CVI	9	77	77	0.13	0.13	0.14	0.02	0.03	0.01	0.25	0.02	0.09	0.01	0.13	8	2	CVI	CT
24	F	CVI	12	47	49	0.14	0.20	0.28	0.97	0.27	1.00	0.98	0.10	0.19	0.06	0.24	11	4	CVI	CT

Table S4. Thrombosis-free survival analyses according to platelet autoantibodies, antiphospholipid antibodies, and complement levels in SLE.

(A) Restricted mean thrombosis-free survival time (RMST) with 95% confidence intervals for each group. Patients were stratified as negative, low positive (below median), or high positive (above median) for each antibody; complement C3 and C4 were categorized into tertiles (low/mid/high). Time is expressed in years; thrombotic events were coded as events and all others as censored. RMST was truncated at the largest observed follow-up time due to tail censoring.

(B) Global between-group comparisons (df=2) using three standard tests: logrank (Mantel–Cox), Gehan–Breslow–Wilcoxon, and Tarone–Ware (intermediate weighting). *NE indicates not estimable due to sparse group size (e.g., anti-annexin V IgG with only one positive sample), precluding meaningful stratified estimation.*

A) RMST (95% CI) per group

Group	GPIIbIIIa	GPV	GPIbIX		C3	C4		
Neg	25.13 (22.09-28.17)	26.28 (23.08-29.48)	20.19 (17.65-22.73)	Low	19.78 (16.75-22.80)	20.03 (17.24-22.82)		
Low	10.54 (6.22-14.86)	16.48 (12.01-20.94)	24.08 (18.26-29.89)	Mid	25.96 (21.63-30.30)	23.98 (19.20-28.75)		
High	18.97 (13.96-23.99)	15.08 (10.34-19.83)	14.81 (10.05-19.56)	High	16.24 (12.41-20.07)	17.55 (13.76-21.34)		
Group	**CLg**	**CLm**	**b2g**	**b2m**	**PSPTg**	**PSPTm**	**AVg**	**AVm**
Neg	24.75 (21.85-27.66)	25.22 (22.38-28.05)	24.26 (21.42-27.10)	19.58 (17.18-21.98)	24.76 (21.93-27.59)	25.63 (22.77-28.49)	NE	24.95 (22.10-27.81)
Low	16.20 (9.20-23.20)	9.67 (1.86-17.47)	11.25 (1.64-20.86)	27.42 (21.58-33.25)	15.17 (7.38-22.96)	13.00 (6.97-19.03)	NE	12.00 (4.75-19.25)
High	15.11 (7.95-22.27)	15.89 (11.39-20.40)	20.75 (16.93-24.57)	13.65 (8.66-18.64)	13.87 (4.40-23.33)	13.91 (8.54-19.27)	NE	14.94 (10.00-19.89)

B) Overall comparisons (df=2)

	GPIIbIIIa		GPV		GPIbIX		C3		C4	
Test (SPSS)*	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p
Logrank (Mantel-Cox)	5.32	0.07	4.26	0.12	3.69	0.16	4.02	0.13	1.25	0.54
Gehan-Breslow-Wilcoxon	4.10	0.13	2.41	0.30	2.88	0.24	3.24	0.20	2.09	0.35
Tarone-Ware	4.65	0.10	3.22	0.20	3.25	0.20	3.62	0.16	1.66	0.44

	CLg		CLm		b2g		b2m		PSPTg		PSPTm		AVg		AVm	
Test (SPSS)*	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p	χ^2	p
Logrank (Mantel-Cox)	1.59	0.45	7.04	0.030	1.90	0.39	4.82	0.09	2.31	0.32	5.61	0.06	0.36	0.55	3.53	0.17
Gehan-Breslow-Wilcoxon	1.34	0.51	7.05	0.029	2.66	0.27	3.71	0.16	2.03	0.36	4.04	0.13	0.34	0.56	1.51	0.47
Tarone-Ware	1.45	0.49	7.07	0.029	2.30	0.32	4.24	0.12	2.15	0.34	4.81	0.09	0.36	0.55	2.37	0.31

Table S5. Platelet counts and thrombocytopenia by anti-platelet glycoprotein antibody status across disease activity states

Platelet counts and frequencies of thrombocytopenia stratified by anti-platelet glycoprotein antibody status and disease activity state. Data are shown separately for (A) anti-GPIIb/IIIa, (B) anti-GPV, and (C) anti-GPIb/IX. Frequencies indicate the number of samples positive/negative for each antibody in the high- and low-disease activity states. Platelet counts are presented as median (interquartile range, IQR). Thrombocytopenia is summarized using two cut-offs (PLT <150×10⁹/L and PLT <100×10⁹/L), expressed as n/N (%) within each antibody stratum and disease activity state. *PLT = platelet count. High/Low denote the two disease activity states as defined in the main manuscript.*

A)

Antibody	GPIIb/IIIa+		GPIIb/IIIa-	
Disease activity	High	Low	High	Low
Frequency	24/89 (27%)	23/89 (26%)	65/89 (73%)	66/89 (74%)
PLT, median (IQR)	229 (201-262)	248 (234-290)	235 (186-286)	238 (190-279)
PLT <150×10⁹/L	2/24 (8%)	1/23 (4%)	6/65 (9%)	5/66 (8%)
PLT <100×10⁹/L	0/24 (0%)	0/23 (0%)	1/65 (2%)	1/66 (1%)

B)

Antibody	GPV+		GPV-	
Disease activity	High	Low	High	Low
Frequency	43/89 (48%)	21/89 (24%)	46/89 (52%)	68/89 (76%)
PLT, median (IQR)	213 (186-248)	248 (208-286)	259 (200-302)	242 (197-286)
PLT <150×10⁹/L	6/43 (14%)	2/21 (10%)	2/46 (4%)	4/68 (6%)
PLT <100×10⁹/L	1/43 (2%)	0/21 (0%)	0/46 (0%)	1/68 (1%)

C)

Antibody	GPIb/IX+		GPIb/IX-	
Disease activity	High	Low	High	Low
Frequency	48/89 (54%)	27/89 (30%)	41/89 (46%)	62/89 (70%)
PLT, median (IQR)	223 (193-262)	253 (210-286)	246 (195-299)	240 (190-285)
PLT <150×10⁹/L	4/48 (8%)	1/27 (4%)	4/41 (10%)	5/62 (8%)
PLT <100×10⁹/L	1/48 (1%)	0/27 (0%)	0/41 (0%)	1/62 (2%)

Table S6. Overall thrombocytopenia frequency by disease activity and platelet counts by thrombosis status

Overall frequency of thrombocytopenia by disease activity state and platelet counts by thrombosis status. (A) Thrombocytopenia prevalence in the high and low disease activity states using cut-offs PLT <150×10⁹/L and PLT <100×10⁹/L. (B) Platelet counts (median, IQR) in patients with and without thrombotic events during follow-up. PLT, platelet count; IQR, interquartile range. Thrombosis refers to incident thrombotic events during follow-up as defined in Methods.

A)

Thrombocytopenia	High	Low
PLT <150×10⁹/L	8 (9%)	6 (7%)
PLT <100×10⁹/L	1 (1%)	1 (1%)

B)

Thrombosis	Yes (n24)	No (n65)
PLT, median (IQR)	229 (177-266)	249 (202-277)

Figure S1. Correlation matrix for antibodies, clinical laboratory results and SLEDAI-2K

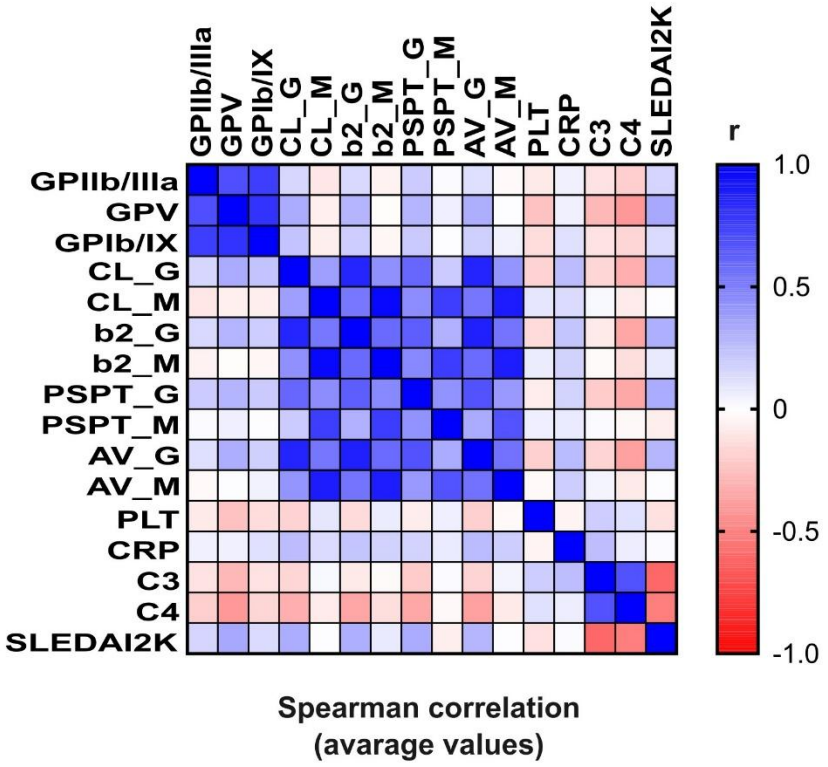
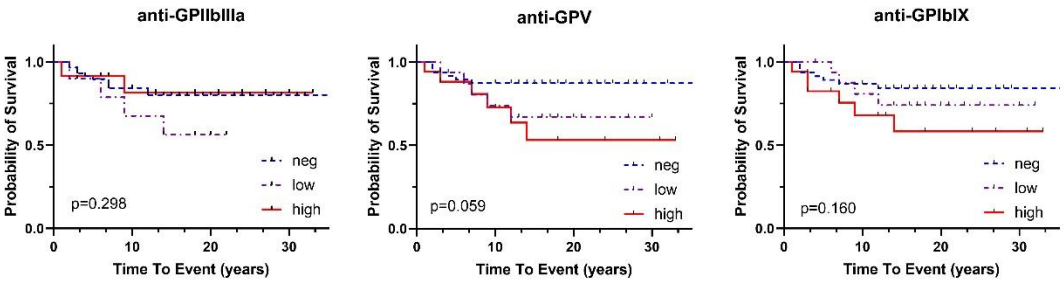


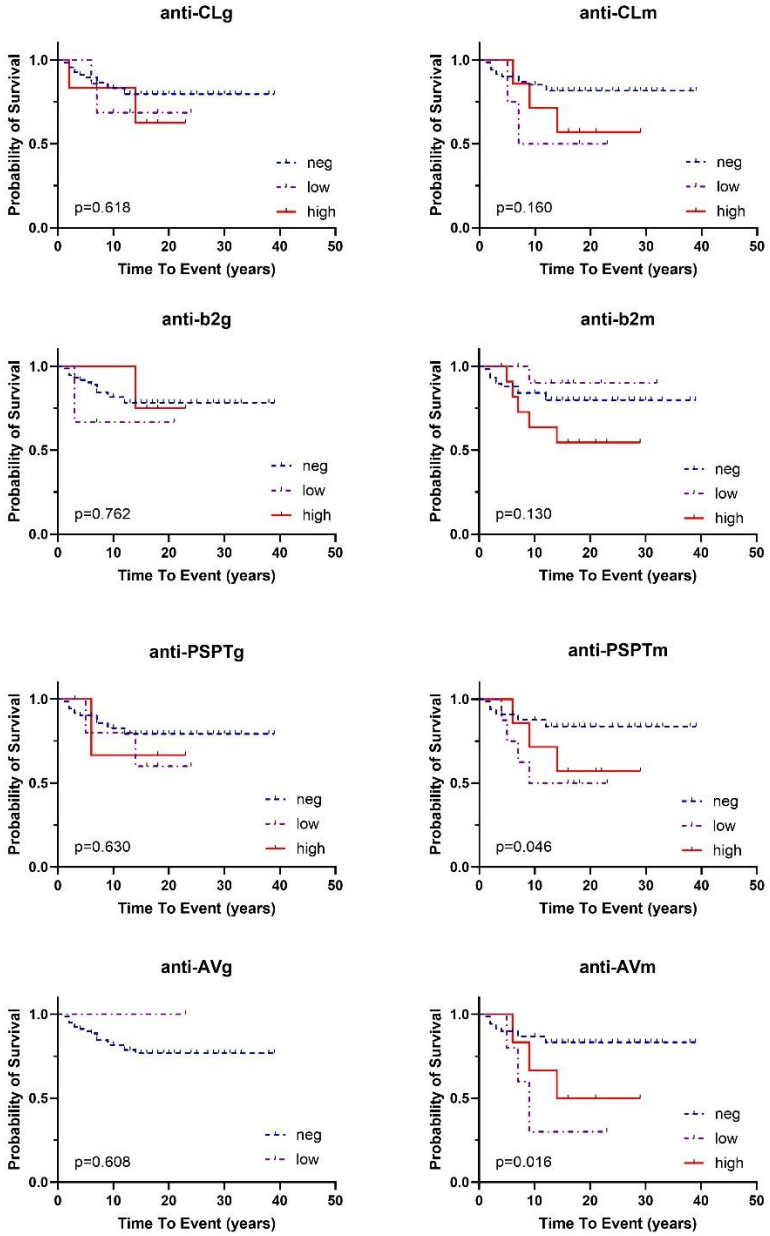
Figure S1. Correlation between average values from baseline sample (H) and follow up (L). Both anti-GP and aPL categories of antibodies showed a strong correlation within each group. A weaker, but significant correlation was detected between anti-GPV and IgG type aPL, and between anti-GPIb/IX and anti-CLG. Average levels of anti-GPV, IgG type anti-cardiolipin (CL_G), anti-β2 glycoprotein 1 (b2_G), anti-PS/PT (PSPT_G) and anti-AV (AV_G) correlated significantly with SLEDAI-2K. anti-GPV, CL_G, b2_G, PSPT_G and AV_G also correlated significantly with C4, but only GPV showed a significant correlation with C3.

Supplementary Figure S2

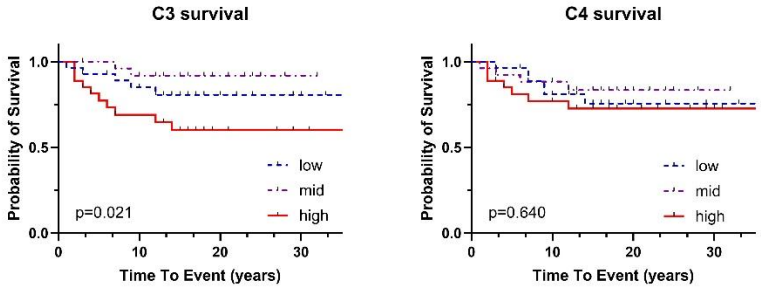
A



B



C



Kaplan–Meier curves were compared using the log-rank (Mantel–Cox) test. Log-rank p-values are displayed in (A) platelet-specific anti-GP antibodies, (B) antiphospholipid antibody (aPL) positivity, and (C) complement proteins. For antibodies, patients were stratified as negative, low positive (below median), or high positive (above median). For complement C3 and C4, levels were divided into tertiles: low, medium, and high. For anti-annexin V IgG (AVg), only one positive sample was available, precluding further stratification. Anti-CL = anticardiolipin; anti-b2 = anti-β2 glycoprotein I; anti-PSPT = anti-phosphatidylserine/prothrombin; anti-AV = anti-annexin V; g = IgG isotype; m = IgM isotype. Supplementary robustness analyses using the log-rank test for trend and the Gehan–Breslow–Wilcoxon test are shown in Supplementary Table S4. Anti-GPV showed a borderline separation by the log-rank test ($p = 0.059$), with a significant linear trend across groups ($p = 0.0187$). PS/PT IgM and anti–Annexin V IgM demonstrated significant separation by the log-rank test ($p = 0.0456$ and $p = 0.0156$), confirmed in Wilcoxon testing. High C3 levels were significantly associated with reduced thrombosis-free survival (log-rank $p = 0.0207$). No other antibody specificities showed significant differences by any of the three methods.
Median thrombosis-free survival time pending analysis. Hazard ratios are provided in Supplementary Table S4.