IgG phosphatidylserine/prothrombin antibodies as a risk factor of thrombosis in antiphospholipid antibody carriers

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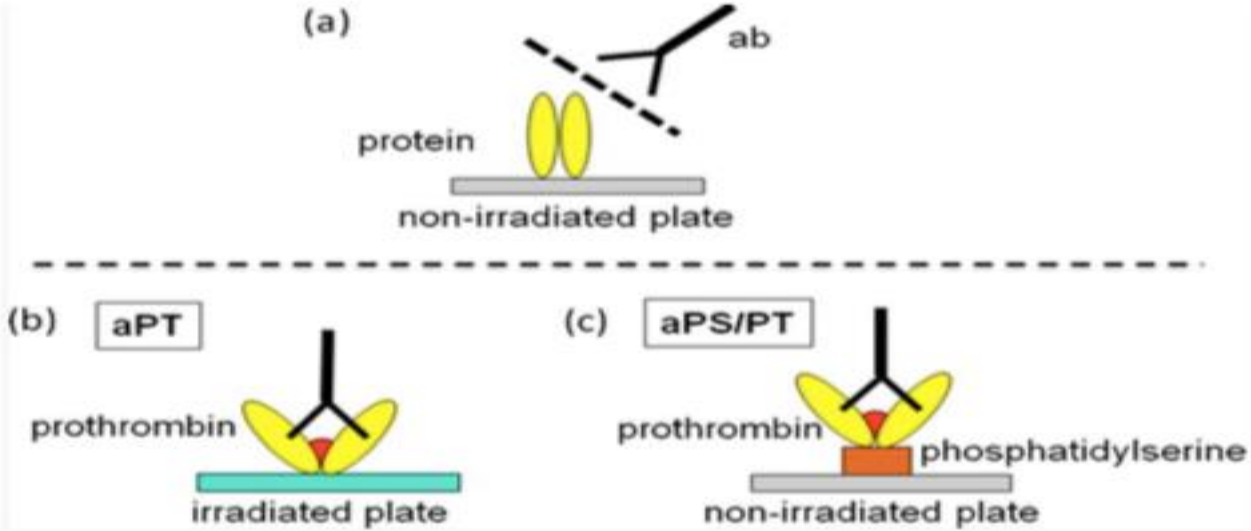
Faculty Disclosure

Company	Nature of Affiliation
• INOVA	

Off-Label Product Usage

Background



Sciascia S, Curr Rheumatol Rep. 2014

Anti-prothrombin (aPT) and anti-phosphatidylserine/prothrombin (aPS/PT) antibodies and the risk of thrombosis in the antiphospholipid syndrome

A systematic review

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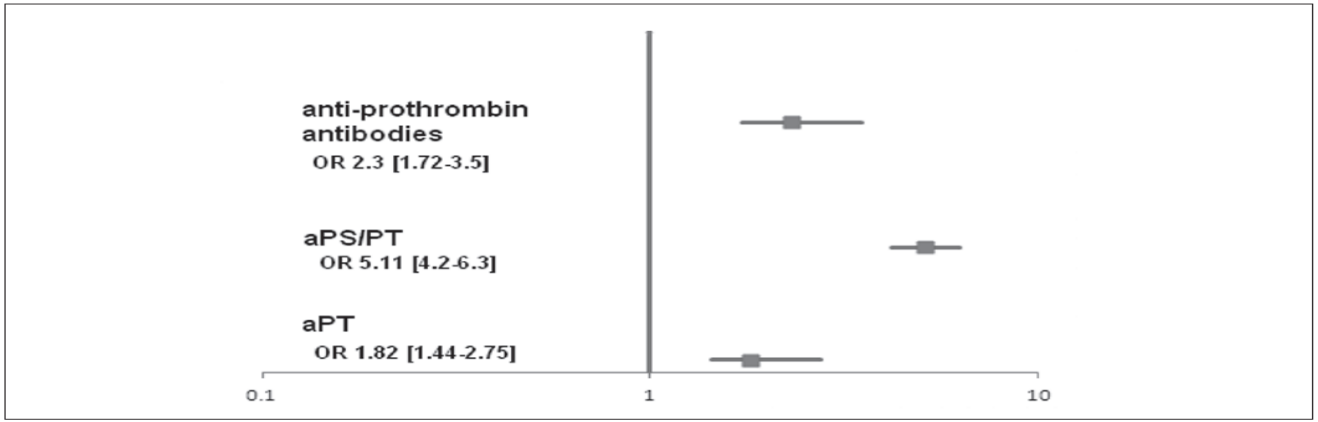

Lupus (2012) 21, 787–789
http://lup.sagepub.com

SPECIAL ARTICLE

Antiphosphatidylserine/prothrombin antibodies in primary antiphospholipid syndrome

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Table 2 The relationship of IgG/IgM aPS/PT antibodies with clinical features of PAPS

Antibody	*Thrombosis* n(%) (n = 102)	*Pregnancy morbidity* n(%) (n = 56)	*Controls* n (%) (n = 214/n = 172*)	*Odds ratio for thrombosis* (95% *CI*)	p-*value*	*Odds ratio for pregnancy morbidity* (95% *CI*)	p-*value*
IgG aPS/PT	39 (38.2)	5 (8.9)	5 (2.3)/4 (2.3)*	25.7 (9.7–68.1)	<0.001	4.0 (1.0–15.8)	0.043
IgM aPS/PT	56 (54.9)	11 (19.6)	6 (2.8)/4 (2.3)*	42.0 (17.0–103.3)	<0.001	10.2 (3.1–33.5)	<0.001

aPS/PT: antiphosphatidylserine/prothrombin; PAPS: primary antiphospholipid syndrome; CI: confidence interval;
*Male patients have been excluded in the statistical comparison with pregnancy morbidity.

Ariela Hoxha*, Amelia Ruffatti, Elena Mattia, Lauro Meneghel, Marta Tonello, Elisa Salvan, Vittorio Pengo and Leonardo Punzi

Relationship between antiphosphatidylserine/prothrombin and conventional antiphospholipid antibodies in primary antiphospholipid syndrome

Table 1 Multivariate logistic regression for the presence of LA.

	β-Coefficient	OR	95% CI	p-Value
IgG aPS/PT	2.0	7.6	2.9–20.0	<0.0001
IgM aPS/PT	1.5	4.5	2.0–9.8	<0.0001
IgG anti-β2GPI	1.3	3.8	1.5–9.3	0.004

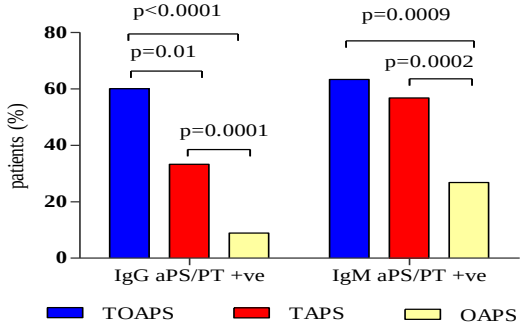
LA, lupus anticoagulant; aPS/PT, antiphosphatidylserine/prothrombin antibodies; anti-β2GPI, anti-β2-glycoprotein I antibodies.

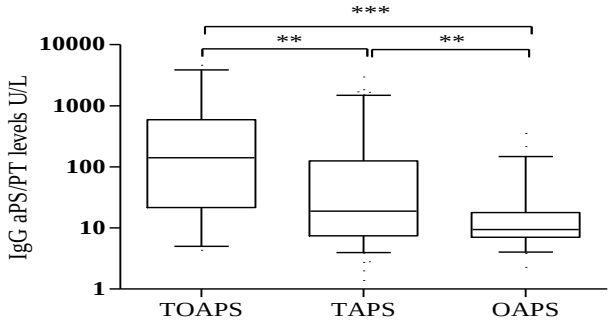
128 APS-seronegative patients

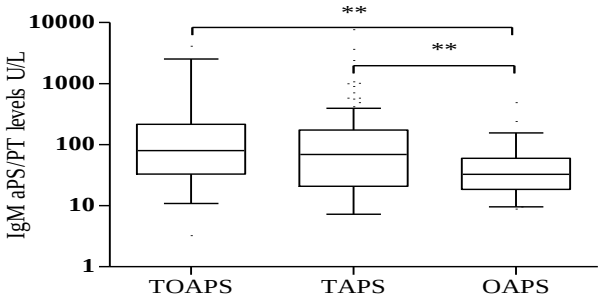
- IgG/IgM aPS/PT Abs were positive 12/128 (9.4%) *vs* 2/100 (2%) [p=0.043]
- aPS/PT antibodies were more frequent in the thrombosis than in pregnancy morbidity subset (p = 0.01, OR 3.4, 95% CI 1.3– 9.0).

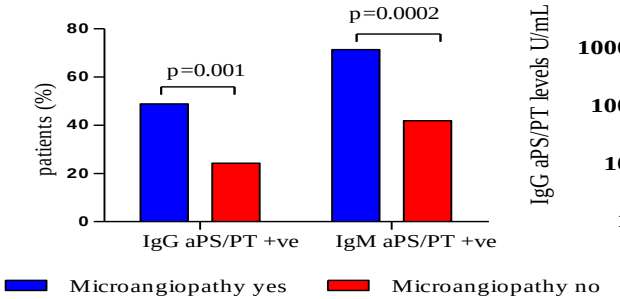
Ariela Hoxha*, Elena Mattia, Marta Tonello, Chiara Grava, Vittorio Pengo and Amelia Ruffatti

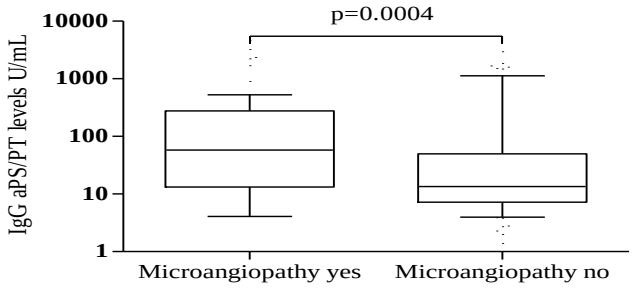
Antiphosphatidylserine/prothrombin antibodies as biomarkers to identify severe primary antiphospholipid syndrome

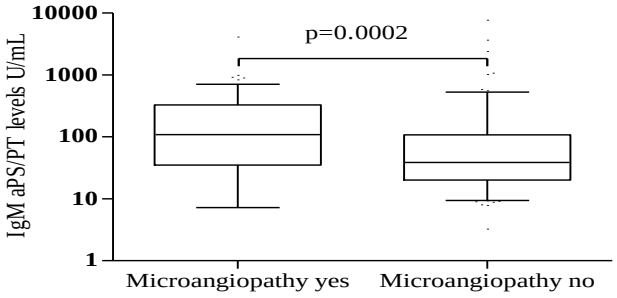












CCLM 2016

Antiphosphatidylserine/prothrombin Antibodies in Antiphospholipid Syndrome with Intrauterine Growth Restriction and Preeclampsia

Valentina Canti, Stefania Del Rosso, Marta Tonello, Roberta Lucianò, Ariela Hoxha, Lavinia A. Coletto, Isadora Vaglio Tessitore, Susanna Rosa, Angelo A. Manfredi, Maria Teresa Castiglioni, Amelia Ruffatti, and Patrizia Rovere-Querini

Table 2. Outcomes of 47 pregnancies followed during this study. Values are mean ± SD or n (%) unless otherwise specified.

Outcomes	All aPL, n = 47	aPS/PT+, n = 33	aPS/PT−, n = 14	p*
wg	33.7 ± 4.9	33.1 ± 4.7	36.2 ± 3.4	**0.04**
Newborn weight, g	2227 ± 993	2058 ± 964	2784 ± 746	**0.04**
Placental weight, g	448 ± 197	420 ± 184	503 ± 223	NS
Pregnancy loss < 10 wg	1	0	1 (7)	NS
Pregnancy loss >10 wg	1	1 (3)	0	NS
IFD	4	2 (6)	2 (14)	NS
IUGR	13	12 (36)	1 (7)	**0.05**
Hypertension	3	2 (6)	1 (7)	NS
Preeclampsia and/or HELLP	12	12 (36)	0	**0.006**
Preterm delivery, without IUGR and/or preeclampsia	10	6 (18)	4 (28)	NS
Secondary APS	16	14 (42)	2 (14)	NS
SLE	9	8 (24)	1 (7)	NS
Other autoimmune diseases	7	6 (18)	1 (7)	NS
Treatment during pregnancy	47	33 (100)	14 (100)	NS
HCQ	6	5 (15)	1 (7)	NS
Corticosteroids	11	10 (30)	1 (7)	NS
LDA	39	27 (82)	12 (86)	NS
LMWH	47	33 (100)	14 (100)	NS
LDA + LMWH	39	27 (82)	12 (86)	NS
Azathioprine	4	3 (9)	1 (7)	NS
Plasmapheresis and/or IVIG	18	18 (100)	0	**0.002**

J Rheum 2018

Aim of the study

To explore the role of aPS/PT antibodies as a risk factor of thrombosis in antiphospholipid antibodies carrier

Patients

- Study population
  - 191 aPL carriers (between 2000-2018)
  - Inclusion criteria
    - At least two consecutive positive results for IgG/IgM anti-β2GPI and/or IgG/IgM aCL antibodies (both at medium or high titers) and/or LAC
    - Absence of APS clinical manifestations
  - Follow up 81.1 months±18.4 SD (range 12-216 months)

Methods

- Autoantibodies detection
  - IgG/IgM anti-cardiolipin and anti-β2glycoprotein I ELISA in house

    Tincani A et al, Thromb Res 2004
    Reber G et al, JTH 2004
  - Lupus anticoagulant

    Pengo V et al, JTH 2009
  - IgG/IgM aPS/PT ELISA commercial kit (INOVA diagnostics, USA)

Demographic and clinical charateristics of aPL carriers (total n=191)

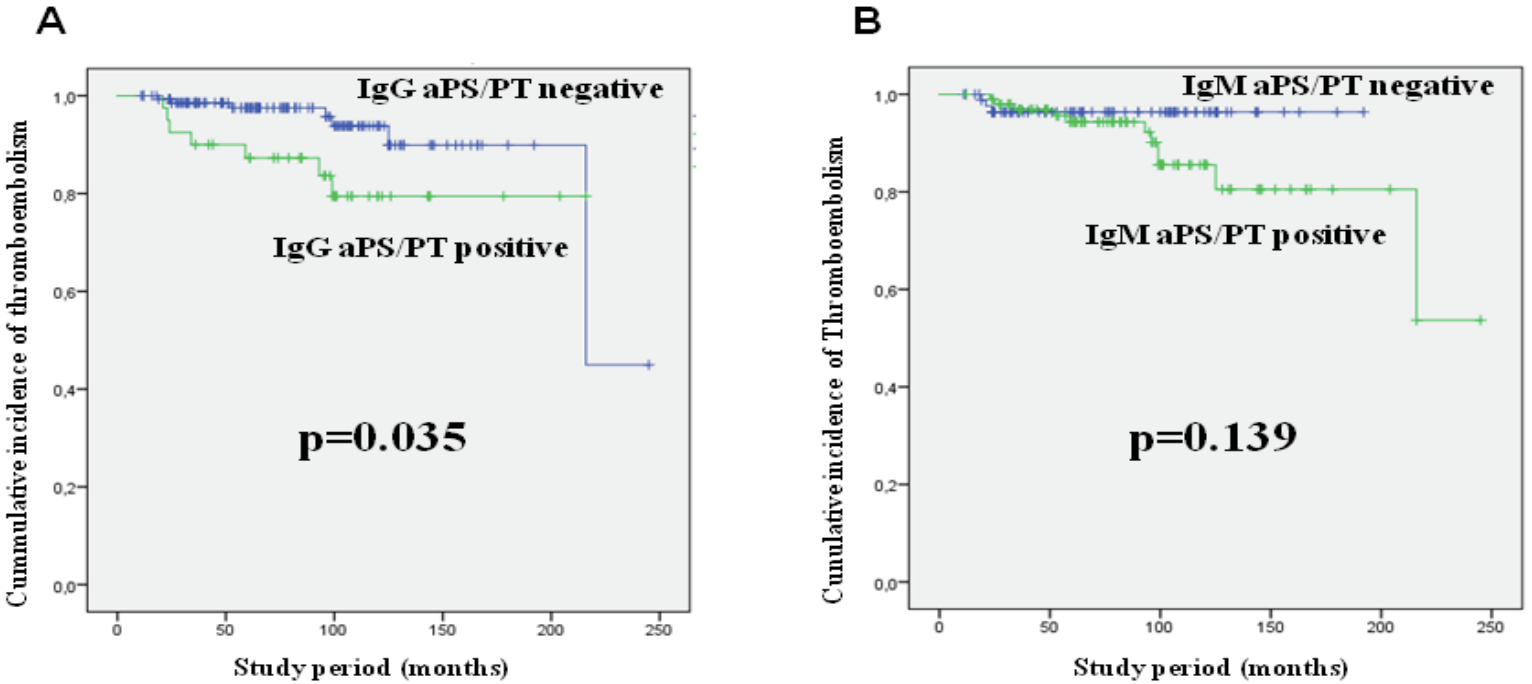
Mean age (years±SD)	38.4±11.3
Female n (%)	176 (92.1)
Reasons for initial testing n (%)	
Autoimmune disorders n (%)	115 (60.2)
Screening before pregnancy n (%)	26 (13.6)
Prolonged aPTT n(%)	40 (20.9)
Family history of aumtoimmunity n (%)	11 (5.8)
Risk factors for thromboembolic events	
Arterial thrombosis	35 (19.5)
Venous thrombosis	19 (10.6)

- IgG aPS/PT abs were positive in 40 aPL carriers (20.9%)
- IgM aPS/PT abs were positive in 102 aPL carriers (53.4%)

Antiphospholipid antibodies profiles in IgG/IgM aPS/PT carriers

	IgG aPS/PT+ve (40)	IgG aPS/PT-ve (151)	p-value
(IgG/IgM) aβ2GPI and aCL and LAC, n (%)	27 (67.7)	28 (18.5)	0.000
(IgG/IgM) aCL and LAC, n (%)	3 (7.5)	8 (5.3)	ns
(IgG/IgM) aβ2GPI and LAC, n (%)	2 (5.0)	0	ns
(IgG/IgM) aβ2GPI and aCL, n (%)	2 (5.0)	44 (29.1)	0.003
LAC, n (%)	1 (2.5)	13 (8.6)	ns
(IgG/IgM) aCL, n (%)	2 (5.0)	29 (19.2)	ns
(IgG/IgM) aβ2GPI, n (%)	3 (7.5)	29 (19.2)	ns
	IgM aPS/PT+ve (102)	IgM aPS/PT-ve (89)	p value
(IgG/IgM) aβ2GPI and aCL and LAC, n (%)	45 (44.1)	10 (1.1)	0.000
(IgG/IgM) aCL and LAC, n (%)	8 (7.8)	3 (3.4)	ns
(IgG/IgM) aβ2GPI and LAC, n (%)	2 (1.9)	0	ns
(IgG/IgM) aβ2GPI and aCL, n (%)	16 (15.7)	30 (33.7)	0.006
LAC, n (%)	13 (12.7)	1 (1.2	0.005
(IgG/IgM) aCL, n (%)	13 (12.7)	18 (20.2)	ns
(IgG/IgM) aβ2GPI, n (%)	5 (4.9)	27 (30.3)	0.000

- 14 (7.3%) of aPL carriers developed a thrombotic event
  - 8/14 (57.1%) venous thrombosis
  - 6/14 (42.9%) arterial thrombosis
- Incidence of thrombotic event
  - 1.4 % patient/year


A
IgG aPS/PT negative
IgG aPS/PT positive
p=0.035
Cummulative incidence of thromboembolism
Study period (months)
B
IgM aPS/PT negative
IgM aPS/PT positive
p=0.139
Cumulative incidence of Thromboembolism
Study period (months)

Risk factors for a first thrombotic event

	aPL carriers	carriers became APS	p value
IgG aPS/PT, n (%)	33 (18.6)	7 (50)	**0.015**
IgM aPS/PT, n(%)	91 (51.4)	11 (78.6)	0.092
(IgG/IgM) aβ2GPI and aCL and LAC, n (%)	45 (25.4)	10 (71.4)	**0.0008**
(IgG/IgM) aCL and LAC, n (%)	10 (5.6)	1 (7.1)	0.715
(IgG/IgM) aβ2GPI and LAC, n (%)	2 (1.1)	0 (0)	0.335
(IgG/IgM) aβ2GPI and aCL, n (%)	44 (24.9)	2 (14.2)	0.571
LAC, n (%)	13 (7.3)	1 (7.1)	0.613
(IgG/IgM) aCL, n (%)	31 (17.5)	0 (0)	0.182
(IgG/IgM) aβ2GPI, n (%)	32 18.1)	0 (0)	0.170
Thromboembolic risk factor	40 (22.6)	11 (78.6)	**0.0000**
Autoimmune disordes	102 (57.6)	13 (92.9)	**0.021**

Indipendent risk factors for a first thrombotic event

- Triple aPL positivity
  - (OR 4.725, 95% CI: 1.135-19.674, p=0.033)
- Thromboembolic risk factor
  - (OR 12.451, 95% CI: 2.519-61.537, p=0.002)
- IgG aPS/PT
  - (3.962, 95% CI: 1.174-13.37)

Conclusion (I)

- IgG aPS/PT abs are independent risk factor for thrombosis in aPL carriers
- Triple aPL positivity and the presence of risk factors for thrombosis are confirmed as independently risk factors for the development of thrombotic events

Conclusion (II)

- The addition of IgG aPS/PT abs detection to the conventional aPL algorithm of testing could be a useful tool for a better risk assessment in aPL carriers and could thus justify the cost of their detection.
- The association of IgM aPS/PT abs to isolated LAC along with the lack of their significant prevalence in aPL carriers developing thrombosis suggest that these abs may be useful to identified aPL carriers at low risk for thrombosis

Thank you for your attention…