

Follow-up of LA positive patients

ECAT Symposium 2022

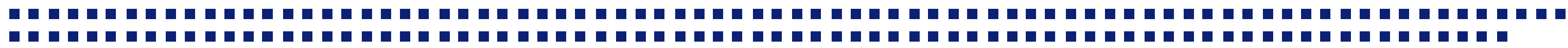
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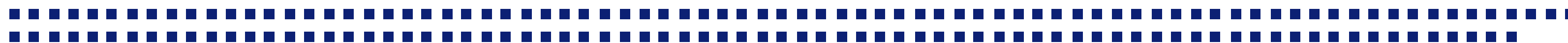
Disclosures AJG Jansen

(potential) disclosures	
<ul style="list-style-type: none">• Speaker's fee and travel costs• Advisory board• Research funding	<ul style="list-style-type: none">• 3SBIO, Novartis, Celgene, Technoclone, Amgen• Novartis• CSL Behring, Principa Biopharma Inc, Argenx



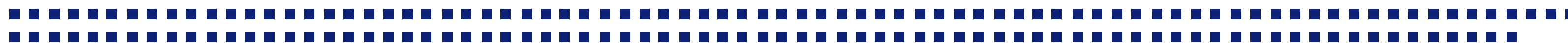
Overview

- Introduction
- aPL at Erasmus MC
- Clinical practice / case report



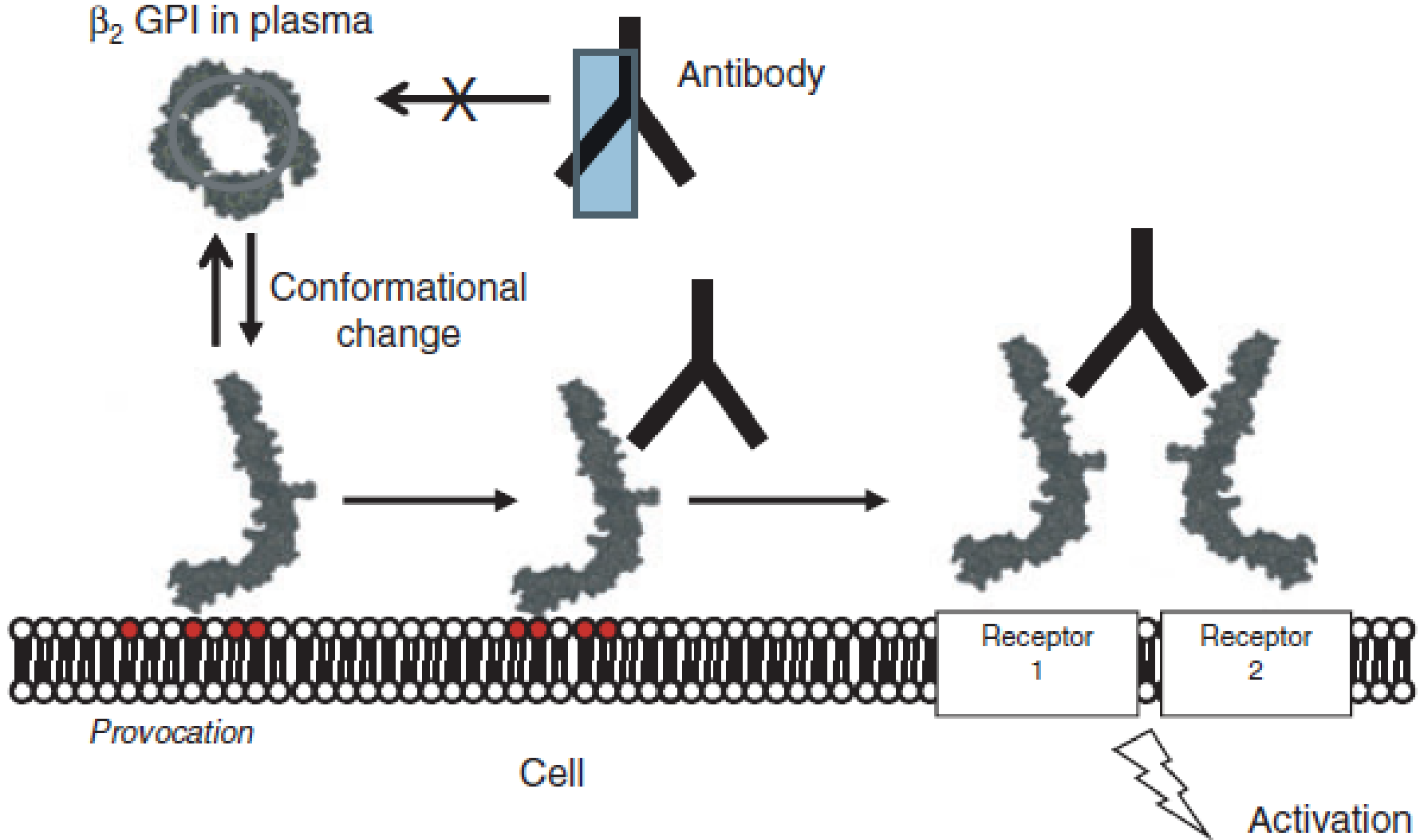
Introduction

- Lupus anticoagulants and other aPLs
- Autoantibodies interacting with phospholipids, antiphospholipid binding proteins or both



Introduction

Lupus anticoagulans *in vivo*



Introduction

10% healthy blood donors positive for ACL antibodies, and 1% positive for LAC. After 1 year, <1% still positive for these tests¹

20% - 30% of patients with SLE have aPL profiles associated with increased risk of clinical symptoms²

Presence of aPL associated with increased risk of thrombosis and/or obstetric complications

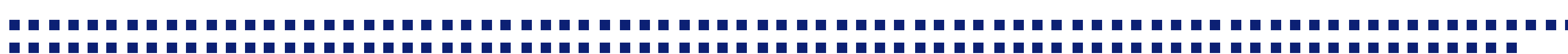
¹Thromb Haemost 1994

²Eur J Rheumatol 2016

Introduction

aPLs are routinely measured:

- assess underlying risk factors for obstetric and/or thrombotic complications
- diagnostic workup suspected autoimmune diseases



aPL at Erasmus MC



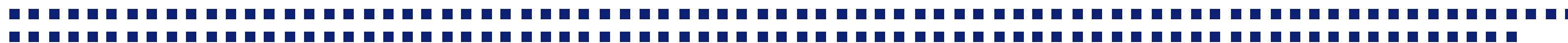
aPL at Erasmus MC

Erasmus MC:

± 1000 aPL tests/year

± 770 patients per year

± 240 tests are positive



aPL at Erasmus MC

Total amount of positive aPL in the period June 2015- April 2018

	aCL IgM	aCL IgG	aCL total	a β 2GPI IgM	a β 2GPI IgG	a β 2GPI total	dRVVT-ratio	APTT-L- ratio	Total
2015	31	38	69	16	20	36	14	11	130
2016	46	63	109	21	34	55	40	31	235
2017	27	81	108	12	37	49	45	37	239
2018	15	51	66	5	14	19	24	19	128
Total	119	233	352 (48.1%)	54	105	159 (21.7%)	123 (16.8%)	98 (13.4%)	732

¹ Rheumatol Adv Pract 2021

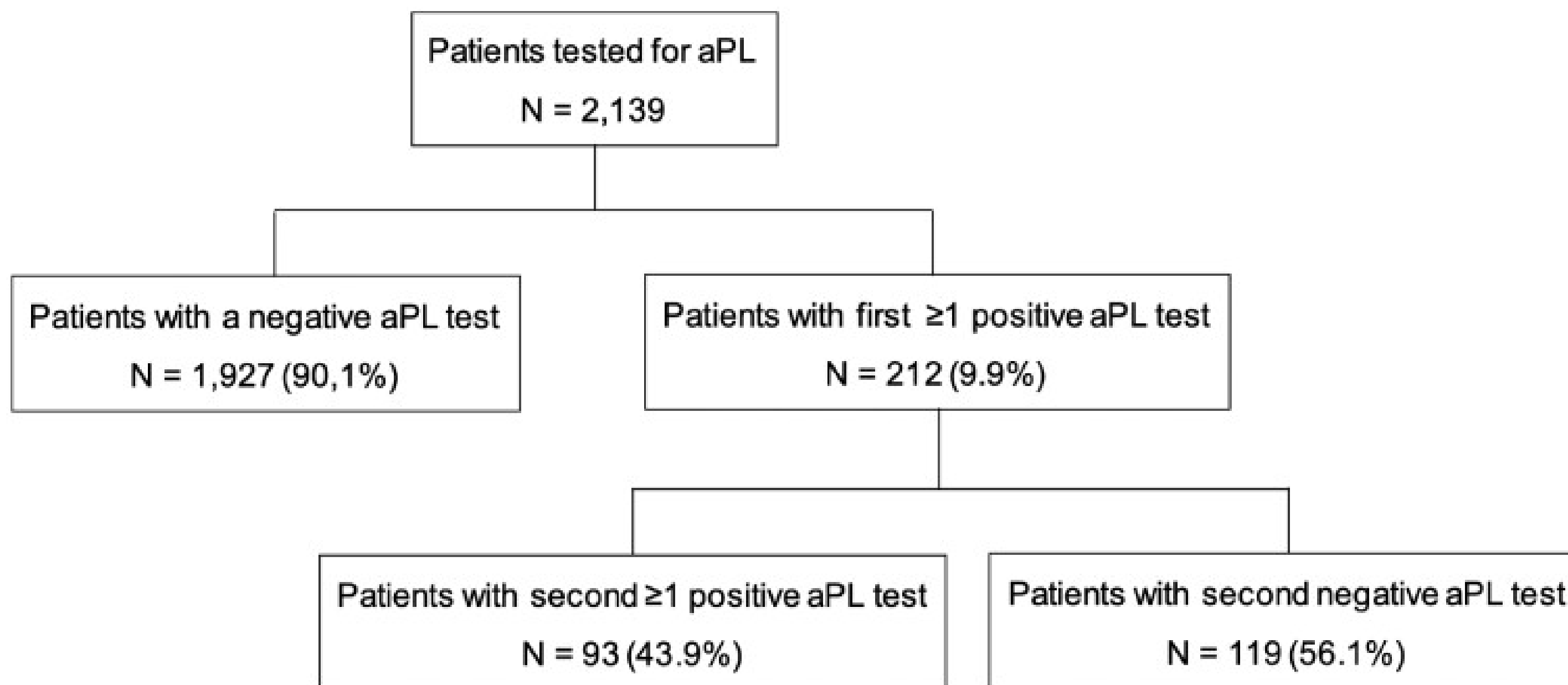
aPL at Erasmus MC

Retrospective study

June 2015 - April 2018

16.847 aPL tests in 2.139 patients

Flowchart



Patient characteristics

	First positive aPL (N=212)	Second positive aPL (N=93)	APS patients (N=74)
Age (yrs)	39.6 ± 18.1	41.3 ± 15.6	40.0 ± 13.4
Sex			
Male (%)	53 (25.0)	18 (19.4)	14 (18.9)
Female (%)	159 (75.0)	75 (80.6)	60 (81.1)
Specialism			
Obstetrics (%)	37 (17.5)	19 (20.4)	19 (25.7)
Internal Medicine (%)	145 (68.4)	61 (65.6)	45 (60.8)
Neurology (%)	26 (12.3)	12 (12.9)	10 (13.5)
Other (%)	3 (1.4)	0 (0.0)	0 (0.0)
Unknown (%)	1 (0.5)	1 (1.1)	0 (0.0)

Patient characteristics

	First positive aPL (N=212)	Second positive aPL (N=93)	APS patients (N=74)
Antibody			
No antibody known (%)	172 (81.1)	61 (65.6)	38 (51.4)
Antibodies known (%)	39 (18.4)	31 (33.3)	36 (48.6)
Unknown (%)	1 (0.5)	1 (1.1)	0 (0.0)
aPL			
Single (%)	55 (25.9)	24 (25.8)	19 (25.7)
Double (%)	21 (9.9)	15 (16.1)	12 (16.2)
Triple (%)	19 (9.0)	11 (11.8)	16 (21.6)
Incomplete (%)	117 (55.2)	43 (46.2)	27 (36.5)

¹ Rheumatol Adv Pract 2021

Indication for testing

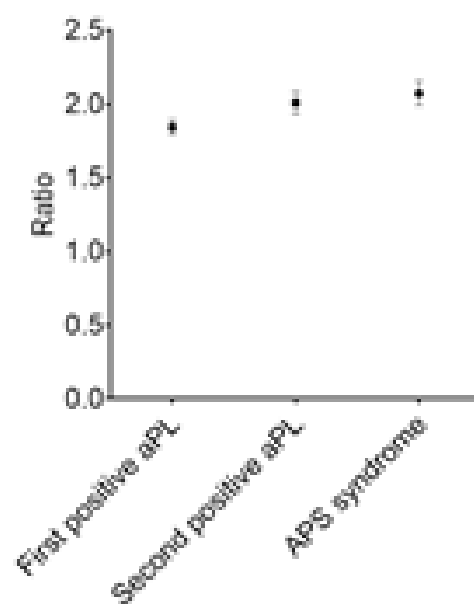
1. Diagnostic/FU autoimmune diseases (including APS) (33.6%)
2. Thrombosis (21.4%)
 - 9.4% arterial thrombosis
 - 12.0% venous thrombosis
3. Obstetric complications (28.0%)
 - 10.6% recurrent pregnancy loss
 - 17.4% screening/follow-up PE or HELLP syndrome

Indication and aPL positivity

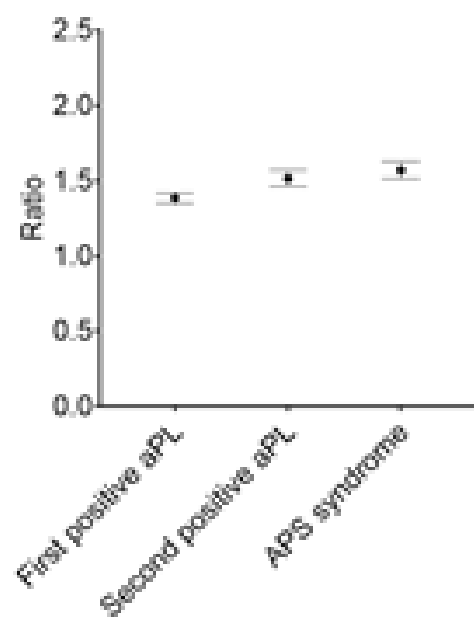
- Diagnostic/FU autoimmune diseases
first positive aPL test 12.5%
sec positive aPL test 5.4%
- Venous and arterial thrombosis
first positive aPL test 14.5% and 9.0%
second positive aPL test 6.3% and 4.5%
- Obstetrical indication
first positive aPL test 5.9%
sec positive aPL test 2.7%

aPL titers

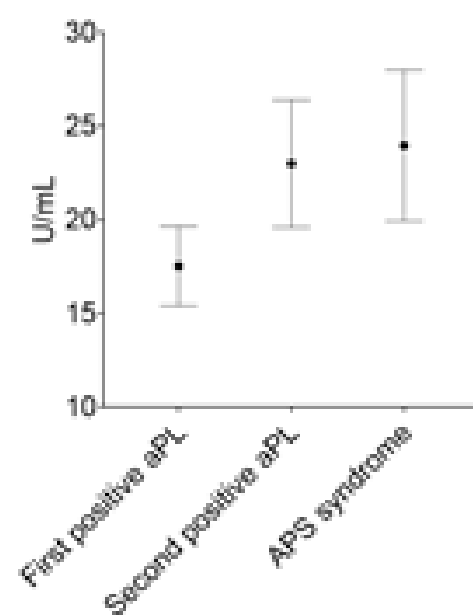
A) APTT ratio



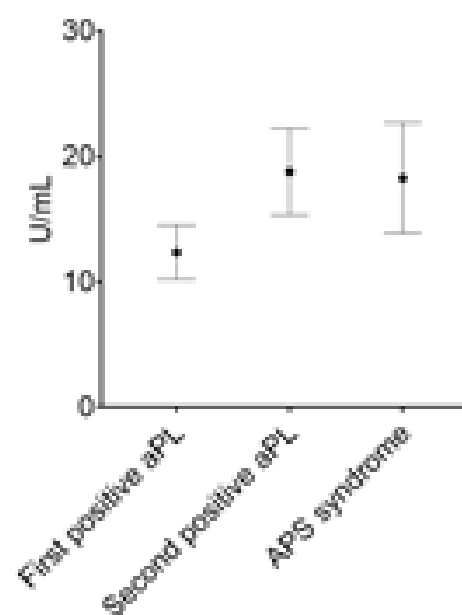
B) DRVVT ratio



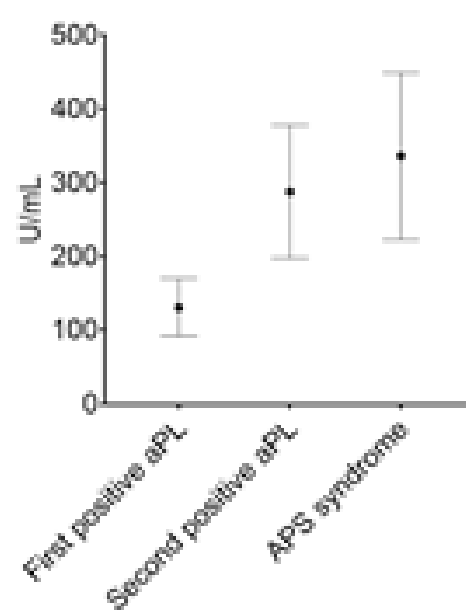
C) Anticardiolipine IgM



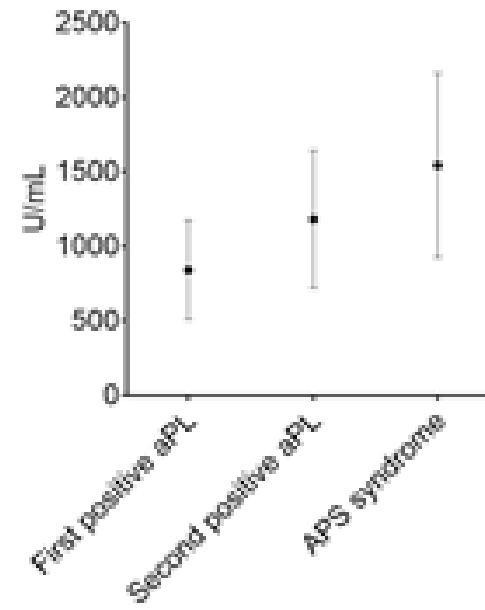
E) Anti-β2 GP IgM



D) Anticardiolipin IgG

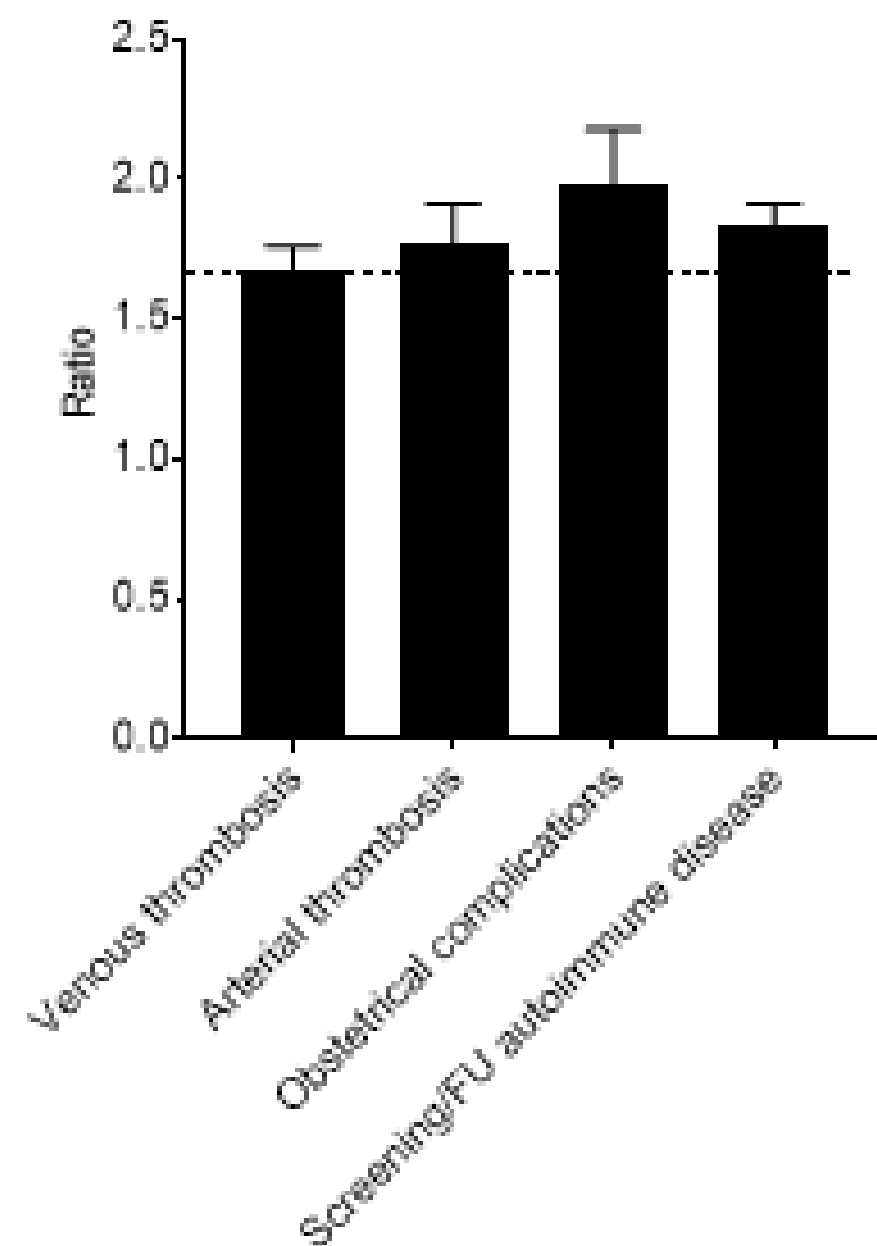


F) Anti-β2 GP IgG

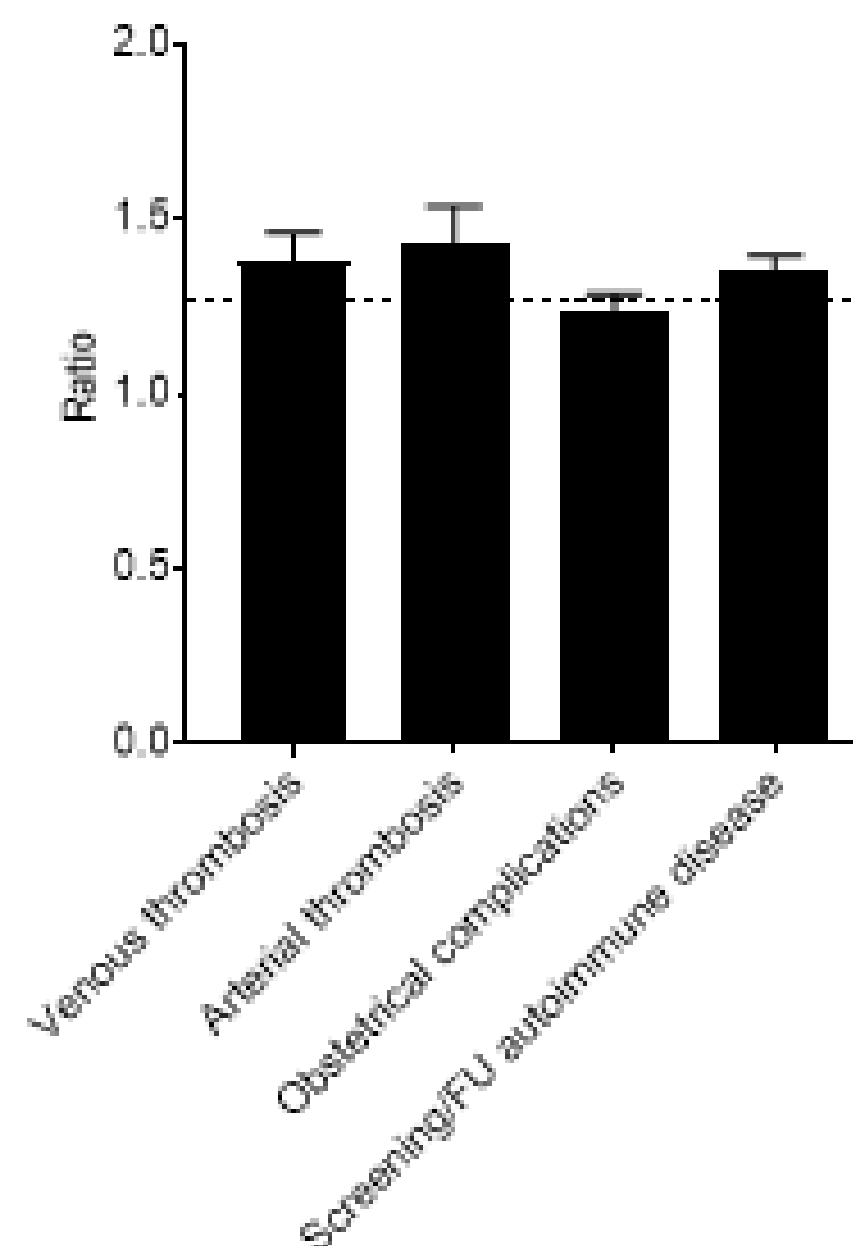


aPL titers and indication

A) DRVVTratio

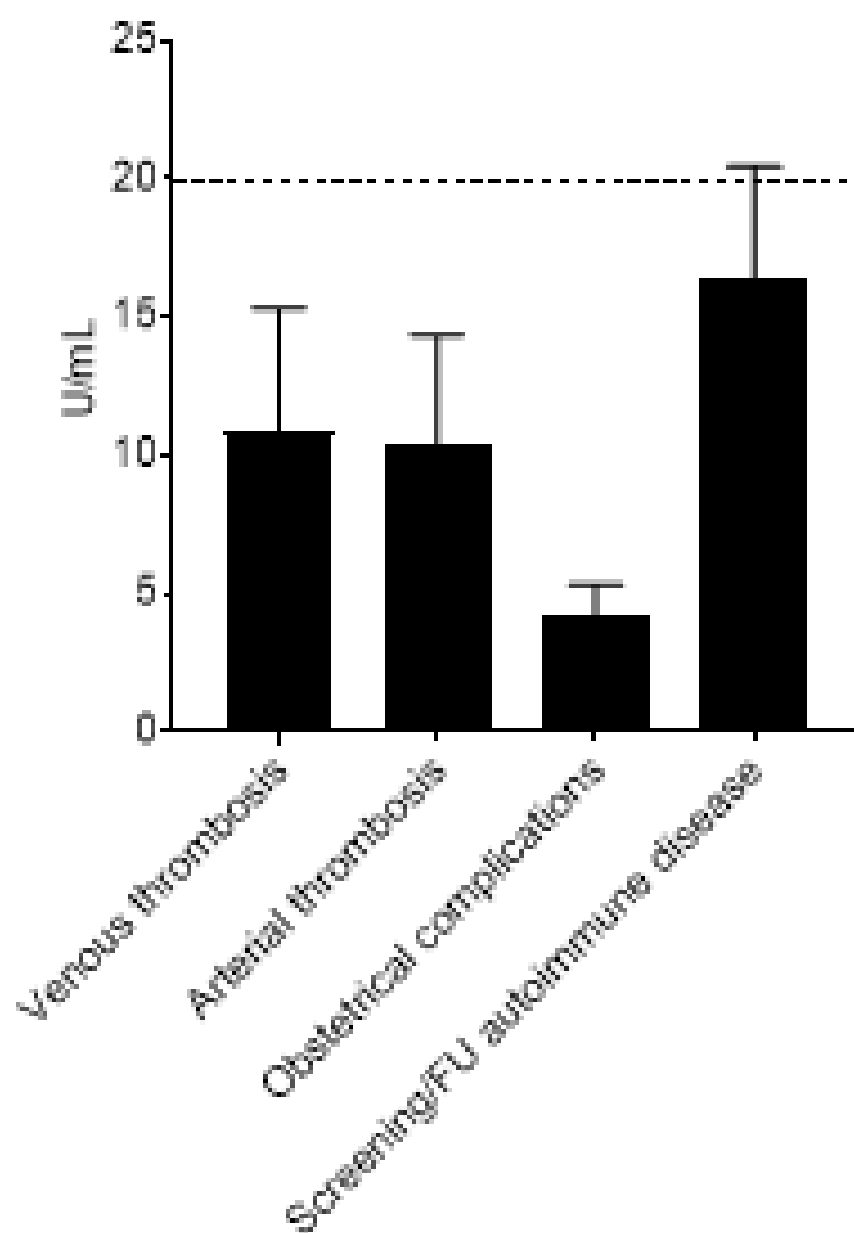


B) APTTratio

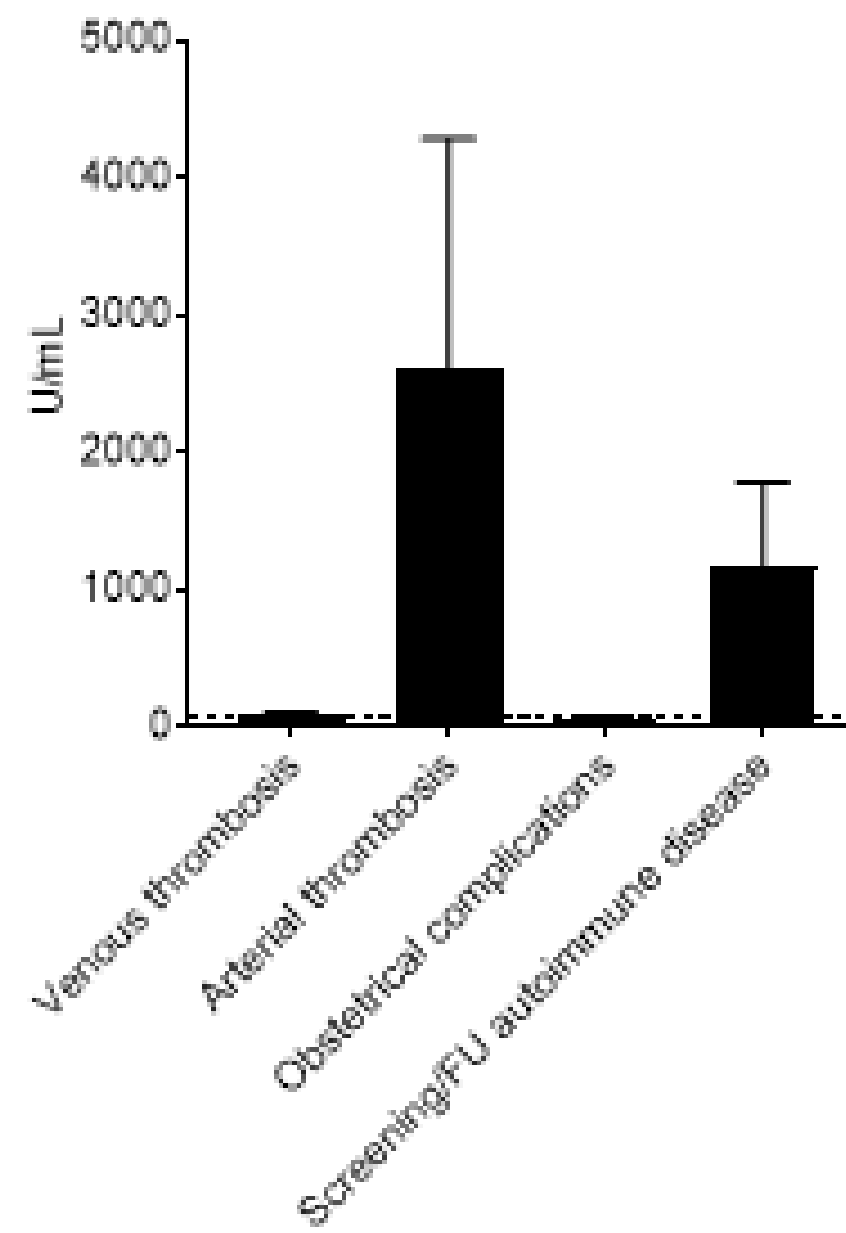


aPL titers and indication

C) Anti-β2 GP IgM

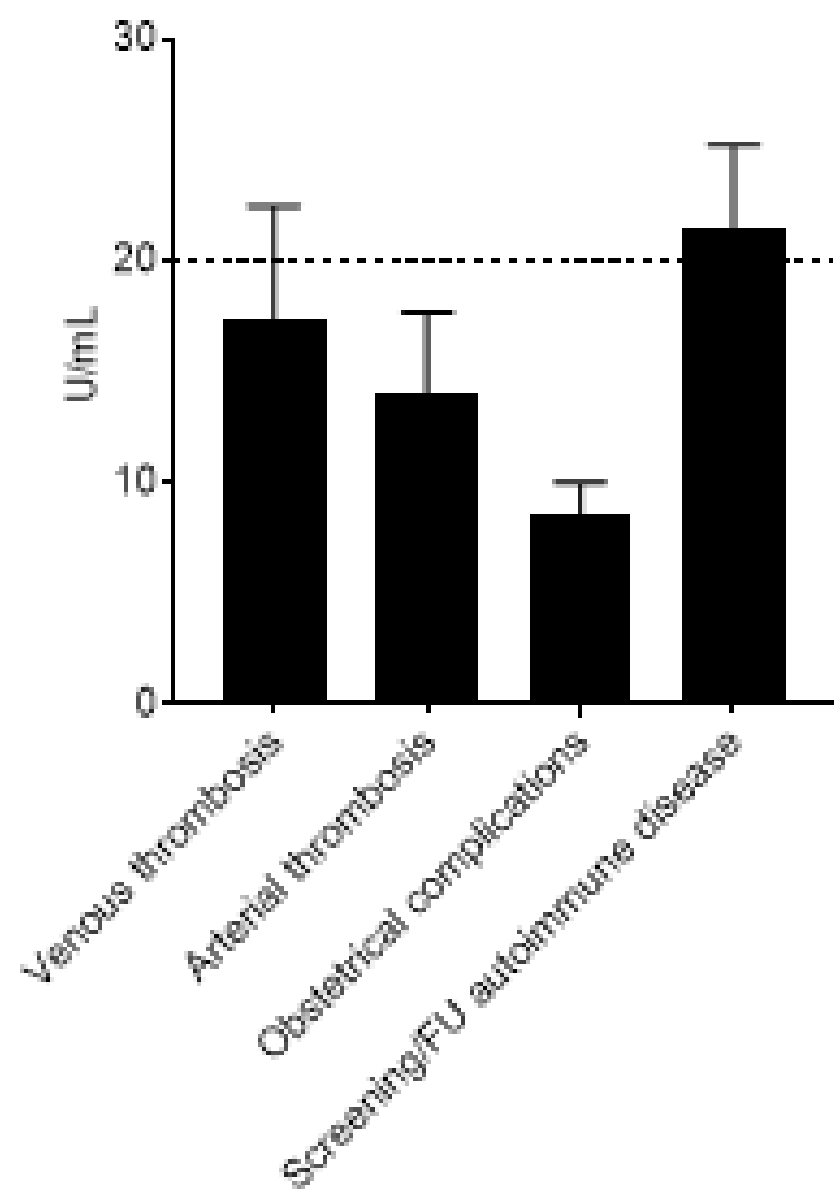


D) Anti-β2 GP IgG

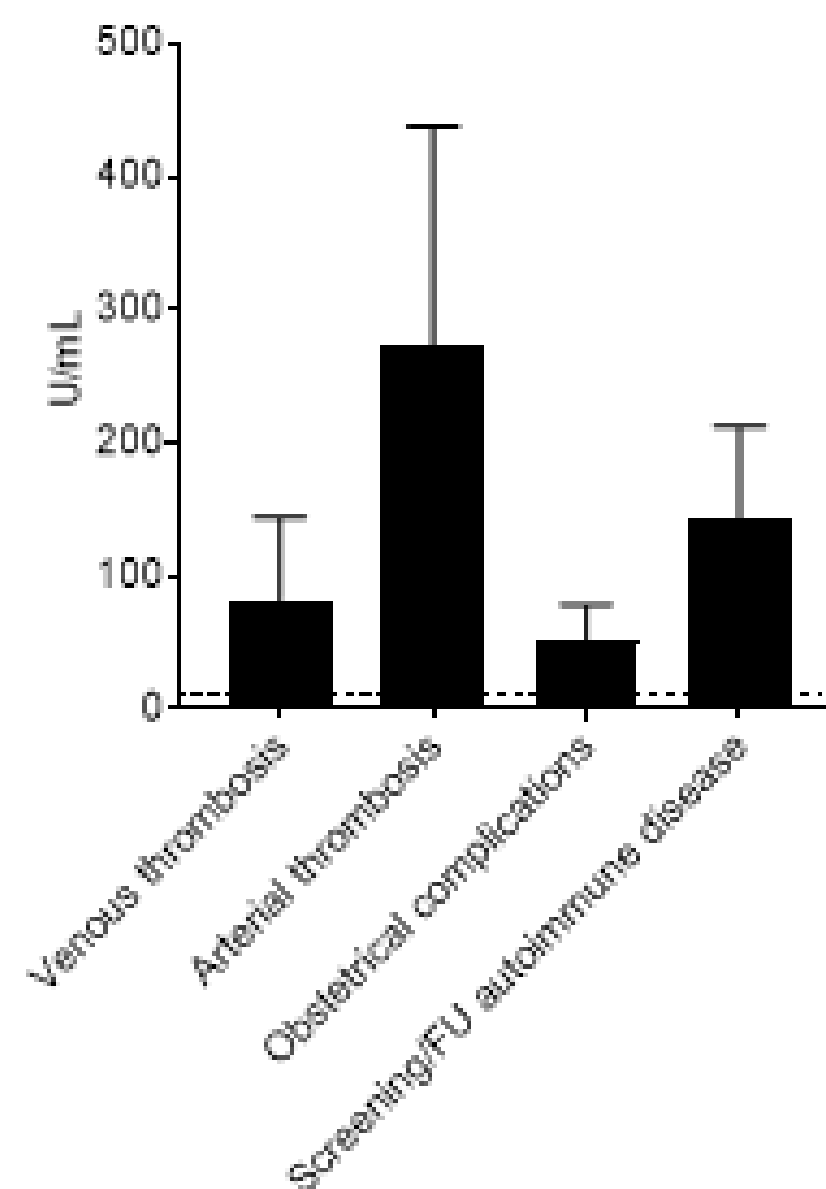


aPL titers and indication

E) Anticardiolipin IgM



F) Anticardiolipin IgG



aPL and indication

Indication, <i>n</i> (%)	Single aPL (<i>n</i> = 55)	Double aPL (<i>n</i> = 21)	Triple aPL (<i>n</i> = 19)
Venous thrombosis	9 (16.4)	3 (14.3)	2 (10.5)
Arterial thrombosis	4(7.3)	3 (14.3)	3 (15.8)
PE/HELLP	11 (20.0)	3 (14.3)	0 (0)
Recurrent pregnancy loss	8 (14.5)	0 (0)	1 (5.3)
Diagnostic workup/follow-up of autoimmune disease	12 (21.8)	12 (57.1)	9 (47.4)
Other	8 (14.5)	0 (0)	3 (15.8)
Combination	1 (1.8)	0 (0)	0 (0)
Unknown	2 (3.6)	0 (0)	1 (5.3)

aPL at Erasmus MC

- Indications for aPL testing were diagnostic workup/follow-up of autoimmune diseases, thrombosis and obstetric complications.
- The prevalence of a first positive aPL was 9.9%, confirmed in 43%; APS was diagnosed in 3.5% (of which 51% new).
- Arterial thrombosis was associated with significantly high anti- β 2GPI IgG and aCL IgG titres.

¹ Rheumatol Adv Pract 2021

aPL at Erasmus MC

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Original article

Indication and outcome of lupus anticoagulant and antiphospholipid antibodies testing in routine clinical practice

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and A.J. Gerard Jansen ¹

Erasmus MC

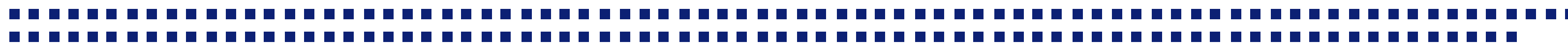


Clinical practice



Case report – March 2018

APTT ratio	1.20
DRVVT ratio (< 1.66)	2.07
ACL IgG (< 20 U/mL)	1098
ACL IgM (< 20 U/mL)	22
Beta2GPI IgG (< 60 U/mL)	6319
Beta2GPI IgM (< 20 U/mL)	13



Case report

Female, 50 years old

Medical history:

Chronic venous insufficiency, hypercholesterolemia, hypertension

2001 Miscarriage (21 weeks)

2 children (16 and 20 year), both premature (cesarean section)

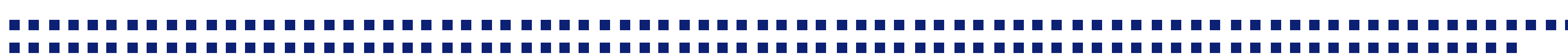
2001 Antiphospholipid syndrome

2005 Ischemic CVA (occipital infarction). Start treatment VKA

2015 Skin lesions (APS PA confirmation)

2016 Subdural hematoma (INR 3.7) neurosurgery

2018 Immunologist: ANA and anti-dsDNA positive, no clinical signs of SLE. No indication immune suppressive therapy



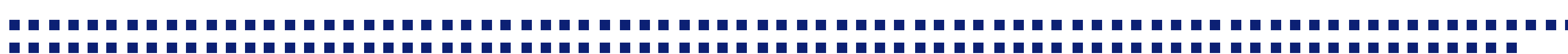
Case report

Sept 2017:

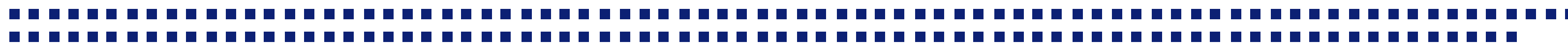
- Spontaneous ulcers upper leg
- Blue coloring foot, arterial occlusion?

Monthly seen by dermatologist and vascular surgeon -> debridement

March 2018 home care nurse worries -> admission internal medicine department



Case report



Catastrophic APS

- 1) Evidence of involvement of three or more organs, systems and/or tissues
- 2) Development of manifestations simultaneously or in less than a week
- 3) Confirmation by histopathology of small vessel occlusion in at least one organ or tissue
- 4) Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant and/or anticardiolipin antibodies)

Definite catastrophic APS

- All four criteria

Catastrophic APS

- 1) Evidence of involvement of three or more organs, systems and/or tissues
- 2) Development of manifestations simultaneously or in less than a week
- 3) Confirmation by histopathology of small vessel occlusion in at least one organ or tissue
- 4) Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant and/or anticardiolipin antibodies)

Probable catastrophic APS

- All four criteria, except for only two organs, systems and/or tissues involvement
- All four criteria, except for the absence of laboratory confirmation at least six weeks apart due to the early death of a patient never tested for aPL before the catastrophic APS
- 1, 2 and 4
- 1, 3 and 4 and the development of a third event in more than a week but less than a month, despite anticoagulation

Asherson, et al. Lupus 2003;12:530-4

Case report

Treated as probable cAPS

Solumedrol 1 gram i.v. for 3 days

Plasmapheresis 7 days

Therapeutic LMWH

Pain medication

Case report



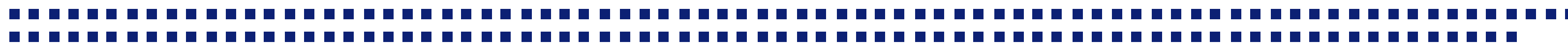
20-03-2018



26-04-2018



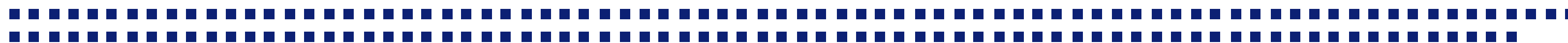
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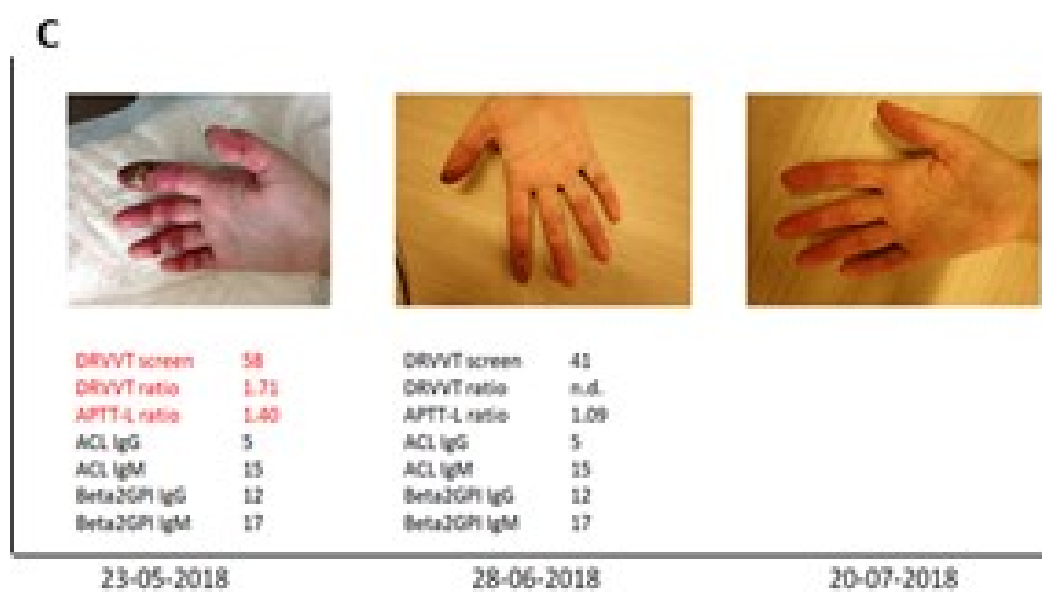
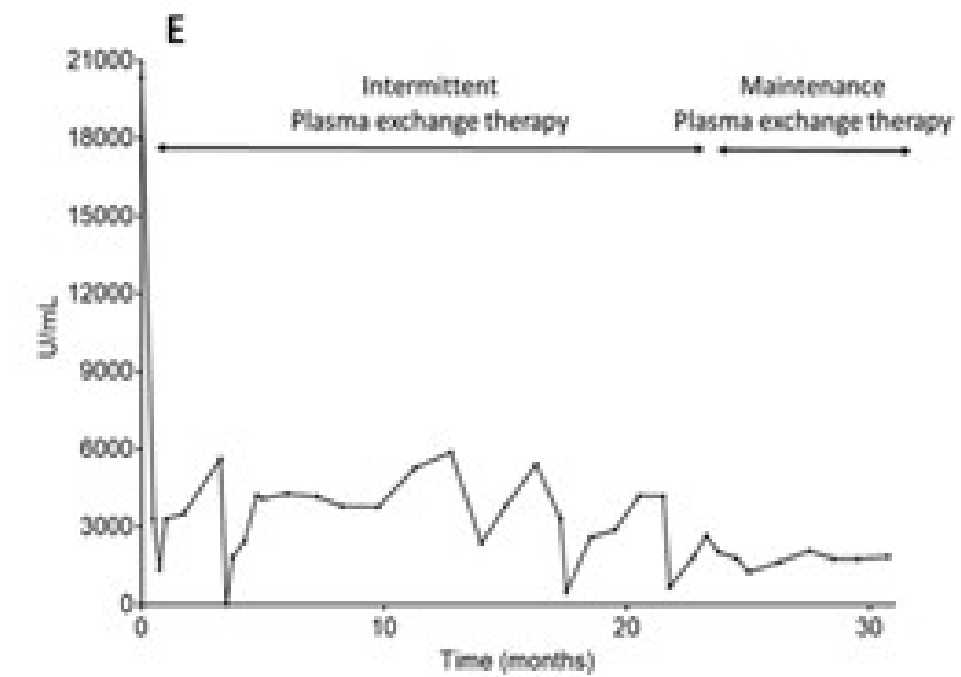
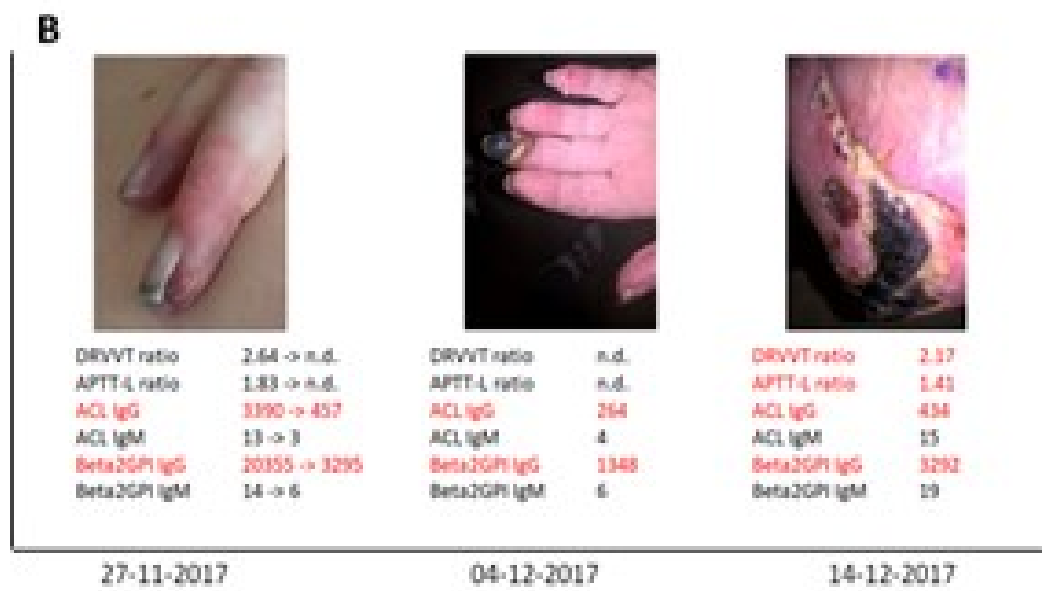
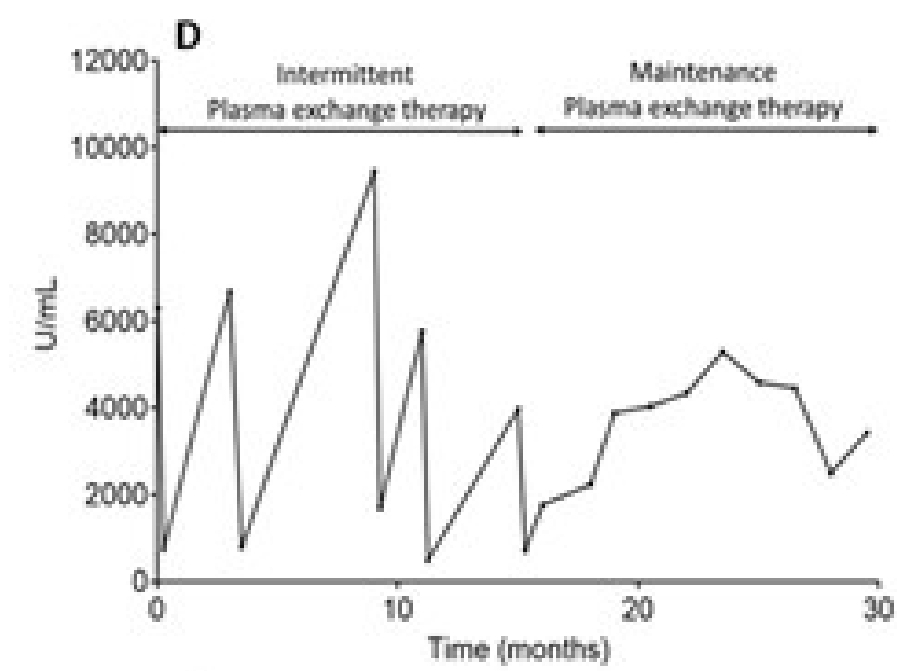


Case report

Lab:

- APTT 31, INR 1.1
- DRVVT screen 81 sec -> 52
- DRVVT ratio 1.99 -> 1.37
- ACL IgG 1098 U/mL -> 127 U/mL
- Beta2GPI IgG 6319 U/mL -> 765 U/mL







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Therapeutic plasma exchange for anticoagulant-refractory antiphospholipid syndrome with severe ischemic and necrotic skin lesions: A case series

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Case report

Vascular necrosis: think about APS

Consider plasma exchange as therapy



Conclusion

Follow-up of LA positive patients

- Indications and results of aPL testing at the Erasmus MC
- APS with vascular necrotic lesions and plasmapheresis

