Sesión bibliográfica
20 sept 2024

Daniel Martín Iglesias

Servicio MI

Hospital de León

MEDICINA CLINICA

Incluida en: Science Direct • Journal Citation Reports • Index Medicus/MEDLINE • Current Contents/Clinical Medicine • Índice Médico Español • Excerpta Medica/EMBASE • Pascal • Scopus • MEDES

Agosto de 2024. Volumen 163 - Suplemento 1

Antiphospholipid Syndrome

Guest Editor: Munther Khamashta

Revisiones

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Review

Hughes syndrome: The discovery of the antiphospholipid syndrome

Munther Khamashta[a,*], Graham R.V. Hughes[b]

[a] Emeritus Professor of Medicine, King's College London, GSK Global Medical Expert-Lupus, Dubai, United Arab Emirates
[b] Emeritus Professor of Rheumatology, King's College London, The London Lupus & Rheumatology Centre, London, United Kingdom

Reseña histórica

- Pacientes "Hughes": lupus raras con trombosis, migraña, abortos, sin apenas casos de nefritis y frecuentemente ANA negativo
- Se identifica en su serología los anticuerpos anticardiolipina
- Presentación y primera descripción en 1983

Table 1
Features in a lupus patient suggesting associated Hughes syndrome.

1. Recurrent pregnancy loss
2. Severe migraine headaches
3. Severe memory loss
4. Stroke and TIA
5. Angina (especially in women under 45)
6. Myelopathy (Spinal thrombosis)
7. Seizures
8. Deep venous thrombosis
9. Marked livedo reticularis
10. Marked visual symptoms
11. Low platelet counts
12. Avascular necrosis of bones

Khamashta M, Hughes GRV. Hughes syndrome: The discovery of the antiphospholipid syndrome. Med Clin (Barc). 2024 Aug;163 Suppl 1:S1-S3

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Special article

Antiphospholipid syndrome: Classification versus diagnosis

Síndrome antifosfolípido: Clasificación versus diagnóstico

Doruk Erkan

Barbara Volcker Center for Women and Rheumatic Diseases, Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, USA

Criterios clasificación:
"crear cohortes homogéneas de pacientes para futura comparación de ensayos clínicos y otros estudios"→ Alta Especificidad

Diagnóstico clínico:
fenotipo clínico + perfil AAF + contexto y comorbilidades

Erkan D. Antiphospholipid syndrome: Classification versus diagnosis. Med Clin (Barc). 2024 Aug;163 Suppl 1:S10-S13.

Table 1
Summary of 2023 ACR/EULAR Antiphospholipid Syndrome (APS) Classification Criteria (please refer to the original publication[2] for details and definitions).

Entry criteria At least one clinical criterion listed below (domains 1–6) *plus* positive antiphospholipid antibody (aPL) test (lupus anticoagulant test, or moderate-to-high titers of anticardiolipin or anti-β_2-glycoprotein-I antibodies [IgG or IgM]) within three years of the clinical criterion	
Clinical domains and criteria:	Weight
Domain 1. Macrovascular (venous thromboembolism [VTE])	
• VTE with a high VTE risk profile	1
• VTE without a high VTE risk profile	3
Domain 2. Macrovascular (arterial thrombosis [AT])	
• AT with a high CVD risk profile	2
• AT without a high CVD risk profile	4
Domain 3. Microvascular[a]	
• Suspected	2
• Established	5
Domain 4. Obstetric	
• Three or more consecutive pre-fetal (<10w) and/or early fetal (10w 0d–15w 6d) deaths	1
• Fetal death (16w 0d–33w 6d) in the absence of pre-eclampsia (PEC) with severe features or placental insufficiency (PI) with severe features	1
• PEC with severe features (<34w 0d) or PI with severe features (<34w 0d) with/without fetal death	3
• PEC with severe features (<34w 0d) and PI with severe features (<34w 0d) with/without fetal death	4
Domain 5. Cardiac valve	
• Thickening	2
• Vegetation	4
Domain 6. Hematology	
• Thrombocytopenia (lowest 20–130 $\times$ 10^9/L)	2
Laboratory (aPL) domains and criteria	Weight
Domain 7. aPL test by coagulation-based functional assay (lupus anticoagulant test [LA])	
• Positive LA (single – one time)	1
• Positive LA (persistent)	5
Domain 8. aPL test by solid phase assay (anti-cardiolipin antibody [aCL] ELISA and/or anti-β_2-glycoprotein-I antibody [aβ_2GPI] ELISA [persistent])[b]	
• Moderate-high positive (IgM) (aCL and/or aβ_2GPI)	1
• Moderate positive (IgG) (aCL and/or aβ_2GPI)	4
• High positive (IgG) (aCL or aβ_2GPI)	5
• High positive (IgG) (aCL and aβ_2GPI)	7
Final assessment *Patients accumulating at least three points each from clinical and laboratory domains are classified as having APS*	

Novedades:

1. Estratificación riesgo en eventos trombóticos
2. Estratificación riesgo anticuerpos
3. Dominios:

- Microvascular
- Valvular
- Trombopenia
- Obstétrico (se amplía)

Erkan D. Antiphospholipid syndrome: Classification versus diagnosis. Med Clin (Barc). 2024 Aug;163 Suppl 1:S10-S13.

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Review

Antiphospholipid antibody testing

Savino Sciascia[a,*], Barbara Montaruli[b], Maria Infantino[c]

[a] University Center of Excellence on Nephrologic, Rheumatologic and Rare Diseases (ERK-Net, ERN-Reconnect and RITA-ERN Member) with Nephrology and Dialysis Unit and Center of Immuno-Rheumatology and Rare Diseases (CMID), Coordinating Center of the Interregional Network for Rare Diseases of Piedmont and Aosta Valley, San Giovanni Bosco Hub Hospital, Department of Clinical and Biological Sciences, University of Turin, Turin, Italy
[b] S.C. Laboratory Analysis, AO Ordine Mauriziano, Turin, Italy
[c] Laboratory of Immunology and Allergy, San Giovanni di Dio Hospital, Florence, Italy

Pedirlos en contexto clínico adecuado

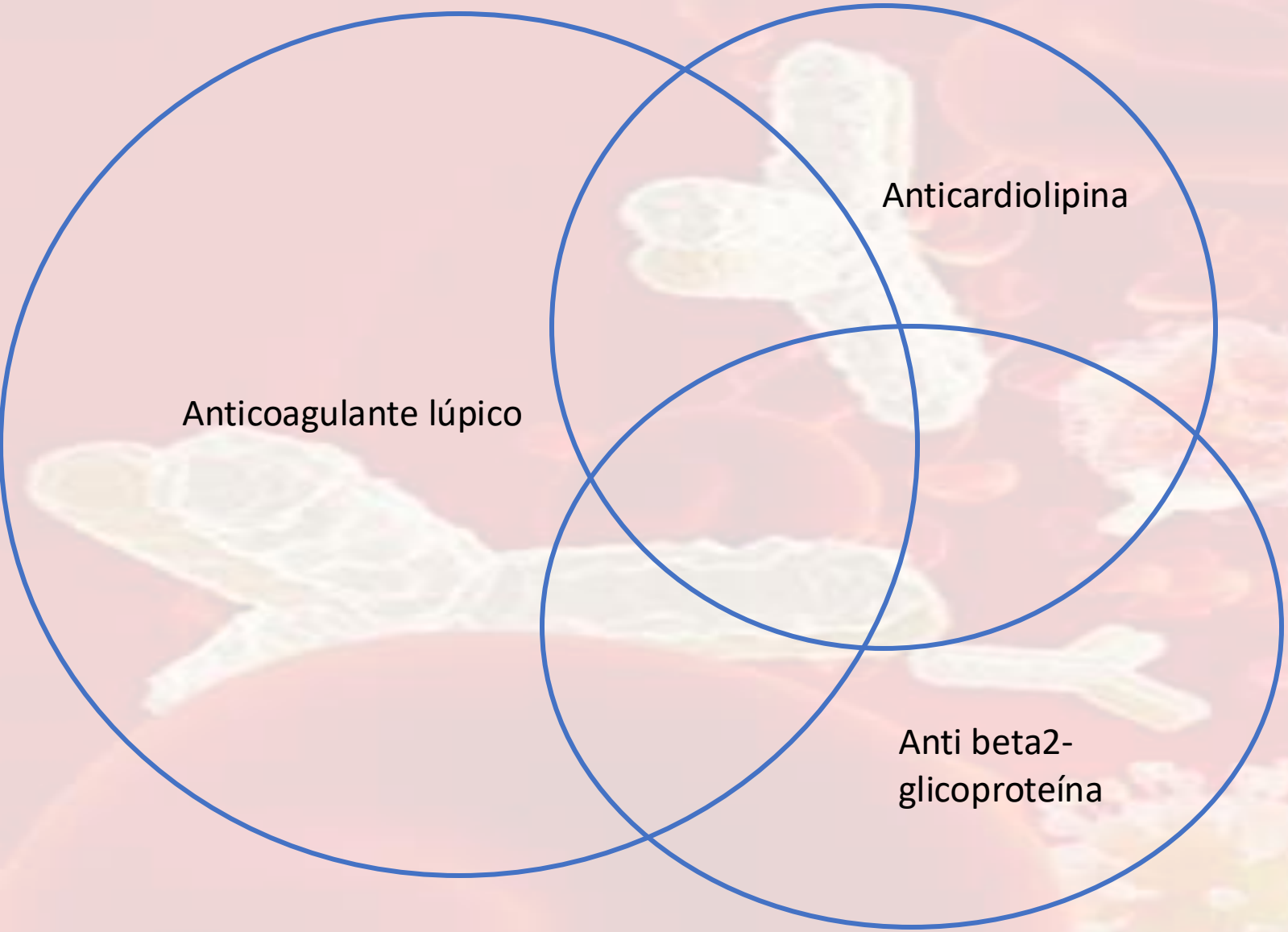
Anticoagulante lúpico

- Test de coagulación
- Varias técnicas (Russel, SCT, TSVT)
- Falsos positivos y negativos (anticoagulantes, PCR elevada, FVIII…)

Anticardiolipina y antibeta2-glicoproteínas

- Inmunoensayo (ELISA)
- IgG más validez que IgM
- IgA si alta sospecha pero resultados negativos
- Títulos > 40 y persistencia en el tiempo

Sciascia S, Montaruli B, Infantino M. Antiphospholipid antibody testing. Med Clin (Barc). 2024 Aug;163 Suppl 1:S4-S9.



Otros:

- Anexina
- Anti D1
- **Anti PT/PS**

Sciascia S, Montaruli B, Infantino M. Antiphospholipid antibody testing. Med Clin (Barc). 2024 Aug;163 Suppl 1:S4-S9.

Perfil de anticuerpos

Perfil de riesgo trombótico

Triple positivo

Más alto riesgo

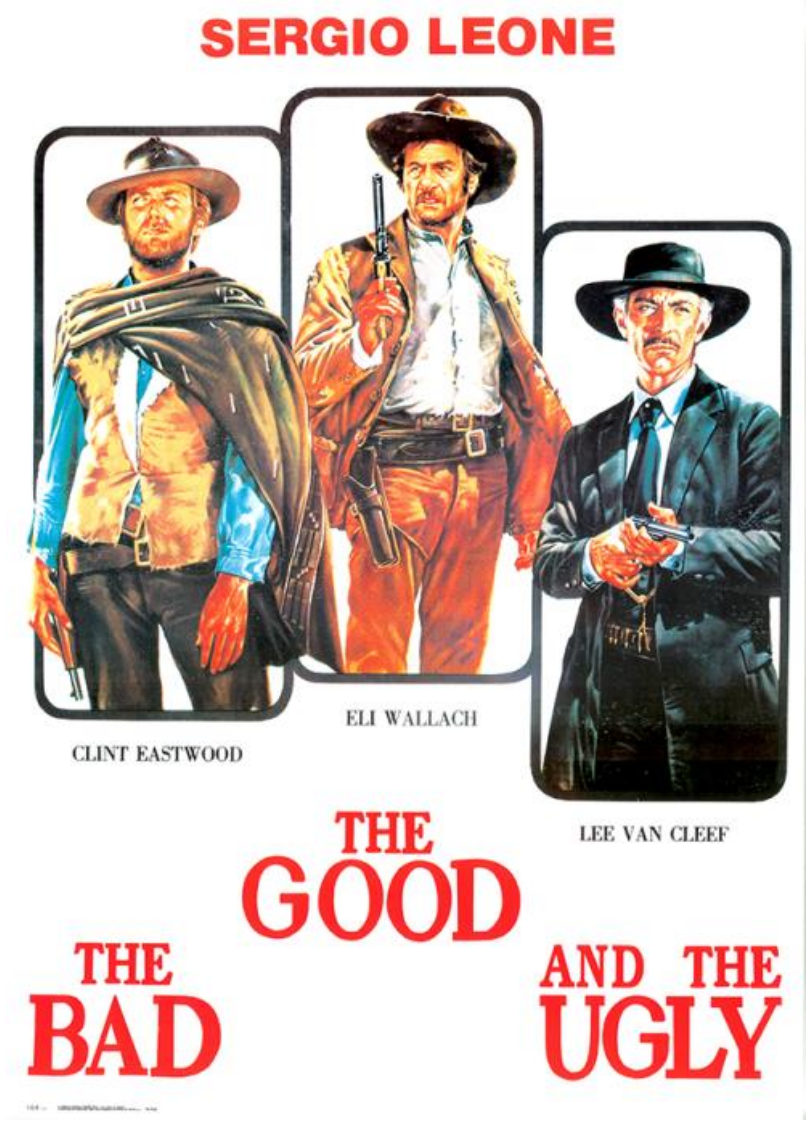


Table 1
The Global AntiPhospholipid Syndrome Score (GAPSS) is a risk assessment tool designed to evaluate the risk of thrombotic/obstetric events in patients with antiphospholipid syndrome (APS).

Risk factor	Points
Anticardiolipin antibodies (IgG/IgM)	5
Lupus anticoagulant	4
Anti-β2 glycoprotein I (IgG/IgM)	4
Anti-phosphatidylserine/prothrombin (IgG/IgM)	3
Hyperlipidemia	3
Arterial hypertension	1

Sciascia S, Montaruli B, Infantino M. Antiphospholipid antibody testing. Med Clin (Barc). 2024 Aug;163 Suppl 1:S4-S9.

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Review

Obstetric antiphospholipid syndrome

Adriana Soto-Peleteiro[a], Cristina Gonzalez-Echavarri[a], Guillermo Ruiz-Irastorza[a,b,*]

[a] *Autoimmune Diseases Research Unit, Department of Internal Medicine, Biobizkaia Health Research Institute, Hospital Universitario Cruces, Spain*
[b] *University of The Basque Country, Bizkaia, The Basque Country, Spain*

Table 1
Obstetric features contained in the Sydney classification criteria for antiphospholipid syndrome.

-One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation. -One or more premature births before week 34 due to eclampsia, pre-eclampsia or placental insufficiency. -3 or more spontaneous abortions (<week 10) not explained by maternal or paternal chromosomal abnormalities or maternal hormonal or anatomical causes.

Adapted from Ref. 4.

Soto-Peleteiro A, Gonzalez-Echavarri C, Ruiz-Irastorza G. Obstetric antiphospholipid syndrome. Med Clin (Barc). 2024 Aug;163 Suppl 1:S14-S21.

Table 2
Obstetric features contained in the 2023 ACR/EULAR antiphospholipid syndrome classification criteria.

Prefetal death (preembryonic or embryonic loss):
Otherwise unexplained pregnancy loss before 10 weeks 0 days of gestation.*

Fetal death:
Otherwise unexplained pregnancy loss between 10 weeks 0 days and 15 weeks 6 days gestation (early fetal death), or between 16 weeks 0 days and 34 weeks 0 days gestation.

Preeclampsia with severe features:
Preeclampsia AND one or more of the following "severe features"
-Severe blood pressure elevation: Systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥110 mm Hg on 2 occasions at least 4 h apart while the patient is on bed rest
-Central nervous system dysfunction: New-onset headache unresponsive to medication and not accounted for by alternative diagnosis.
-Visual disturbances.
-Pulmonary edema.
-Impaired liver function: abnormally elevated blood concentrations of liver enzymes or severe persistent right upper quadrant or epigastric pain unresponsive to medications, not accounted by alternative diagnosis.
-Renal dysfunction: serum creatinine concentration > 1.1 mg/dl or a doubling of the serum creatinine concentration in the absence of other renal disease.
-Thrombocytopenia: platelet count of $<100 \times 10^9$/liter.

Placental insufficiency with severe features:
Intrauterine fetal growth restriction AND one or more of the following "severe features":
-Abnormal or non-reassuring fetal surveillance test(s) suggestive of fetal hypoxemia.
-Abnormal Doppler flow velocimetry waveform analysis suggestive of fetal hypoxemia.
-Severe intrauterine fetal growth restriction suggested by fetal biometry indicating an estimated fetal or postnatal birth weight of <3rd percentile for gestational age.
-Oligohydramnios.
-Maternal vascular malperfusion on placental histology.

Adapted from Ref. 3.

Soto-Peleteiro A, Gonzalez-Echavarri C, Ruiz-Irastorza G. Obstetric antiphospholipid syndrome. Med Clin (Barc). 2024 Aug;163 Suppl 1:S14-S21.

Claves

- Consulta preconcepcional
- Seguimiento protocolizado
- Tratamiento personalizado

Table 4
Cruces Autoimmune Diseases Unit treatment protocol for obstetric antiphospholipid syndrome.

Asymptomatic aPL carriers:
- LDA100 mg/d since positive pregnancy test.
- Antithrombotic prophylaxis during pregnancy and in the puerperium according to the calculation of thrombotic risk at week 9.

Recurrent early miscarriages (<10 weeks):
- Preconceptional LDA 100 mg/d.
- Prophylactic LMWH since positive test according to clinical considerations and risk factors for thrombosis.

Previous fetal loss (≥10 weeks):
- LDA 100 mg/d preconceptional.
- Prophylactic LMWH since positive test

Previous thrombosis:
- With the first positive pregnancy test (before week 6), replace VKAs with LDA 100 mg/d + LMWH at anticoagulant dose.

Ovarian stimulation techniques:
- In women with high-risk aPL, we recommend LMWH at prophylactic doses from the time of embryo transfer. It can be stopped at week 12 in case of no indication according to the thrombotic/obstetric profile and in the setting of a normal first trimester uterine Doppler study.

aPL: antiphospholipid antibodies; LDA: low dose aspirin; LMWH: low molecular weight heparin; VKAs: vitamin K antagonists.

Soto-Peleteiro A, Gonzalez-Echavarri C, Ruiz-Irastorza G. Obstetric antiphospholipid syndrome. Med Clin (Barc). 2024 Aug;163 Suppl 1:S14-S21.

Table 5
Cruces Autoimmune Diseases Unit protocol for the management of pregnancy and puerperium in aPL carriers or women with antiphospholipid syndrome.

Preconceptional visit:
- *Indicated for all women.*
- *Assess organ damage.*
- *Assess the risk of complications during pregnancy.*
- *Identify women at high risk for preeclampsia.*
- *Adjust treatment if the woman is on drugs contraindicated during pregnancy.*
- *Confirm indication of preconceptional LDA in women with obstetric APS.*

Telephone call when pregnancy is confirmed:
- *In patients with APS on anticoagulants: stop VKAs and start LDA 100 mg/d +LMWH therapeutic dose.*
- *Start LDA 100–150 mg/day from the first positive pregnancy test if not taken preconceptional.*
- *Start LMWH prophylactic dose if indicated for obstetric history.*
- *Book combined visit with the obstetrician for week 9 of pregnancy.*

Week 9, first visit:
- *Estimate thrombotic risk. Start LMWH if required (depending on risk score).*

Week 12:
- *Screening for chromosomopathies.*
- *Screening for preeclampsia risk, including uterine artery Doppler ultrasonography.*
  - If high risk on screening, add acetylsalicylic acid 100–150 mg/day if not previously taken.
- *Urine analysis and blood pressure measurement.*

Week 16:
- *Routine visit with urine analysis and blood pressure measurement.*

Week 20:
- *Fetal morphological scan.*
- *If uterine artery Doppler results were abnormal at week 12, repeat Doppler.*
- *Urine analysis and blood pressure measurement.*

Weeks 24–37:
- *Continue coordinated visits in accordance with standard pregnancy monitoring and depending on disease activity.*
- *Coordinate blood tests, ensuring one TSH and 25 (OH) vitamin D test per trimester.*
- *Check urine for proteinuria and measure blood pressure at every visit.*

Day 1 postpartum:
- *Book postnatal visit at 4 weeks postpartum.*
- *Adjust medication on discharge from hospital.*
- *Adjust anticoagulant therapy:*
  - If LMWH was not taken during pregnancy, give thromboprophylaxis for 10 days-6 weeks postpartum depending on overall thrombotic risk status.
  - If prophylactic LMWH was taken during pregnancy (for any reason, even if aPL negative), give thromboprophylaxis for 6 weeks postpartum.
  - In women on long-term anticoagulant therapy, change to vitamin K antagonists no sooner than 4 days after delivery, check INR regularly and continue LMWH until the target INR is achieved.
  - In all cases, do not start LMWH therapy until 6 h after removing the epidural catheter.
- *Ensure adequate calcium and vitamin D intake after hospital discharge, especially in women who are breastfeeding and on LMWH.*

Week 4 after delivery:
- *Postnatal visit.*
- *Assess disease activity in women with SLE.*
- *Measure ferritin, 25 (OH) vitamin D and TSH.*
- *Adjust treatment depending on clinical status.*

APS: antiphospholipid syndrome; aPL: antiphospholipid antibodies; LDA: low dose aspirin; LMWH: low molecular weight heparin; VKAs: vitamin K antagonists.

Soto-Peleteiro A, Gonzalez-Echavarri C, Ruiz-Irastorza G. Obstetric antiphospholipid syndrome. Med Clin (Barc). 2024 Aug;163 Suppl 1:S14-S21.

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Review

Thrombotic antiphospholipid syndrome: From guidelines to clinical management

Diana Paredes-Ruiz[a], Daniel Martin-Iglesias[a], Guillermo Ruiz-Irastorza[a,b,*]

[a] *Autoimmune Diseases Research Unit, Department of Internal Medicine, Biobizkaia Health Research Institute, Hospital Universitario Cruces, Spain*
[b] *University of The Basque Country, Bizkaia, The Basque Country, Spain*

Consideraciones antes de plantear tratamiento

- Perfil AAF
- Factores de riesgo CV
- Factores de riesgo de sangrado
- Paciente (enf. de base, preferencias, etc)

Herramientas terapéuticas

- AVK
- Heparina
- Antiagregantes
- ACOD
- Otros: HCQ, estatinas

Paredes-Ruiz D, Martin-Iglesias D, Ruiz-Irastorza G. Thrombotic antiphospholipid syndrome: From guidelines to clinical management. Med Clin (Barc). 2024 Aug;163 Suppl 1:S22-S30

Profilaxis primaria

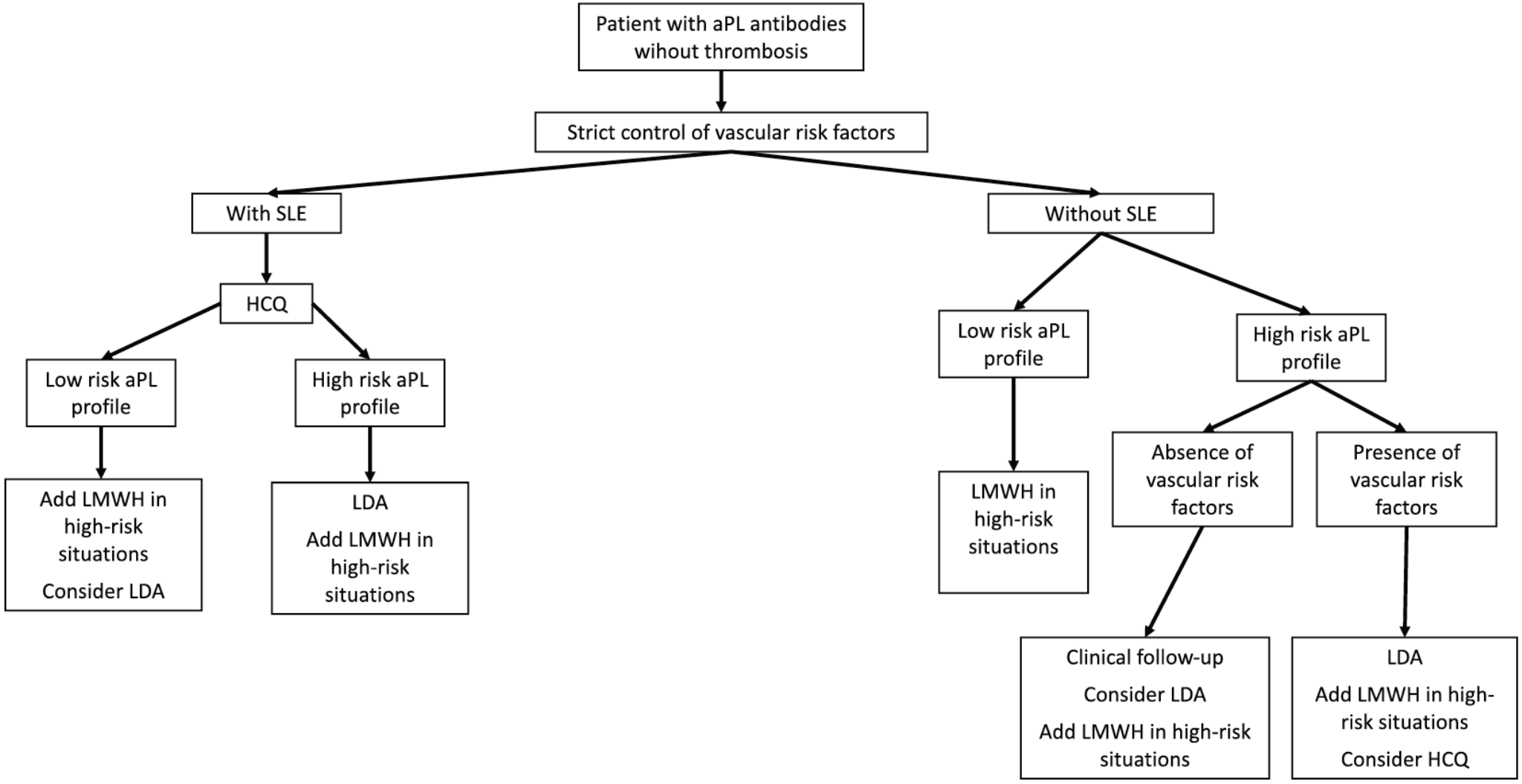


Fig. 1. Algorithm for primary thromboprophylaxis. aPL: antiphospholipid; SLE: systemic erythematosus lupus; HCQ: hydroxychloroquine; LMWH: low-molecular-weight-heparin; LDA: low-dose aspirin.

Paredes-Ruiz D, Martin-Iglesias D, Ruiz-Irastorza G. Thrombotic antiphospholipid syndrome: From guidelines to clinical management. Med Clin (Barc). 2024 Aug;163 Suppl 1:S22-S30

Profilaxis secundaria

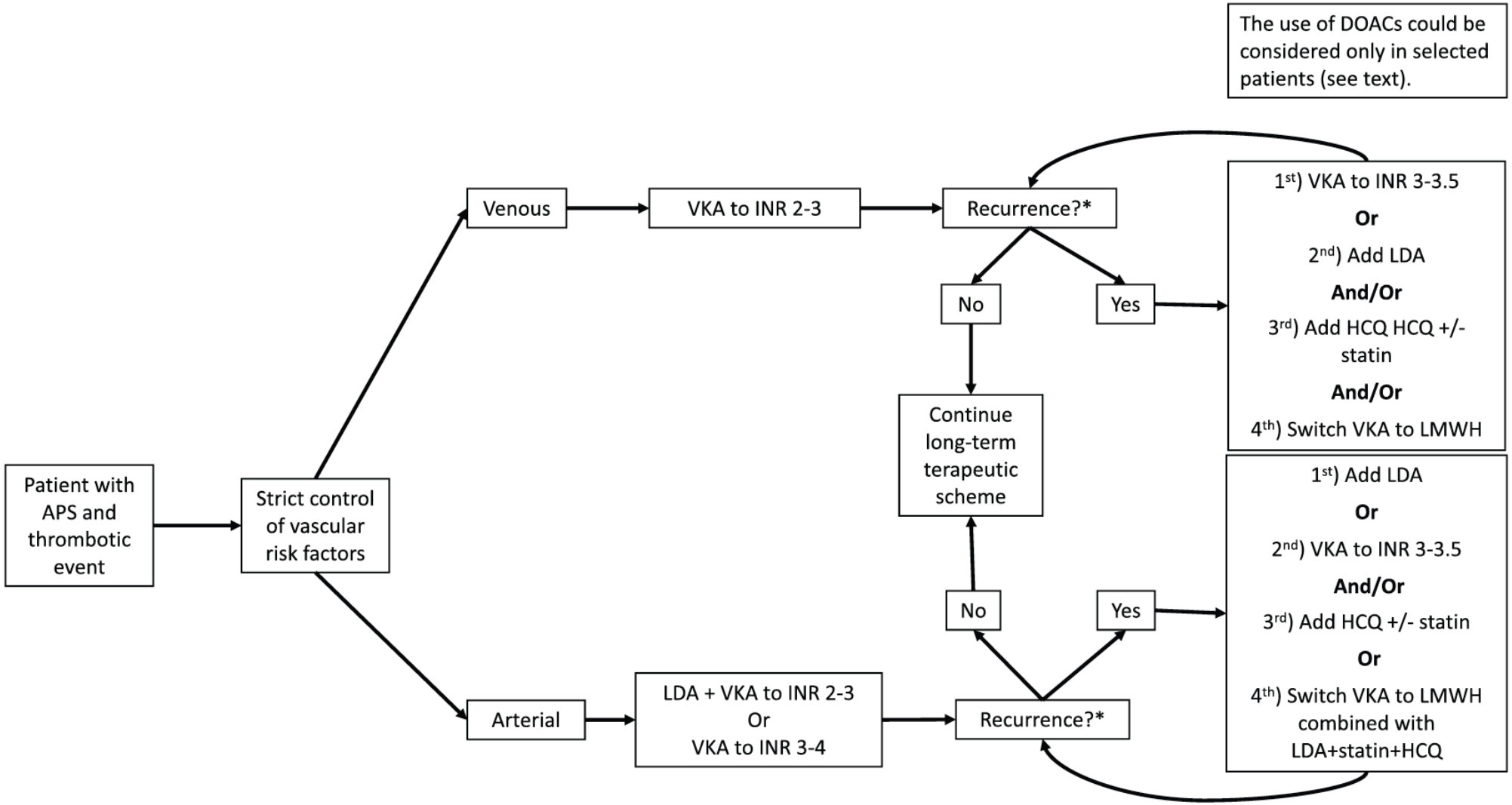


Fig. 2. Algorithm for the therapy of first and recurrent thrombotic events. * First assure adherence and in-range INR levels before the recurrent event. APS: antiphospholipid syndrome; VKA: vitamin K antagonist; INR: international normalized ratio; LDA: low-dose aspirin; HCQ: hydroxychloroquine; LMWH: low-molecular-weight heparin; DOACs: direct oral anticoagulant drugs.

Paredes-Ruiz D, Martin-Iglesias D, Ruiz-Irastorza G. Thrombotic antiphospholipid syndrome: From guidelines to clinical management. Med Clin (Barc). 2024 Aug;163 Suppl 1:S22-S30

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Review

Catastrophic antiphospholipid syndrome: Lessons from the "CAPS Registry"

Ignasi Rodriguez-Pintó, Gerard Espinosa, Ricard Cervera*

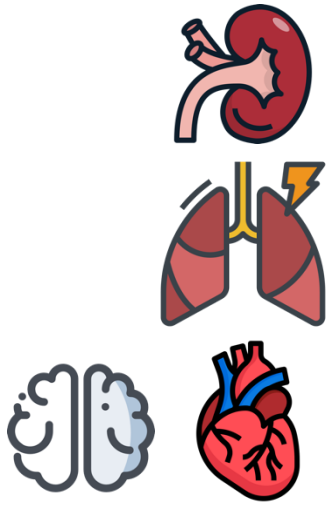
Department of Autoimmune Diseases, Reference Centre for Systemic Autoimmune Diseases (UEC, CSUR) of the Catalan and Spanish Health Systems/Member of ERN-ReCONNET, Hospital Clínic, Barcelona, Catalonia, Spain

SAF catastrófico

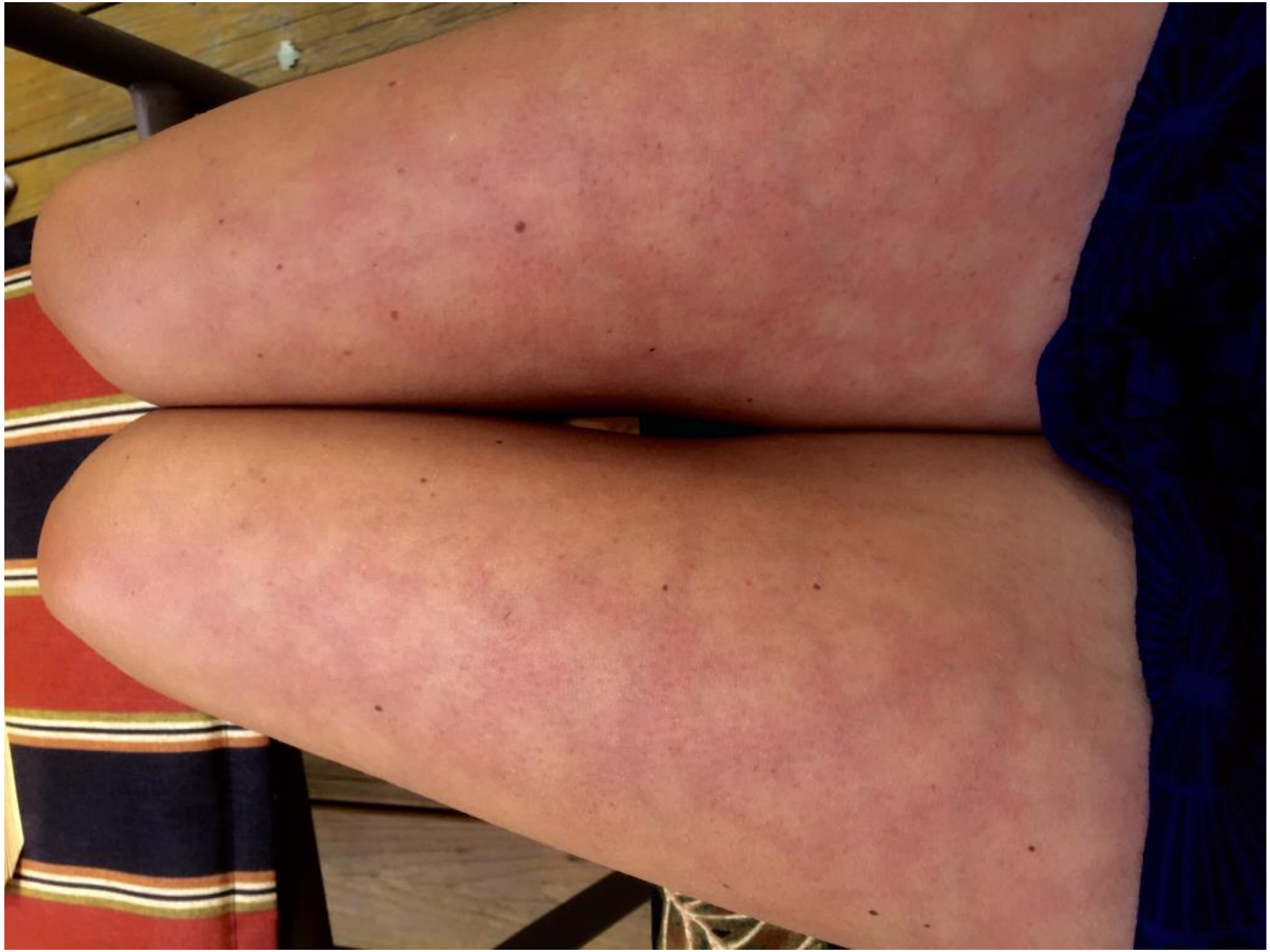
- trombosis macro y microvascular periodo recortado tiempo (1 semana)
- Muy raro: incidencia 9 por 10000 pacientes con SAF

Presentación clínica

- Factor desencadenante
- Renal 73%
- Pulmonar 60%
- Cerebral 56%
- Cardiaca 50%
- Cutánea 47%
- TVP 37%



Rodriguez-Pintó I, Espinosa G, Cervera R. Catastrophic antiphospholipid syndrome: Lessons from the "CAPS Registry". Med Clin (Barc). 2024 Aug;163 Suppl 1:S31-S35.



Rodriguez-Pintó I, Espinosa G, Cervera R. Catastrophic antiphospholipid syndrome: Lessons from the "CAPS Registry". Med Clin (Barc). 2024 Aug;163 Suppl 1:S31-S35.

Diagnóstico diferencial

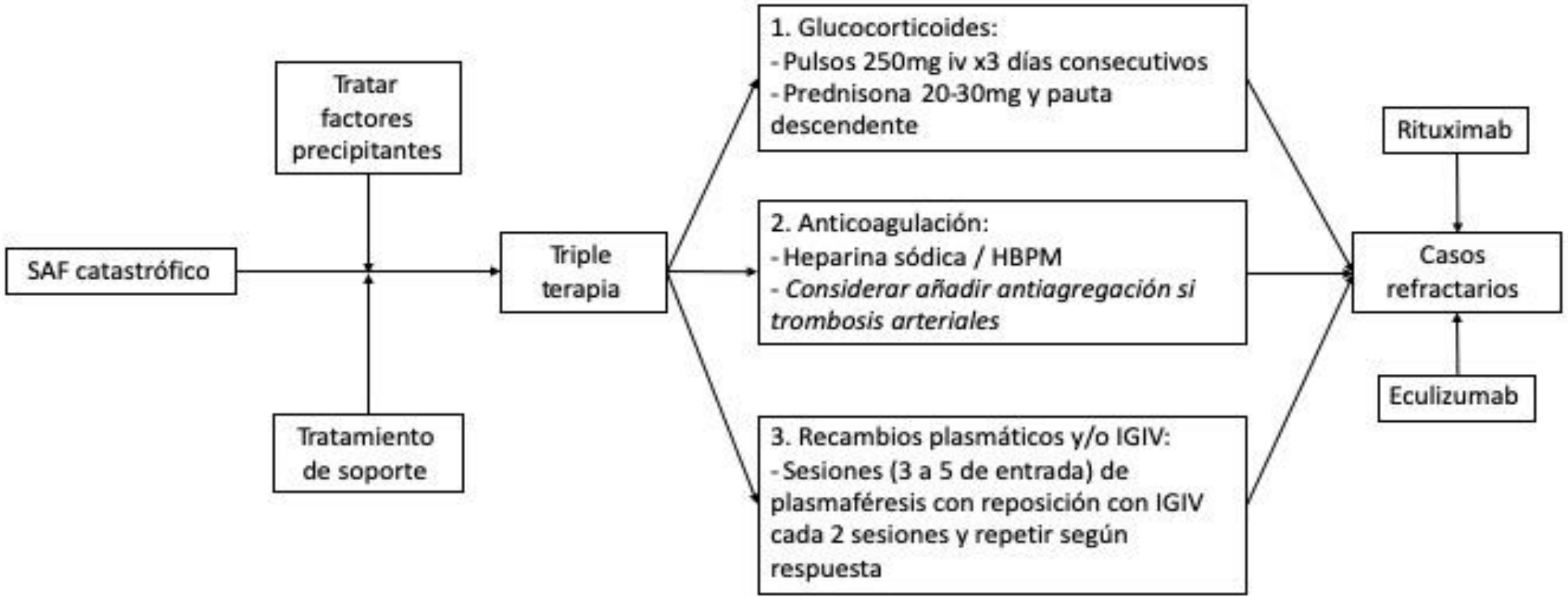
- Sepsis con CID
- Microangiopatías trombóticas (PTT/SHU)
- Trombopenia por heparina
- HELLP

Table 3
Selected tests for patients with microangiopathic features and suspicion of CAPS.

- Peripheral blood smear
- Chest X-ray
- Funduscopic examination
- ADAMTS13 activity
- Stool culture
- Anti-nuclear, anti-DNA, anti-Sm, and anti-RNP antibodies
- Antiphospholipid antibodies (LA, aCL IgG and IgM, aβ2GPI IgG and IgM)
- Bone marrow biopsy
- Positron emission tomography-computed tomography
- Anti-HPF4 antibodies
- Biopsy of affected tissues/organs
- Complement factor H, factor B, and factor I levels

Abbreviations: LA, lupus anticoagulant, aCL, anticardiolipin, aβ2GPI, anti-β2-glycoprotein, HPF4, heparin-platelet factor 4.

Rodriguez-Pintó I, Espinosa G, Cervera R. Catastrophic antiphospholipid syndrome: Lessons from the "CAPS Registry". Med Clin (Barc). 2024 Aug;163 Suppl 1:S31-S35.



Rodriguez-Pintó I, Espinosa G, Cervera R. Catastrophic antiphospholipid syndrome: Lessons from the "CAPS Registry". Med Clin (Barc). 2024 Aug;163 Suppl 1:S31-S35.

Table I. Treatment protocol for catastrophic antiphospholipid syndrome.

Day 1	Pulse of methylprednisolone 250-500 mg + mechanical thrombectomy + **plasma exchange** with replacement with FFP	LMWH 1mg/kg/bid
Day 2	Pulse of methylprednisolone 250-500 mg + **plasma exchange** with replacement with FFP	LMWH, same dose
Day 3	Pulse of methylprednisolone 250-500 mg + IVIG 200 mg/kg)	LMWH, same dose
Day 4	Methylprednisolone 20 mg/day+ **plasma exchange** with replacement with FFP	LMWH, same dose
Day 5	Methylprednisolone 20 mg/day	LMWH, same dose
Day 6	Methylprednisolone 20 mg/day+ **plasma exchange** with replacement with FFP	LMWH, same dose
Day 7	Methylprednisolone 20 mg/day + IVIG 200 mg/kg	LMWH, same dose
Day 8	Methylprednisolone 20 mg/day+ **plasma exchange** with replacement with FFP	LMWH, same dose
Day 9	Methylprednisolone 20 mg/day	LMWH, same dose + HCQ 200 mg/day
Day 10	Methylprednisolone 20 mg/day+ **plasma exchange** with replacement with FFP	LMWH, same dose + HCQ 200 mg/day
Day 11	Methylprednisolone 15 mg/day + IVIG 200 mg/kg	LMWH, same dose + HCQ 200 mg/day
Day 12 and on the following days	Prednisone 15 mg/day one week, then 10 mg/day with tapering to 5 mg/day over 4-8 weeks + LMWH 1mg/kg/12h + HCQ 200 mg/day	

FFP: fresh-frozen plasma; LMWH: low molecular weight heparin; IVIG: intravenous immunoglobulins; HCQ: hydroxychloroquine..

Soto-Peleteiro A, Ruiz-Irastorza G. Catastrophic antiphospholipid syndrome with massive cerebral venous sinus thrombosis. Clin Exp Rheumatol. 2024 doi: 10.55563/clinexprheumatol/t7uz2j.