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SOCIEDAD LATINOAMERICANA DE CARDIOLOGIA INTERVENCIONISTA

XLIX Jornadas SOLACI

17° Región Centroamérica y el Caribe

7 y 8 de noviembre 2024

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Terapia antiplaquetaria dual (TAPD) en pacientes con alto riesgo de sangrado

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El Salvador 8-nov-2024

Terapia antiplaquetaria dual (TAPD) en pacientes con alto riesgo de sangrado

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- Fellow SIAC y ESC
- PUBLICACIONES:
  - Artículos y capítulo de libro sobre antiagregación plaquetaria
  - Artículos sobre angioplastia primaria
  - Guías SIAC-SOLACI para TAVI (Co-autor)
  - Autor de 3 capítulos del libro de la SIAC (2017)

No tengo conflictos de interés

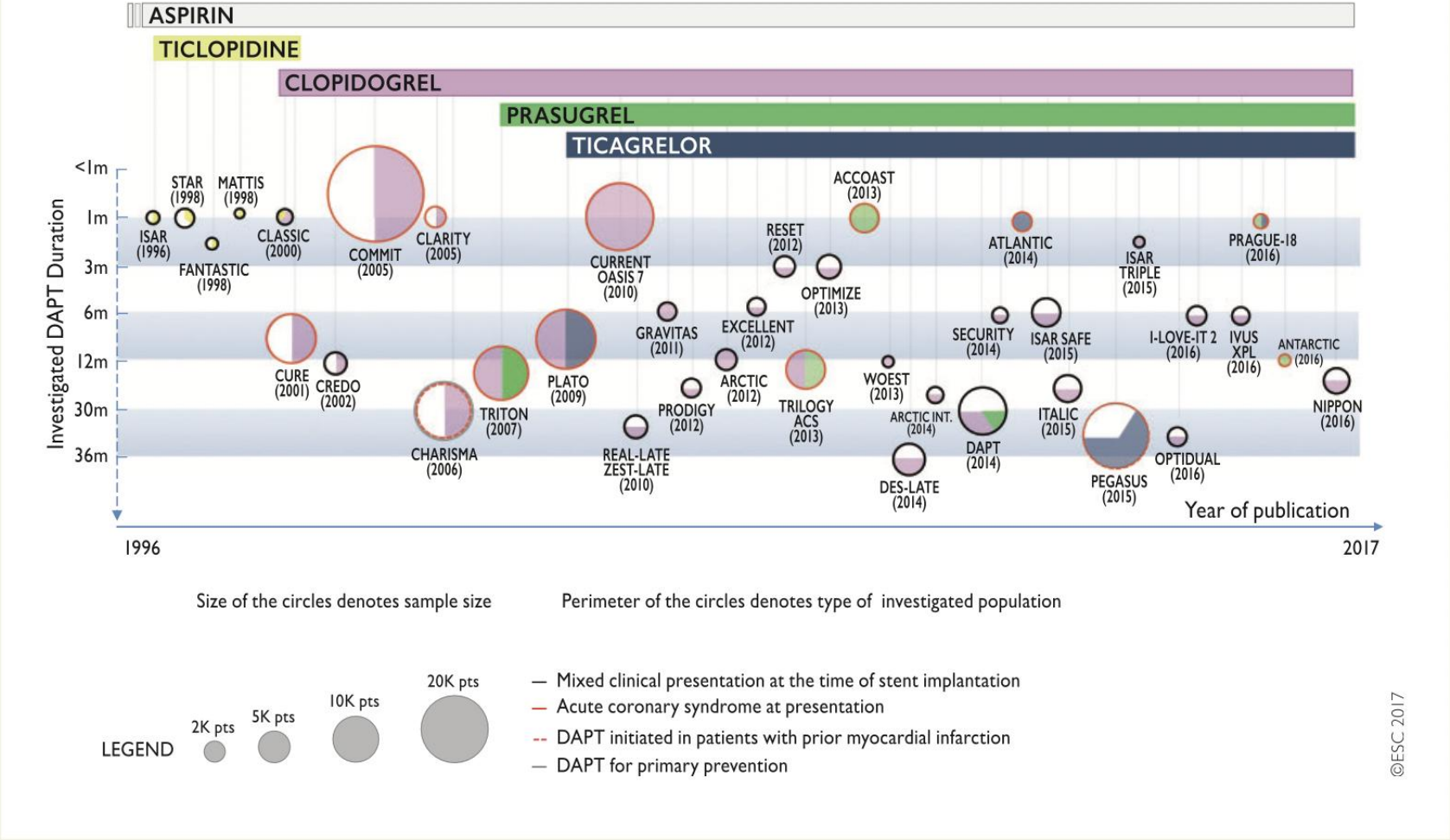

Figure 1 History of dual antiplatelet therapy (DAPT) in patients with coronary artery disease. The size of the circles denotes sample size. The colours of perimeters identify the type of included patient populations within each study. The colours within each circle identify the antiplatelet agent(s) investigated. Head-to-head studies comparing similar durations of two different antiplatelet strategies are shown with a vertical line, whereas those investigating different treatment durations are shown with a horizontal line. Studies investigating different treatment strategies or regimens and not treatment durations or type (e.g. pre-treatment in ACCOAST, tailored therapy in GRAVITAS, double dose of clopidogrel in CURRENT OASIS 7, etc.) are represented with a single colour indicating the $P2Y_{12}$ inhibitor, which was tested on top of aspirin.
pts = patients.

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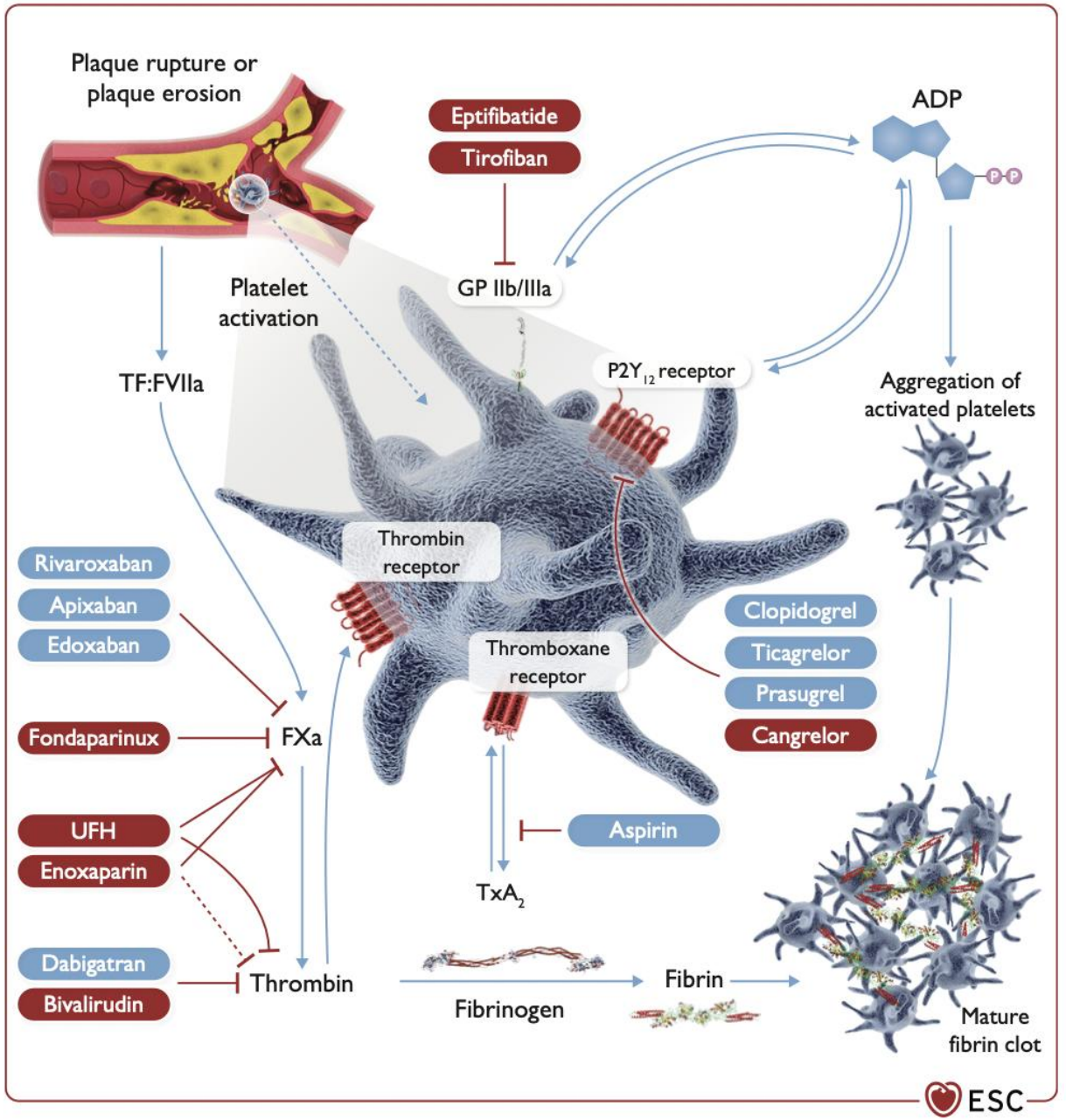

Figure 9 Antithrombotic treatments in acute coronary syndrome: pharmacological targets. ADP, adenosine diphosphate; FVIIa, Factor VIIa; FXa, Factor Xa; GP, glycoprotein; TF, tissue factor; TxA_2, thromboxane A_2; UFH, unfractionated heparin. Drugs with oral administration are shown in blue and drugs with preferred parenteral administration in red.

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TAPD en pacientes con alto riesgo de sangrado (SCA sin indicación de anticoagulación oral)

- Tratamiento antiplaquetario es obligatorio.
- Estrategia recomendada es 12 meses de:
  - Inhibidor potente del receptor $P2Y_{12}$ (Prasugrel o Ticagrelor) + AAS
  - En escenarios específicos esta estrategia puede ser:
    - Corta = <12 meses
    - Extendida = >12 meses
    - Modificada = desescalada

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Use of risk scores as guidance for the duration of dual antiplatelet therapy

Recommendations	Class[a]	Level[b]
The use of risk scores designed to evaluate the benefits and risks of different DAPT durations[c] may be considered.[15,18]	IIb	A

DAPT = dual antiplatelet therapy.
[a]Class of recommendation.
[b]Level of evidence.
[c]The DAPT and PRECISE-DAPT scores are those currently fulfilling these requirements.

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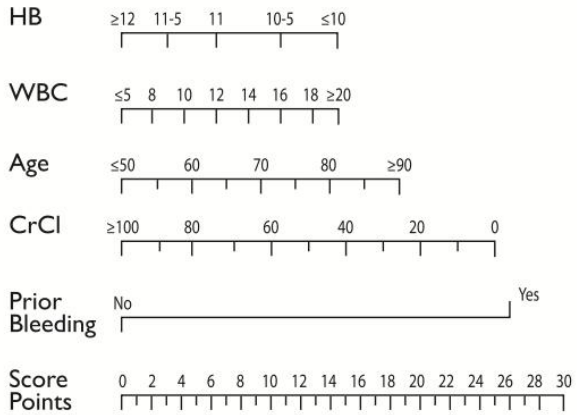
Table 3 **Risk scores validated for dual antiplatelet therapy duration decision-making**

	PRECISE-DAPT score[18]	DAPT score[15]
Time of use	At the time of coronary stenting	After 12 months of uneventful DAPT
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)
Score calculation[a]		Age ≥75 −2 pt 65 to <75 −1 pt <65 0 pt Cigarette smoking +1 pt Diabetes mellitus +1 pt MI at presentation +1 pt Prior PCI or prior MI +1 pt Paclitaxel-eluting stent +1 pt Stent diameter <3 mm +1 pt CHF or LVEF <30% +2 pt Vein graft stent +2 pt
Score range	0 to 100 points	−2 to 10 points
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT	Score ≥2 → Long DAPT Score <2 → Standard DAPT
Calculator	www.precisedaptscore.com	www.daptstudy.org

CHF = congestive heart failure; CrCl = creatinine clearance; DAPT = dual antiplatelet therapy; Hb = haemoglobin; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; WBC = white blood cell count.

[a]For the PRECISE-DAPT score use the score nomogram: mark patient's value for each of the five clinical variables of the score and draw a vertical line to the 'Point' axis to determine the number of points obtained for each clinical variable. Then summate the points obtained for each clinical variable to the total score. A practical case example for score calculation is provided in Web Figure 1 of the Web Addenda.

For the DAPT score summate positive points for each value and subtract values for age to the total score.

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Tabla 1 Escala de sangrado ''Bleeding Academic Research Consortium'' (BARC)

Tipo 0: sin sangrado.

Tipo 1: sangrado no significativo, no requiere estudios o consulta a un servicio médico, hospitalización o manejo por un profesional de salud. Puede incluir la suspensión voluntaria de la medicación antitrombótica por parte del paciente. Ejemplo: sangrado nasal, moretones, sangrado hemorroidal, en general, no se busca atención médica.

Tipo 2: Cualquier signo de hemorragia (cualquier sangrado que sea más de lo esperado, incluyendo sangrado solo identificado por un estudio de imagen), que no cumpla criterios para tipo 3, 4 o 5 pero que requiera al menos uno de los siguientes puntos:

- Intervención médica no quirúrgica por parte de un profesional de salud (ejemplos suspender la medicación antiplaquetaria, antitrombótica, compresión en el sitio de sangrado, uso de medicamentos para revertir el efecto como: la protamina y la vitamina k).
- Requiere hospitalización o aumento del nivel de cuidado.
- Requiere evaluación pronta con exámenes como: el hemograma, el uroanálisis, las pruebas de coagulación, la endoscopia y la tomografía.

Tipo 3

- Tipo 3 a:
- Sangrado con descenso de la hemoglobina de $\geq$ 3 a < 5 g/dl (relacionado con el sangrado).
- Cualquier necesidad de transfusión por sangrado evidente.

Tipo 3 b:

- Descenso en la hemoglobina $\geq$ 5 g/dl (relacionado con el sangrado).
- Taponamiento cardiaco.
- Sangrado que requiera intervención quirúrgica para su control (excluyendo nasal, dental, piel, hemorroides).
- Sangrado que requiera el uso de agentes vasoactivos.
- Tipo 3 c:
- Hemorragia intracraneal (no incluye microhemorragias o transformación hemorrágica. Incluye sangrado intraespinal).
- Subcategorías confirmadas por autopsias o imágenes o punción lumbar.
- Sangrado intraocular con compromiso de la visión.

Tipo 4: sangrado asociado a revascularización miocárdica.

- Sangrado intracraneal perioperatorio dentro de las 48 horas.
- Reoperación luego de cierre de esternotomía con propósito de controlar sangrado.
- Transfusión de $\geq$ 5 unidades de glóbulos rojos, dentro de un período de 48 horas.
- Gasto de tubo a tórax $\geq$ 2 litros en 24 horas.

Tipo 5: sangrado fatal

- Tipo 5 a: Sangrado fatal probable: con sospecha clínica pero no comprobado por autopsia o imagen.
- Tipo 5 b: Sangrado fatal definitivo: confirmado por imagen o autopsia. El sangrado se especifica como: intracraneal, gastrointestinal, pulmonar, pericárdico, genitourinario u otro.

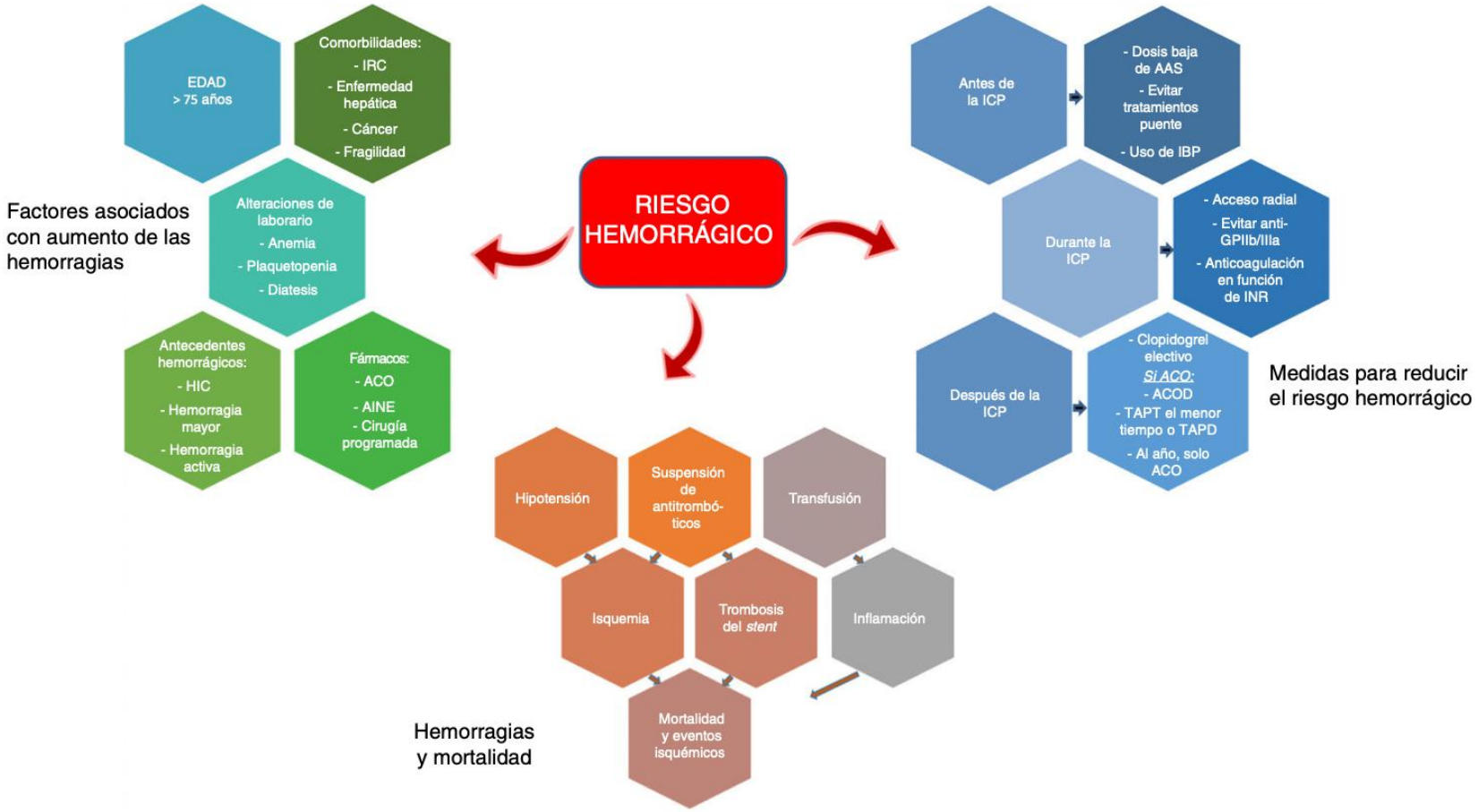

Figura 1. Variables relacionadas con el paciente en alto riesgo hemorrágico sometido a intervención coronaria. En tonos marrones: consecuencias del sangrado. En tonos verdes: factores asociados con el aumento del sangrado. En tonos azules: medidas para reducir el riesgo hemorrágico. AAS: ácido acetilsalicílico; ACO: anticoagulación oral crónica; ACOD: anticoagulantes orales de acción directa; AINE: antiinflamatorios no esteroideos; anti-GPIIb/IIIa: inhibidor de la glucoproteína IIb/IIIa; HIC: hemorragia intracraneal; IBP: inhibidor de la bomba de protones; ICP: intervención coronaria percutánea; INR: razón internacional normalizada; IRC: insuficiencia renal crónica; TAPD: tratamiento doble (ACO y un antiagregante plaquetario); TAPT: tratamiento triple (ACO y 2 antiagregantes plaquetarios). Esta figura se muestra a todo color solo en la versión electrónica del artículo.

Rev Esp Cardiol. 2020;73(7):521–523

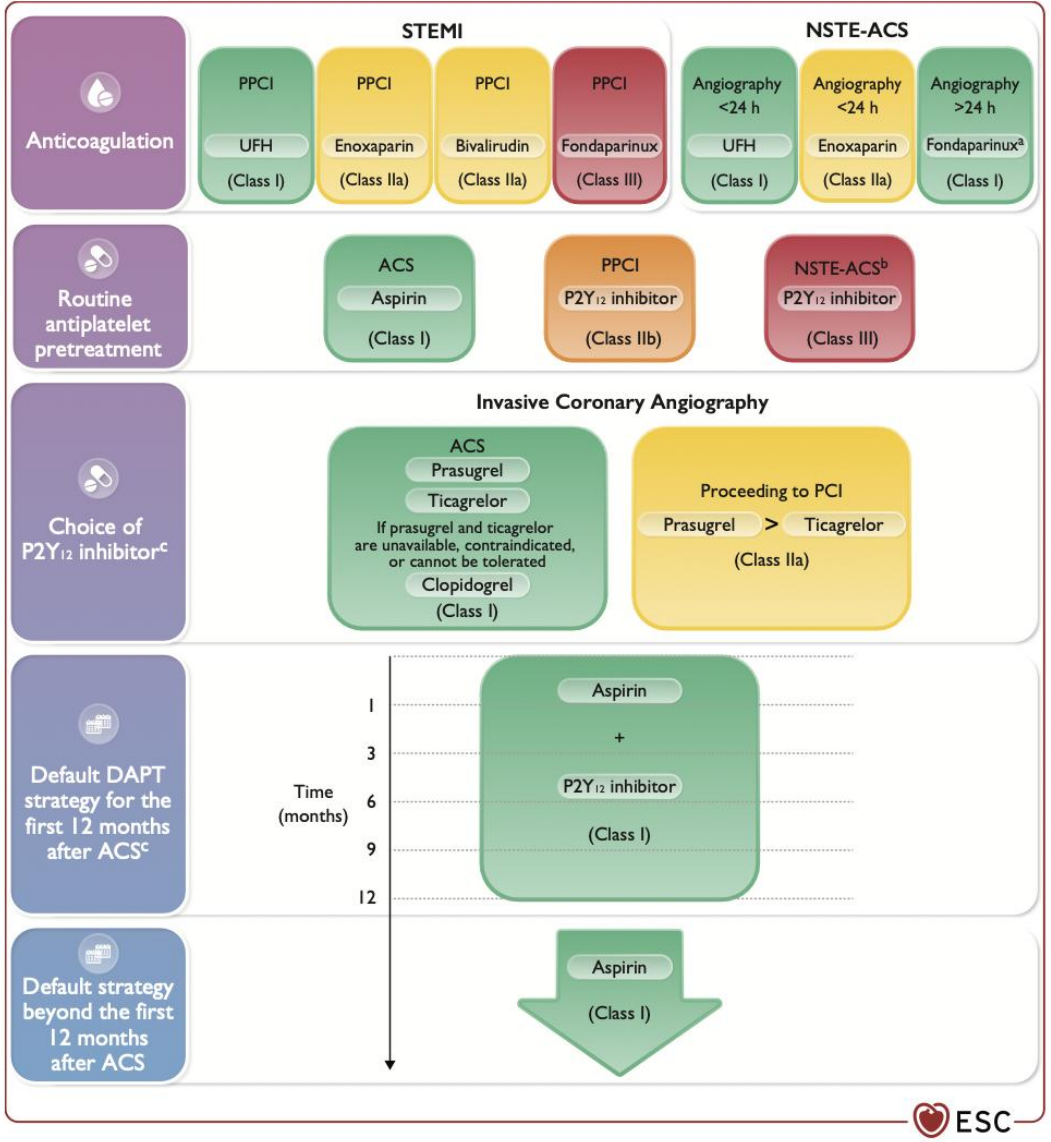

Figure 10 Recommended default antithrombotic therapy regimens in acute coronary syndrome patients without an indication for oral anticoagulation. ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy; HBR, high bleeding risk; NSTE-ACS, non-ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; UFH, unfractionated heparin. Algorithm for antithrombotic therapy in ACS patients without an indication for oral anticoagulation undergoing invasive evaluation. [a]Fondaparinux (plus a single bolus of UFH at the time of PCI) is recommended in preference to enoxaparin for NSTE-ACS patients in cases of medical treatment or logistical constraints for transferring the NSTE-ACS patient to PCI within 24 h of symptom onset. [b]Routine pre-treatment with a $P2Y_{12}$ receptor inhibitor in NSTE-ACS patients in whom coronary anatomy is not known and early invasive management (<24 h) is planned is not recommended, but pre-treatment with a $P2Y_{12}$ receptor inhibitor may be considered in NSTE-ACS patients who are not expected to undergo an early invasive strategy (<24 h) and do not have HBR. [c]Clopidogrel is recommended for 12 months DAPT if prasugrel and ticagrelor are not available, cannot be tolerated, or are contraindicated, and may be considered in older ACS patients (typically defined as older than 70–80 years of age).

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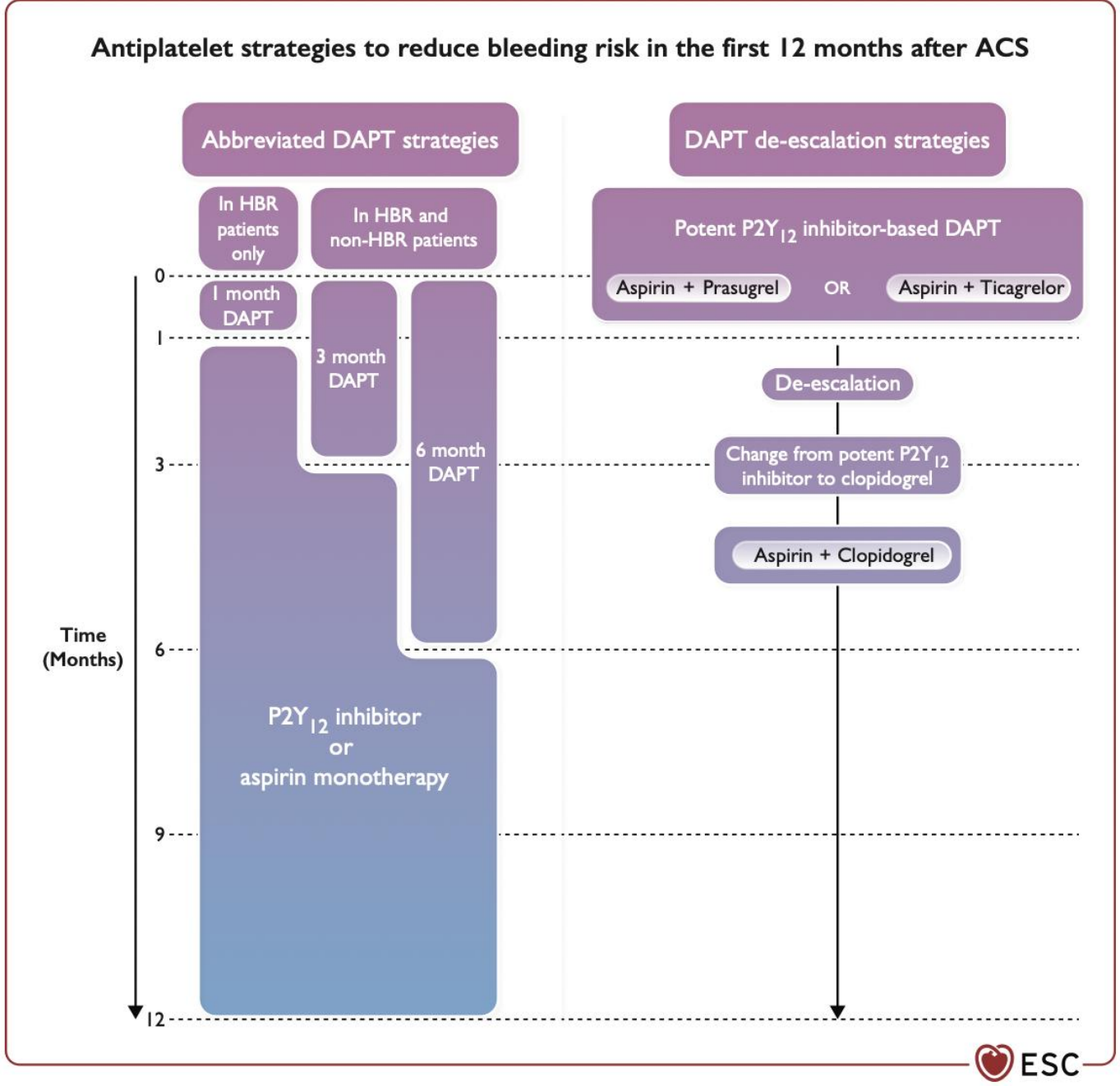

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Figure 11 Alternative antiplatelet strategies to reduce bleeding risk in the first 12 months after an ACS. ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy; HBR, high bleeding risk; PFT, platelet function test.

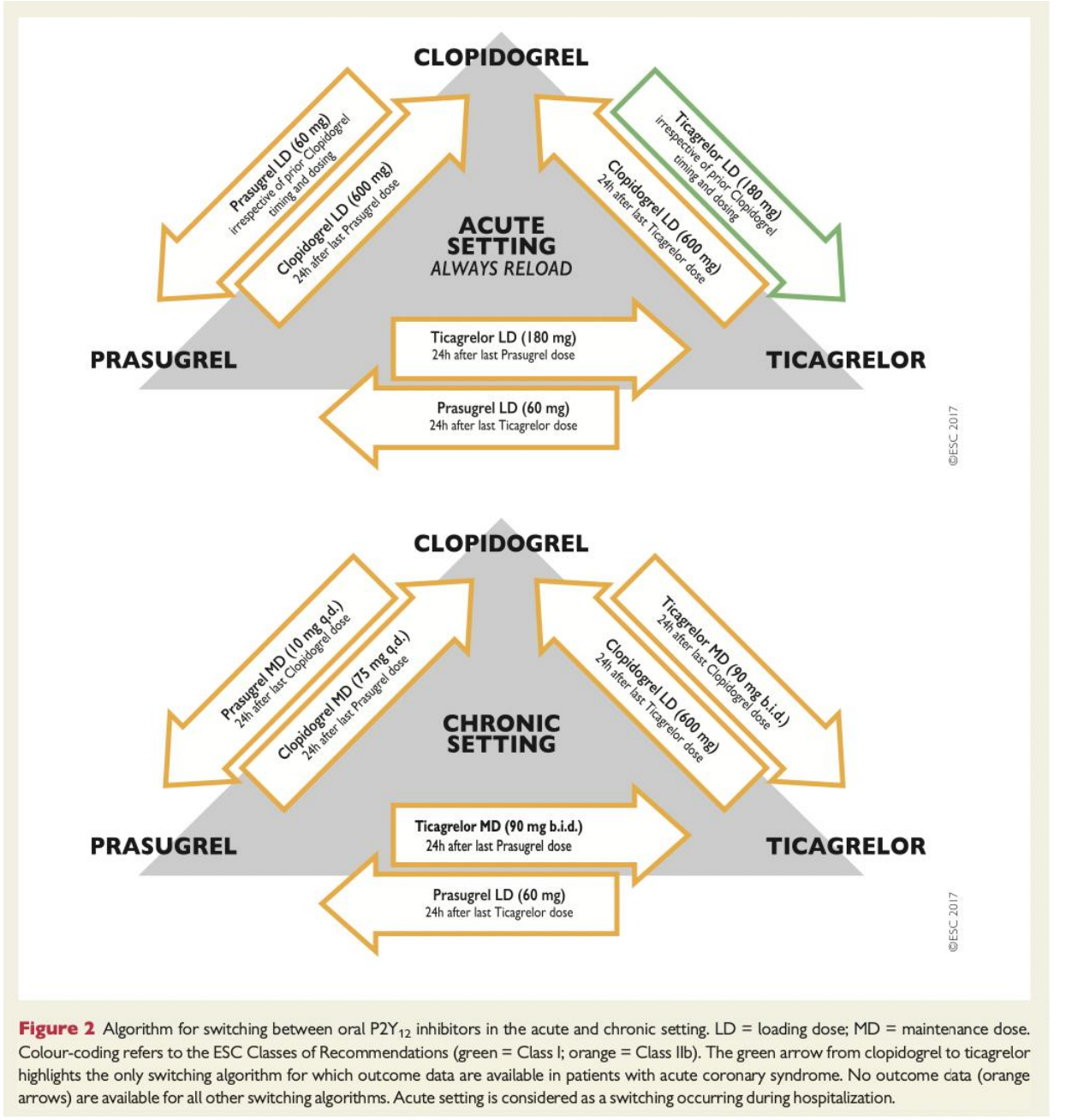

Figure 2 Algorithm for switching between oral $P2Y_{12}$ inhibitors in the acute and chronic setting. LD = loading dose; MD = maintenance dose. Colour-coding refers to the ESC Classes of Recommendations (green = Class I; orange = Class IIb). The green arrow from clopidogrel to ticagrelor highlights the only switching algorithm for which outcome data are available in patients with acute coronary syndrome. No outcome data (orange arrows) are available for all other switching algorithms. Acute setting is considered as a switching occurring during hospitalization.

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Terapia antiplaquetaria en pacientes con indicación de anticoagulación oral

- En 6-8% de los casos.
- Se debe continuar con el anticoagulante oral:
  - No hacer puente con heparina.
- La evidencia en warfarina deriva de análisis de subgrupos de estudios.
- Se ha evaluado la seguridad de los anticoagulantes directos Triple vs doble terapia :
  - Menos sangrado (2.3% de reducción absuluta).
  - Ligero incremento (significativo) en trombosis del STENT (0.4% absoluto).
  - No incremento de MACE.

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Table 7 Suggested strategies to reduce bleeding risk related to percutaneous coronary intervention

- Anticoagulant doses adjusted to body weight and renal function, especially in women and older patients
- Radial artery approach as default vascular access
- Proton pump inhibitors in patients on dual antiplatelet therapy at higher-than-average risk of gastrointestinal bleeds (i.e. history of gastrointestinal ulcer/haemorrhage, anticoagulant therapy, chronic non-steroidal anti-inflammatory drug/corticosteroid use), or two or more of:
  (a) Age ≥65 years
  (b) Dyspepsia
  (c) Gastro-oesophageal reflux disease
  (d) *Helicobacter pylori* infection
  (e) Chronic alcohol use
- In patients on OAC:
  (a) PCI performed without interruption of VKAs or NOACs
  (b) In patients on VKAs, do not administer UFH if INR >2.5
  (c) In patients on NOACs, regardless of the timing of the last administration of NOACs, add low-dose parenteral anticoagulation (e.g. enoxaparin 0.5 mg/kg i.v. or UFH 60 IU/kg)
- Aspirin is indicated but avoid pre-treatment with $P2Y_{12}$ receptor inhibitors
- GP IIb/IIIa receptor inhibitors only for bailout or peri-procedural complications

GP, glycoprotein; INR, international normalized ratio; i.v., intravenous; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulation/anticoagulant; PCI, percutaneous coronary intervention; UFH, unfractionated heparin; VKA, vitamin K antagonist.

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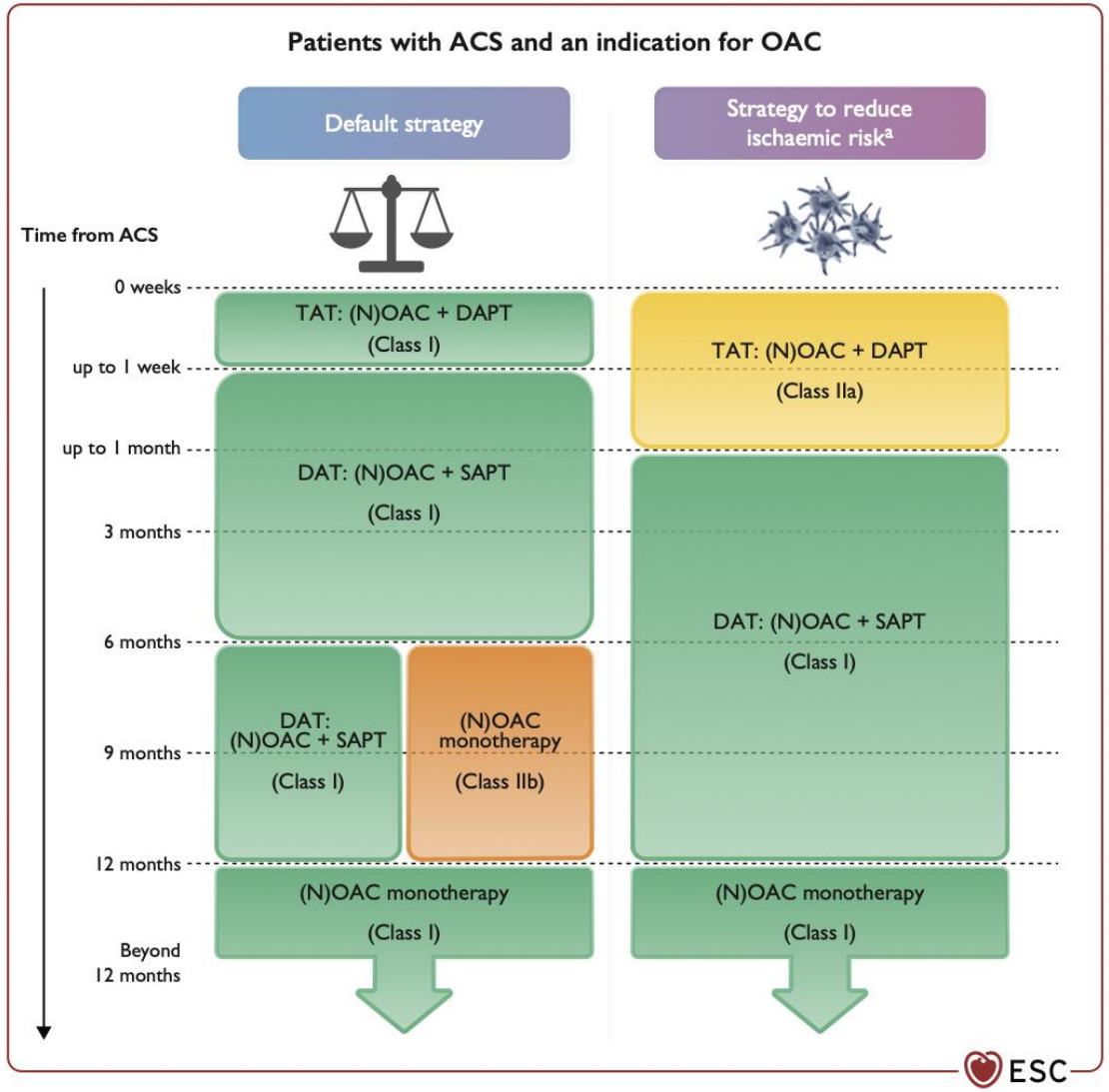

Figure 12 Antithrombotic regimens in patients with acute coronary syndrome and an indication for oral anticoagulation. ACS, acute coronary syndrome; ARC-HBR, Academic Research Consortium for High Bleeding Risk; DAPT, dual antiplatelet therapy; DAT, dual antithrombotic therapy; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulation/anticoagulant; SAPT, single antiplatelet therapy; TAT, triple antithrombotic therapy; VKA, vitamin K antagonist. OAC: preference for a NOAC over VKA for the default strategy and in all other scenarios if no contraindications. For both TAT and DAT regimens, the recommended doses for the NOACs are as follows: Apixaban 5 mg b.i.d., Dabigatran 110 mg or 150 mg b.i.d., Edoxaban 60 mg o.d., Rivaroxaban 15 mg or 20 mg o.d. NOAC dose reductions are recommended in patients based on certain criteria for each of the NOACs (including renal function, body weight, concomitant medications and age). SAPT: preference for a $P2Y_{12}$ receptor inhibitor (usually clopidogrel) over aspirin. See Bleeding risk assessment in Supplementary data online, *Section 8.2.2.3* for details on the ARC-HBR criteria. In addition, patients with a PRECISE-DAPT score of ≥25 are regarded as high bleeding risk. [a]See Supplementary material online, *Table S9* for examples of high-risk features of stent-driven recurrent events.

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CONCLUSIONES

- El manejo de pacientes sometidos a intervención coronaria percutánea, requiere de una adecuada evaluación del riesgo isquémico/hemorrágico
- La terapia antiplaquetaria dual a a corto plazo (1-3 meses), ha demostrado ser una estrategia segura en pacientes de alto riesgo de sangrado.
- En casos de alto riesgo de sangrado en pacientes que requieren anticoagulación oral, debemos reducir la terapia triple a dual, al menor tiempo y a menor intensidad, en donde se haya demostrado seguridad.

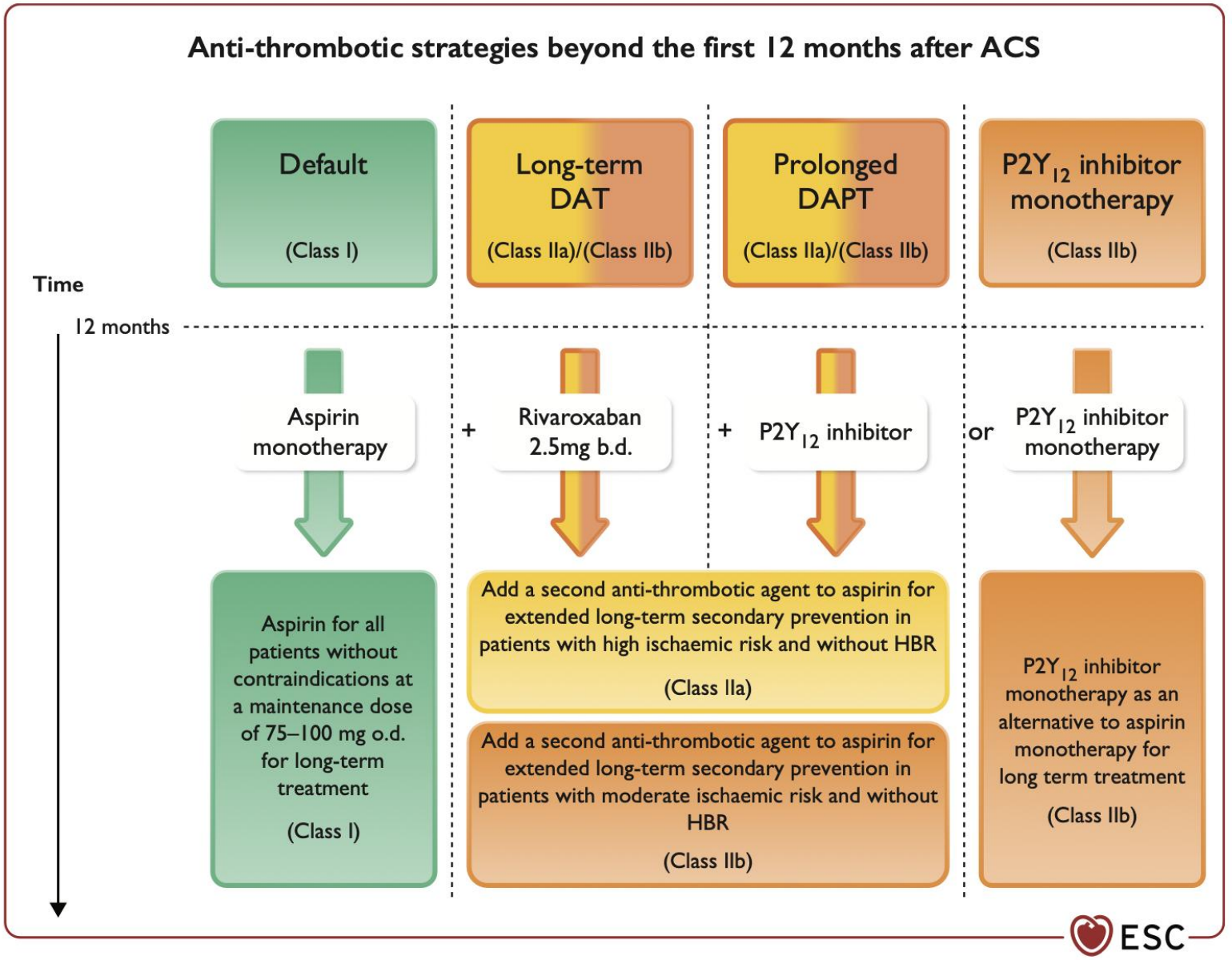

Figure S4 Antithrombotic strategies beyond the first 12 months after ACS. ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy; DAT, dual antithrombotic therapy; HBR, high bleeding risk; MD, maintenance dose; o.d., once a day.

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Table S8 Risk criteria for extended treatment with a second antithrombotic agent

High thrombotic risk (Class IIa)	Moderate thrombotic risk (Class IIb)
Complex CAD and at least one criterion	Non-complex CAD and at least one criterion
Risk enhancers	
Diabetes mellitus requiring medication History of recurrent MI Any multivessel CAD Premature (<45 years) or accelerated (new lesion within a 2-year timeframe) CAD Concomitant systemic inflammatory disease (e.g. human immunodeficiency virus, systemic lupus erythematosus, chronic arthritis) Polyvascular disease (CAD plus PAD) CKD with eGFR 15–59 mL/min/1.73 m^2	Diabetes mellitus requiring medication History of recurrent MI Polyvascular disease (CAD plus PAD) CKD with eGFR 15–59 mL/min/1.73 m^2
Technical aspects	
At least three stents implanted At least three lesions treated Total stent length >60 mm History of complex revascularization (left main, bifurcation stenting with ≥2 stents implanted, chronic total occlusion, stenting of last patent vessel) History of stent thrombosis on antiplatelet treatment	

CAD, coronary artery disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; PAD, peripheral arterial disease.
In line with guideline recommendations, CAD patients are stratified into two different risk groups (high vs. moderately increased thrombotic or ischaemic risk). Stratification of patients towards complex vs. non-complex CAD is based on individual clinical judgment with knowledge of the patient's cardiovascular history and/or coronary anatomy. Selection and composition of risk-enhancing factors are based on the combined evidence of clinical trials on extended antithrombotic treatment in CAD patients and on data from related registries.[141]

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Table S9 High-risk features of stent-driven recurrent ischaemic events

Prior stent thrombosis on adequate antiplatelet therapy
Stenting of the last remaining patent coronary artery
Diffuse multivessel disease, especially in patients with diabetes
Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
At least three stents implanted
At least three lesions treated
Bifurcation with two stents implanted
Total stent length >60 mm
Treatment of a chronic total occlusion

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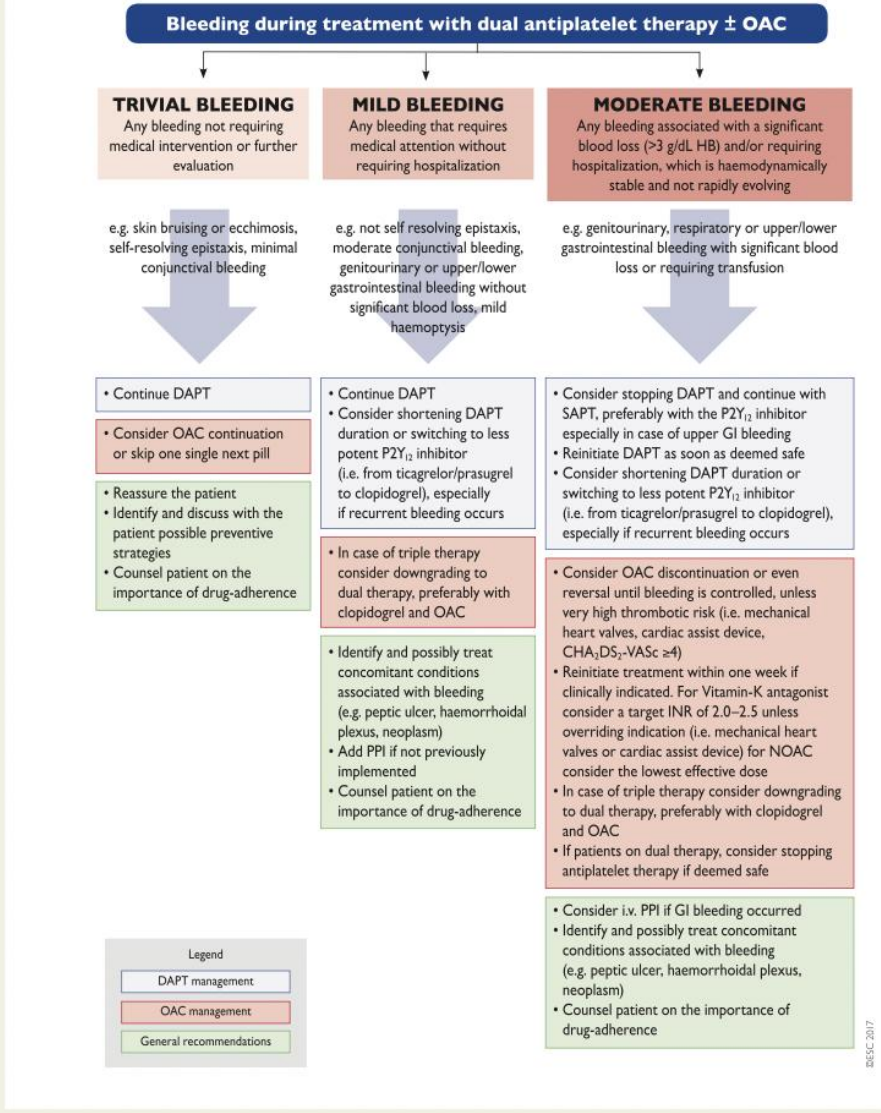

Figure 10 Practical recommendations for the management of bleeding in patients treated with dual antiplatelet therapy with or without concomitant oral anticoagulation. Practical recommendations for the management of bleeding in patients treated with dual antiplatelet therapy with or without concomitant oral anticoagulation. Blue boxes refer to management of antiplatelet therapy. Dark-red boxes refer to the management of oral anticoagulation. Light-green boxes refer to general recommendation for patients' safety.
ACS = acute coronary syndrome; CHA_2DS_2-VASc= cardiac failure, hypertension, age ≥75 (2 points), diabetes, stroke (2 points)–vascular disease, age 65–74, sex category; DAPT = dual antiplatelet therapy; GI = gastrointestinal; HB = haemoglobin; INR = international normalized ratio; i.v. = intravenous; OAC = oral anticoagulant; NOAC = non-vitamin-K antagonist; PPI = proton pump inhibitor; RBC = red blood cell; SAPT = single antiplatelet therapy.

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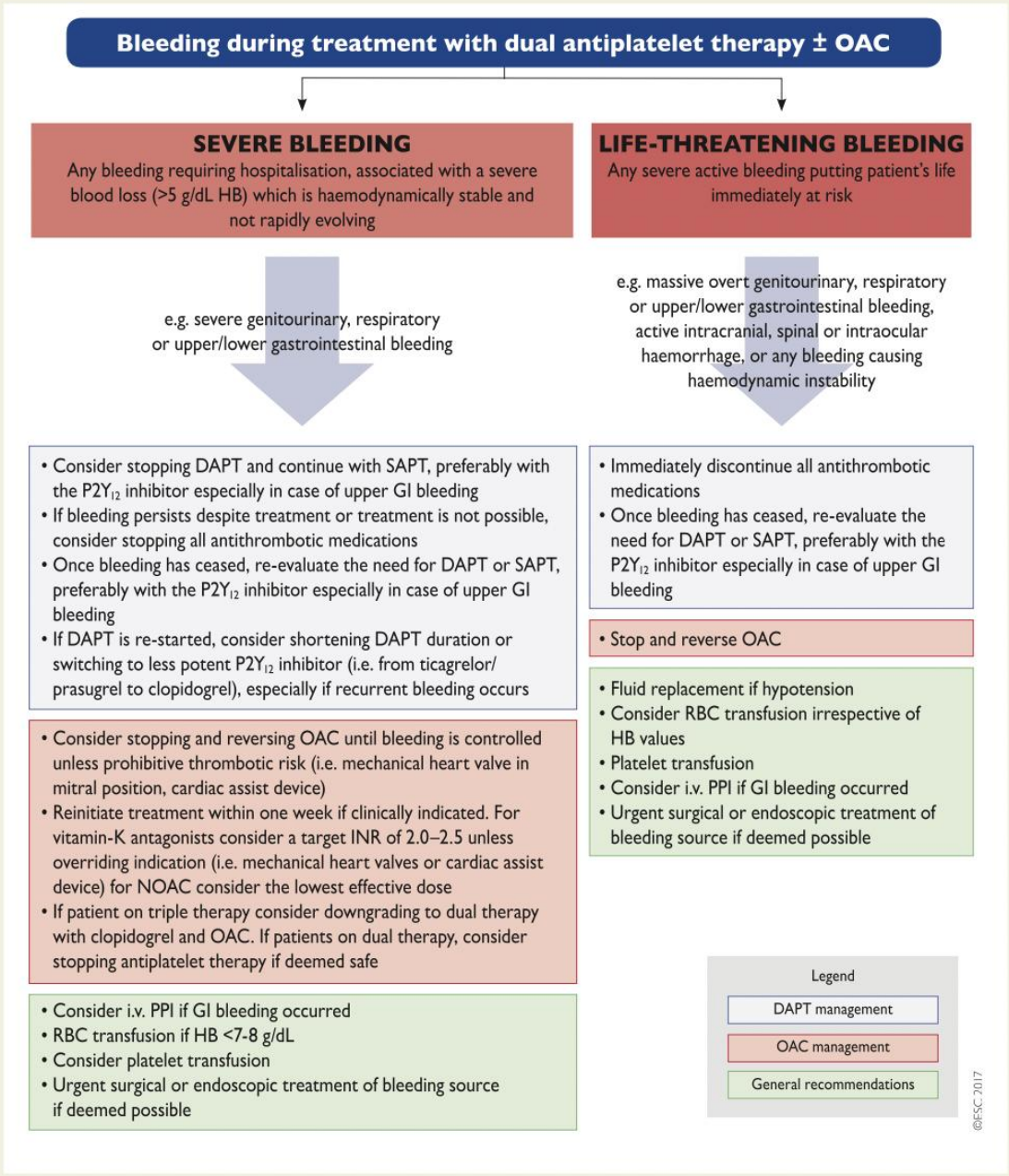

Figure 10 Continued

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