2022

¿Cómo tratar al paciente anticoagulado crónicamente luego de la angioplastia?

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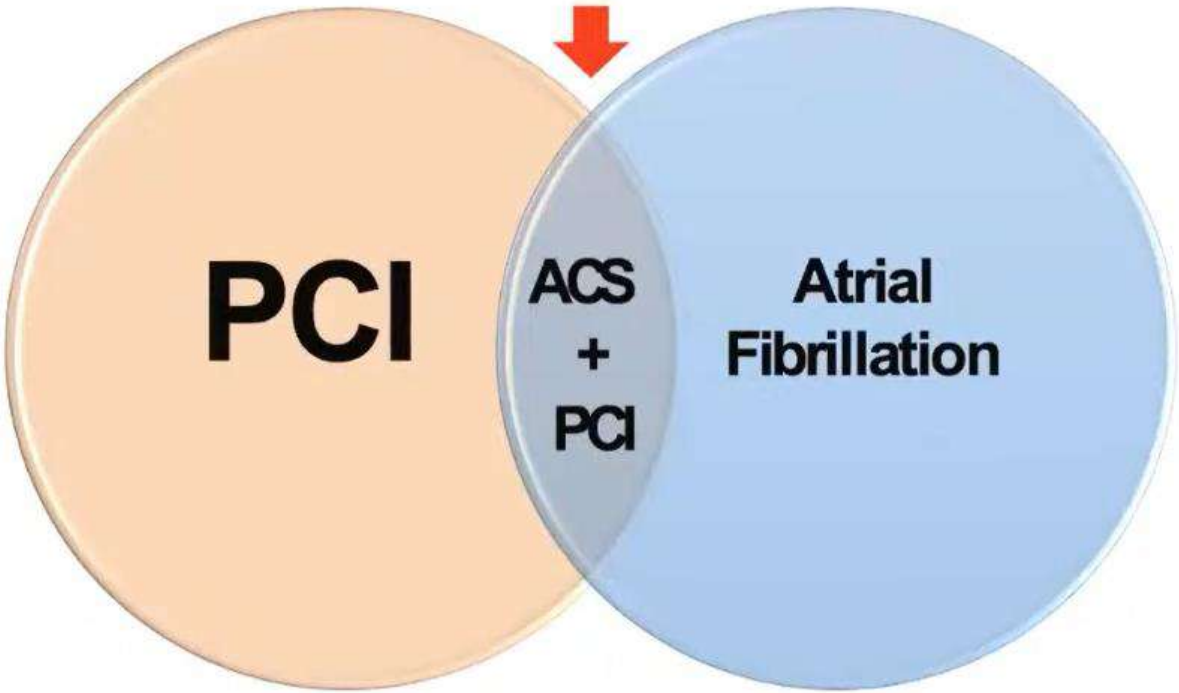
Background

Frecuentemente, pacientes sometidos a ANGIOPLASTIA - requieren A.C.O

- Fibrilacion auricular.
- Trombosis venosa.
- Válvulas protesicas.

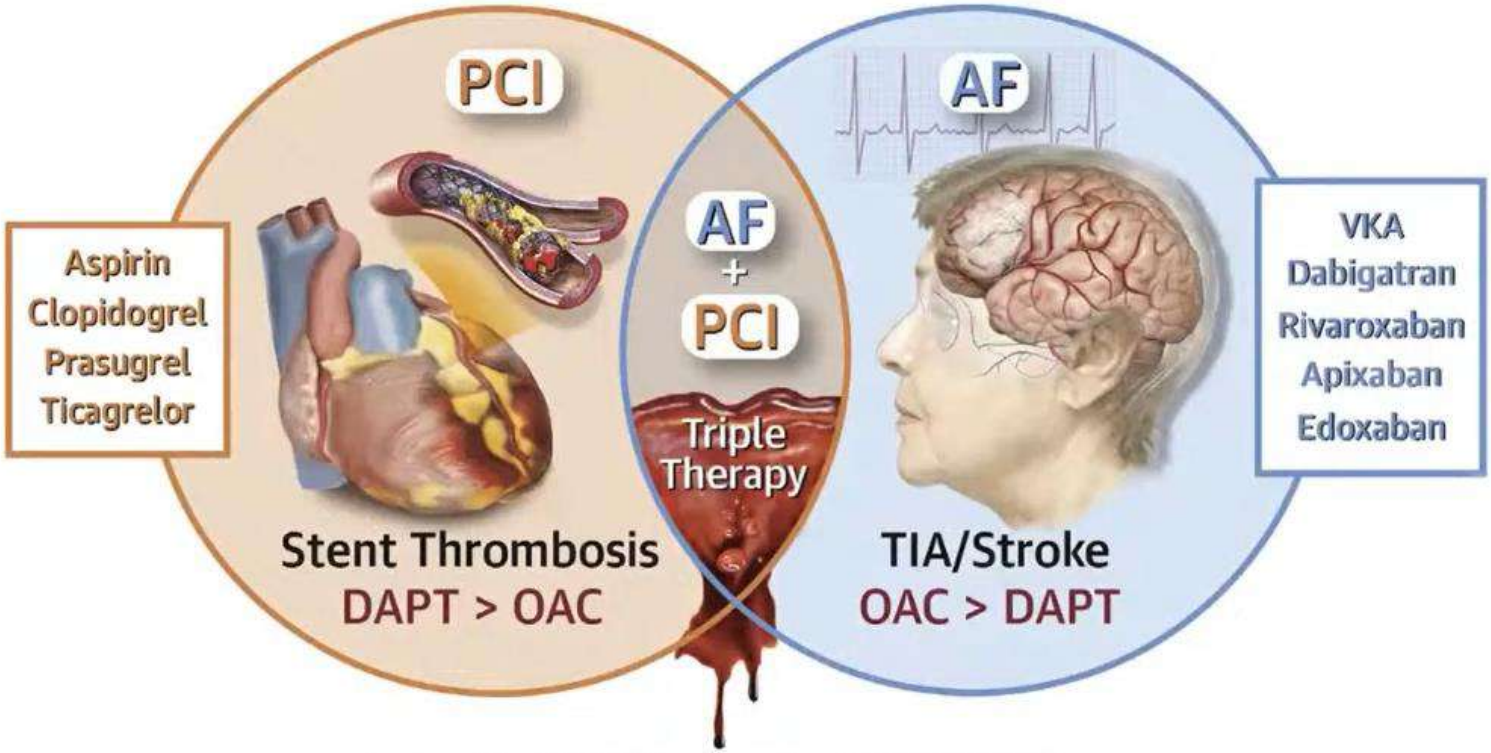
La evidencia más robusta del manejo - deriva de los pacientes con FA.

~5-8% of patients who undergo PCI have atrial fibrillation [1,2]



1. Rubboli A, Colletta M. Dis 2007;18:193-9.
2. Wang TY, Robinson LA. Am Heart J 2008;155:361-8.

DESAFIOS EN PACIENTES CON F.A y PTCA



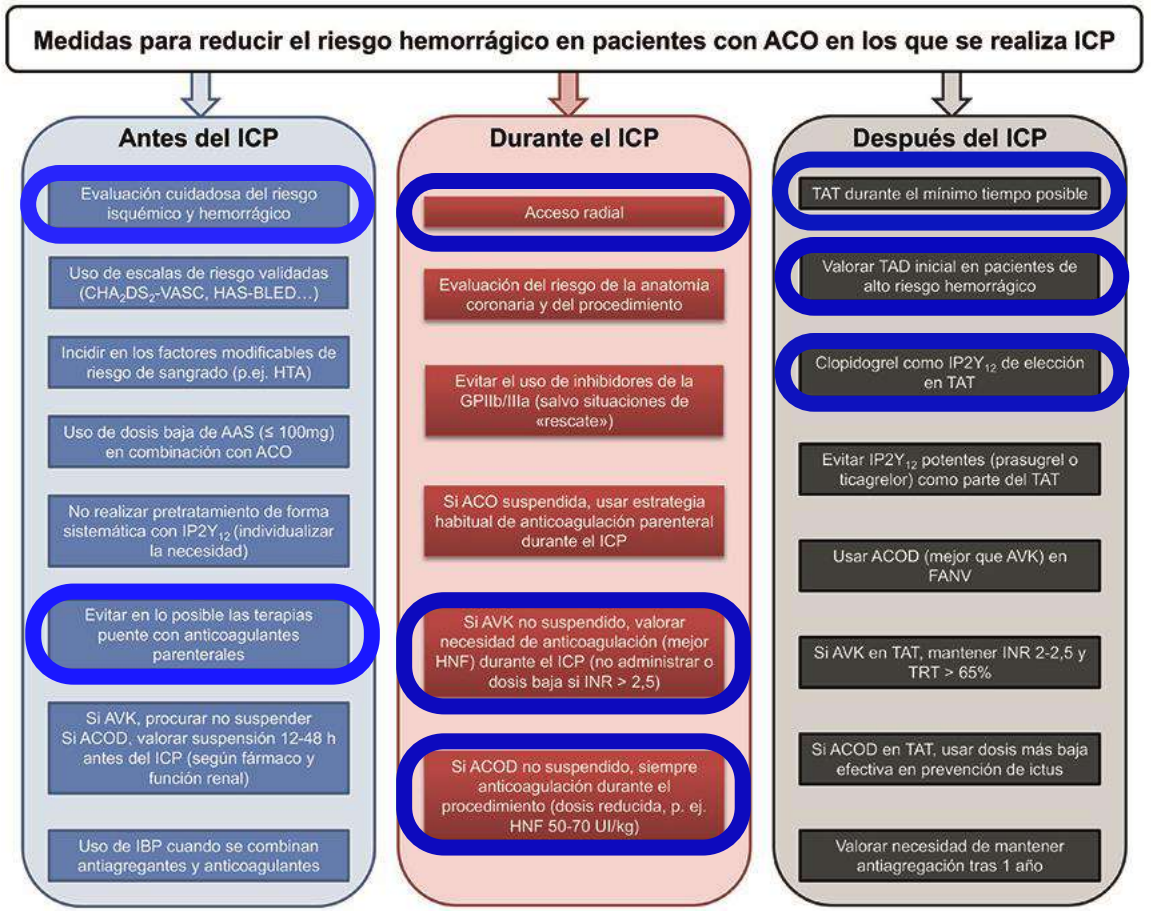
Capodanno D, Angiolillo DJ JACC cardiovasc Interv, 2017;10(11):1086-1088

THROMBOTIC RISK FACTORS

- Diabetes mellitus requiring therapy
- Prior ACS/recurrent myocardial infarction
- Multivessel CAD
- Concomitant PAD
- Premature CAD (occurring at age of <45 y) or accelerated CAD (new lesion within 2 years)
- CKD (eGFR <60 mL/min)
- Clinical presentation (ACS)
- Multivessel stenting
- Complex revascularisation (left main stenting, bifurcation lesion stenting, chronic total occlusion intervention, last patent vessel stenting)
- Prior stent thrombosis on antiplatelet treatment
- Procedural factors (stent expansion, residual dissection, stent length, etc.)

BLEEDING RISK FACTORS

- Hypertension
- Abnormal renal or liver function
- Stroke or ICH history
- Bleeding history or bleeding diathesis (e.g., anaemia with haemoglobin <110 g/L)
- Labile INR (if on VKA)
- Elderly (>65 years)
- Drugs (concomitant OAC and antiplatelet therapy, NSAIDs), excessive alcohol consumption

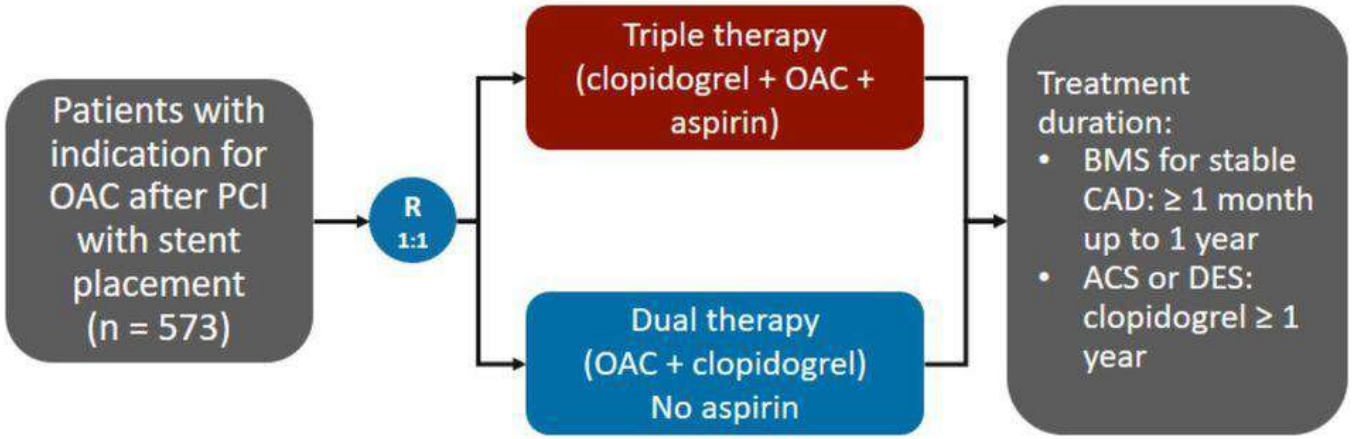


REC Interv Cardiol. 2019;1(1):41-50. doi.org/10.24875/RECIC.M19000006

COMBINACIONES POSIBLES EN S.C.A y FA

ENORME NÚMERO DE COMBINACIONES!!!

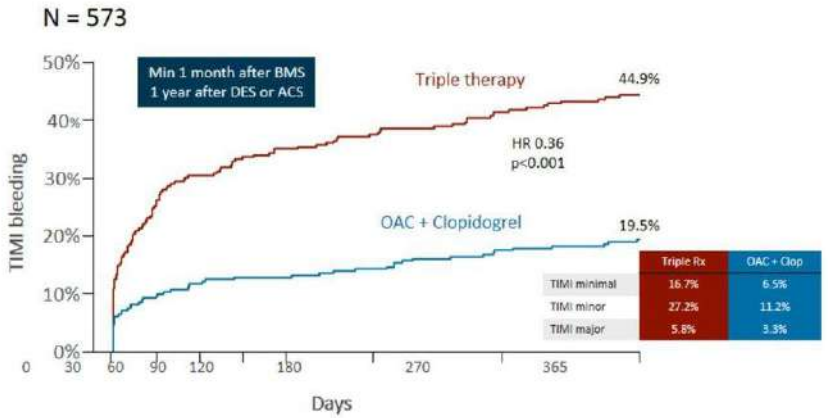
WOEST
Study Design



- Primary endpoint: composite of minor, moderate, and major bleeding according to TIMI and GUSTO criteria
- Secondary endpoint: composite of death, MI, stroke, systemic embolization, target vessel revascularization, and stent thrombosis

Dewilde W, et al. *Am Heart J.* 2009;158:713-718.

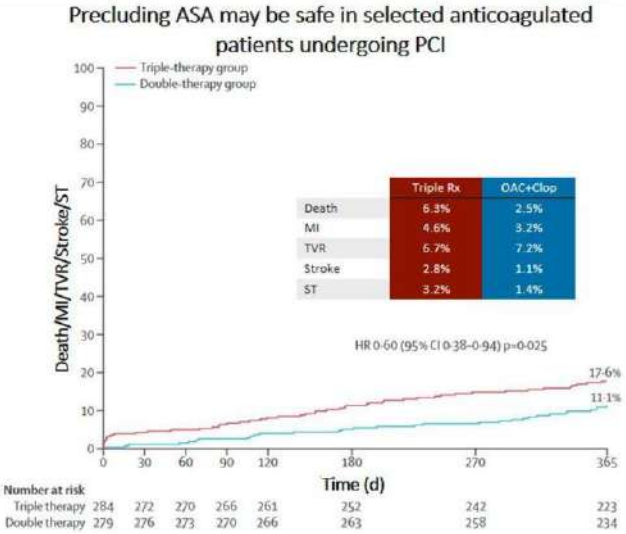
WOEST - VKA in Patients With AF Undergoing PCI Any Bleeding



OAC indication: 69% AF, 11% mechanical prosthesis. Mean INR 1.9 on day of PCI, radial 26%, DES 67%

Dewilde WJ et al. *Lancet* 2013;381:1107-1115.

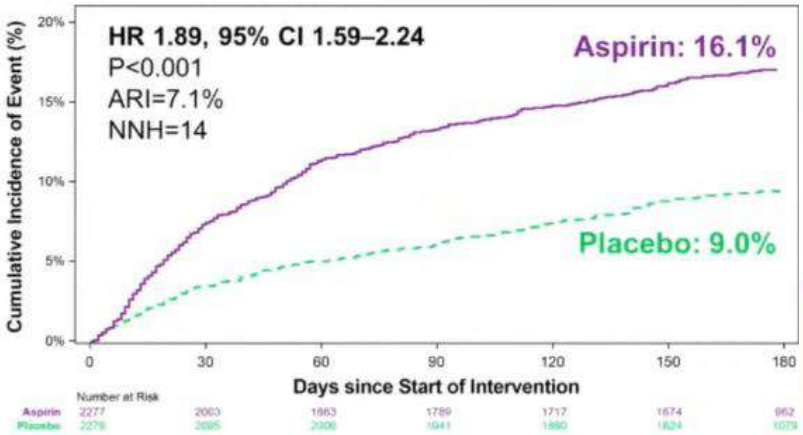
WOEST - VKA in Patients With AF Undergoing PCI Efficacy



Dewilde WJ et al. *Lancet* 2013;381:1107-1115.

AUGUSTUS TRIAL: TRIPLE VS. DUAL THERAPY

Major / CRNM Bleeding
Aspirin vs. Placebo



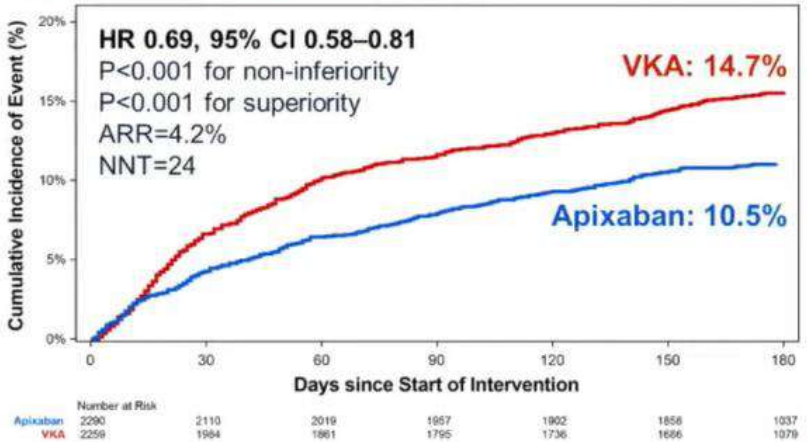
Ischemic Outcomes
Aspirin vs. Placebo

Endpoint	Aspirin (N=2307)	Placebo (N=2307)	HR (95% CI)
Death / Ischemic Events (%)	6.5	7.3	0.89 (0.71–1.11)
Death (%)	3.1	3.4	0.91 (0.66–1.26)
CV Death (%)	2.3	2.5	0.92 (0.63–1.33)
Stroke (%)	0.9	0.8	1.06 (0.56–1.98)
Myocardial Infarction (%)	2.9	3.6	0.81 (0.59–1.12)
Definite or Probable Stent Thrombosis (%)	0.5	0.9	0.52 (0.25–1.08)
Urgent Revascularization (%)	1.6	2.0	0.79 (0.51–1.21)
Hospitalization (%)	25.4	23.4	1.10 (0.98–1.24)

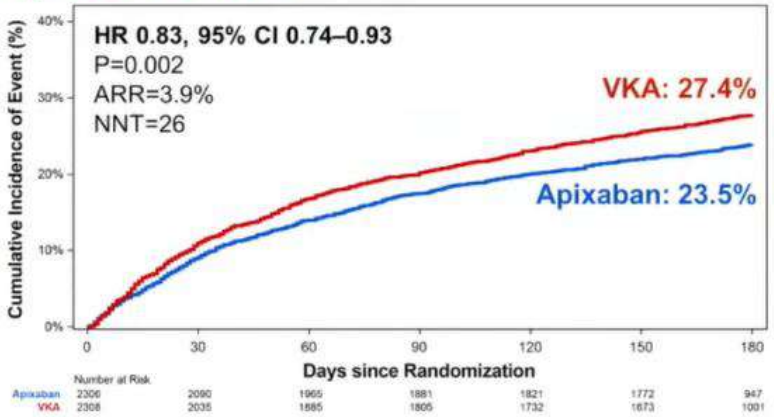
Lopes RD et al. N Engl J Med. 2019;380:1509-24

AUGUSTUS TRIAL: APIXABAN VS. VKA

Major / CRNM Bleeding
Apixaban vs. VKA

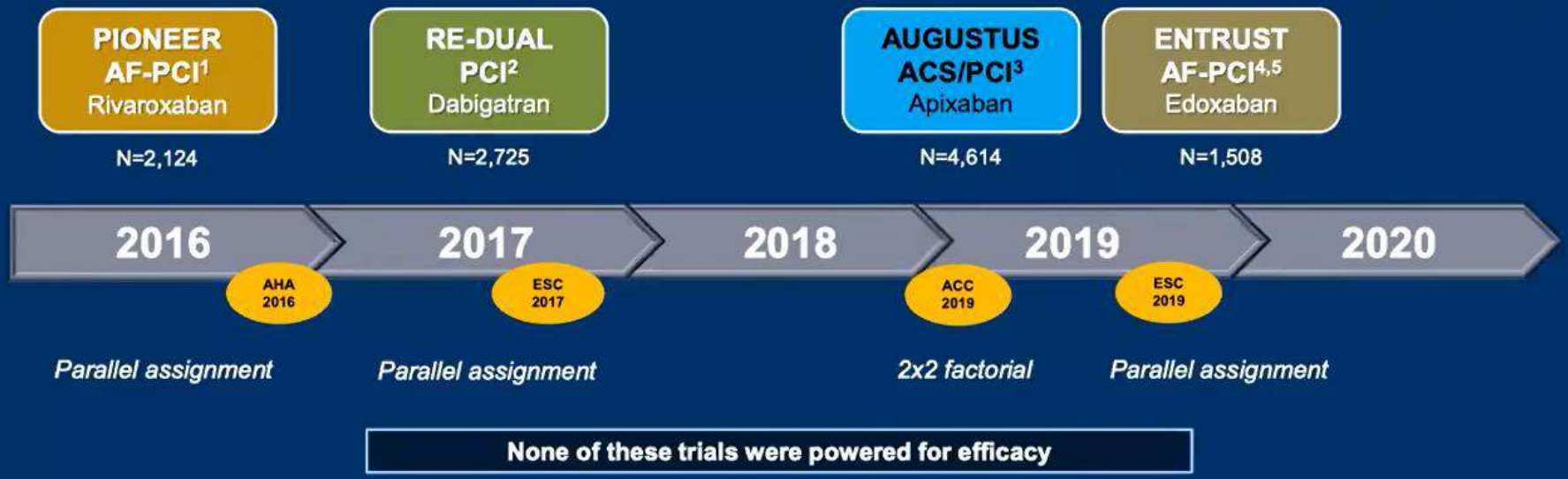


Death / Hospitalization
Apixaban vs. VKA



Lopes RD et al. N Engl J Med. 2019;380:1509-24

Evidencia con DOACS en FA + PCI



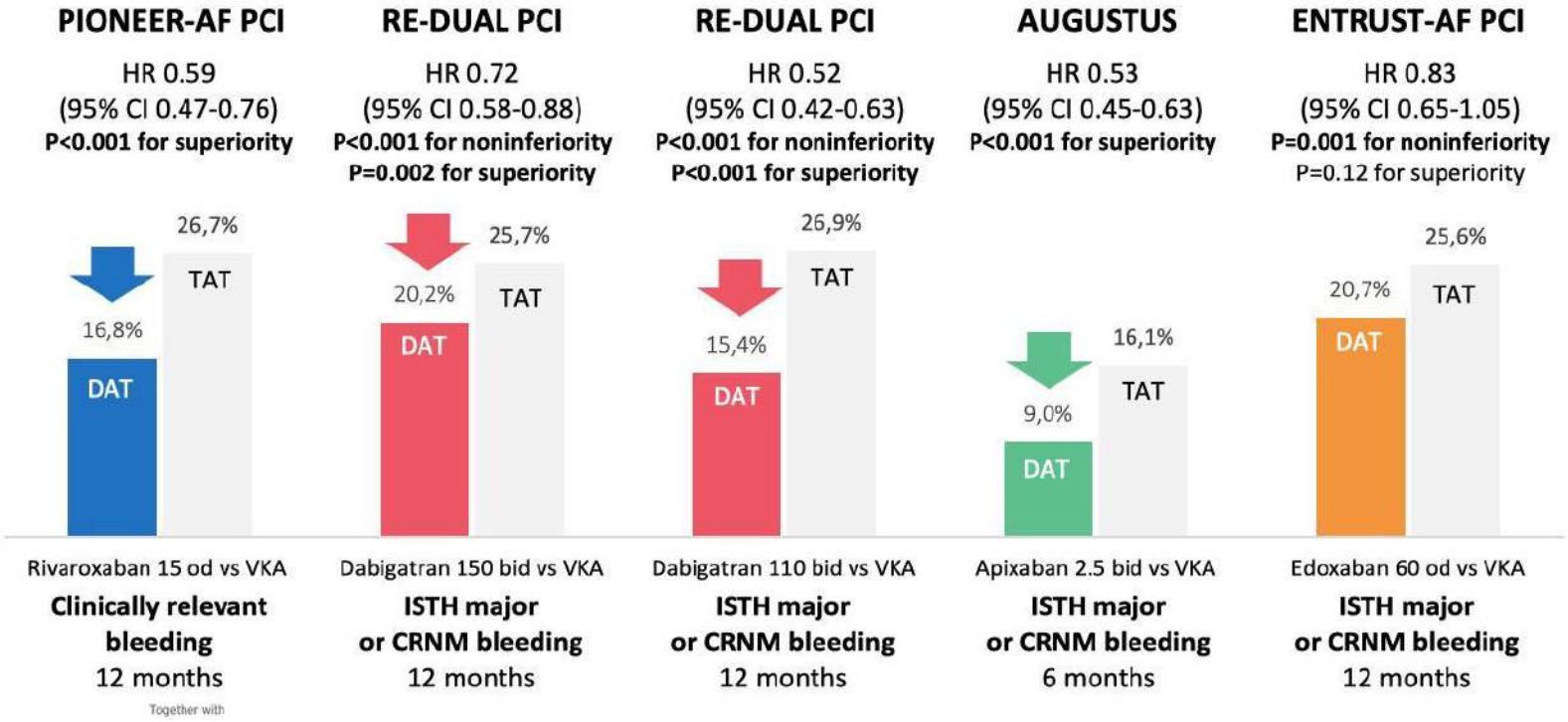
None of these trials were powered for efficacy

Duke Clinical Research Institute
From Thought Leadership to Clinical Practice

ACC, American College of Cardiology; AHA, American Heart Association.
1. Gibson CM, et al. N Engl J Med 2016;375:2423–34; 2. Cannon CP, et al. N Engl J Med 2017;377:1513–24;
3. Lopes RD, et al. N Engl J Med 2019;380:1509–24; 4. Vranckx P, et al. Am Heart J 2018;196:105–12; 5. NCT02866175. Available at: clinicaltrials.gov/ct2/show/NCT02866175. Accessed Aug 2019.

Evolving paradigms in antithrombotic therapy for AF

Comparisons of DAT vs. TAT in trials of NOACs



Together with

TRIPLE O DOBLE TERAPIA: METAANÁLISIS

META-ANALYSIS (ACOD TRIALS IN AF-PCI)

ISTH major or CRNM bleeding

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	204	2279	367	2277	26.8%	0.56 [0.47, 0.65]
ENTRUST AF-PCI	128	751	152	755	22.3%	0.85 [0.68, 1.05]
PIONEER AF-PCI	117	696	178	697	22.7%	0.66 [0.53, 0.81]
RE-DUAL PCI	305	1744	264	981	28.2%	0.65 [0.56, 0.75]
Total (95% CI)		**5470**		**4710**	**100.0%**	**0.66 [0.56, 0.78]**
Total events	754		961			

Heterogeneity: Tau² = 0.02; Chi² = 9.65, df = 3 (P = 0.02); I² = 69%
Test for overall effect: Z = 5.03 (P < 0.00001)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours DAT Favours TAT

TIMI major bleeding

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	29	2279	55	2277	35.6%	0.53 [0.34, 0.82]
ENTRUST AF-PCI	15	751	24	755	17.5%	0.63 [0.33, 1.19]
PIONEER AF-PCI	14	696	20	697	15.6%	0.70 [0.36, 1.38]
RE-DUAL PCI	30	1744	37	981	31.4%	0.46 [0.28, 0.73]
Total (95% CI)		**5470**		**4710**	**100.0%**	**0.54 [0.42, 0.71]**
Total events	88		136			

Heterogeneity: Tau² = 0.00; Chi² = 1.29, df = 3 (P = 0.73); I² = 0%
Test for overall effect: Z = 4.50 (P < 0.00001)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours DAT Favours TAT

Myocardial infarction

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	84	2307	68	2307	46.5%	1.24 [0.90, 1.69]
ENTRUST AF-PCI	29	751	23	755	15.9%	1.27 [0.74, 2.17]
PIONEER AF-PCI	19	694	21	695	12.3%	0.91 [0.49, 1.67]
RE-DUAL PCI	70	1744	29	981	25.4%	1.36 [0.89, 2.08]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.22 [0.99, 1.52]**
Total events	202		141			

Heterogeneity: Tau² = 0.00; Chi² = 1.18, df = 3 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.84 (P = 0.07)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours DAT Favours TAT

Stent thrombosis

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	21	2307	11	2307	38.5%	1.91 [0.92, 3.95]
ENTRUST AF-PCI	8	751	6	755	18.3%	1.34 [0.47, 3.84]
PIONEER AF-PCI	5	694	4	695	11.8%	1.25 [0.34, 4.64]
RE-DUAL PCI	22	1744	8	981	31.4%	1.55 [0.69, 3.46]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.59 [1.01, 2.50]**
Total events	56		29			

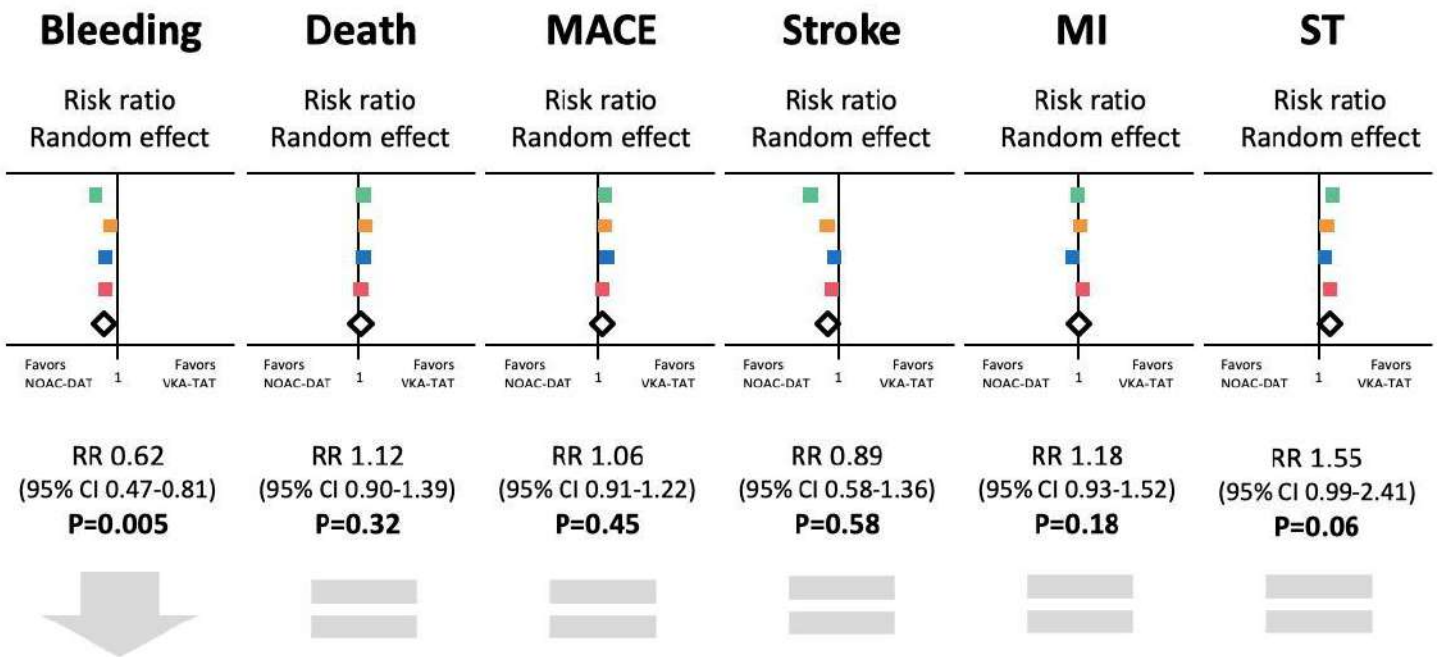
Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 3 (P = 0.92); I² = 0%
Test for overall effect: Z = 2.02 (P = 0.04)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours DAT Favours TAT

Gargiulo G et al. Eur Heart J. 2019; 40:3757-67

7,927 patients from 4 trials of NOACs

Meta-analysis of NOAC-DAT vs VKA-TAT



Adapted from Vranckx P, et al. Lancet 2019 [ePub ahead of print]

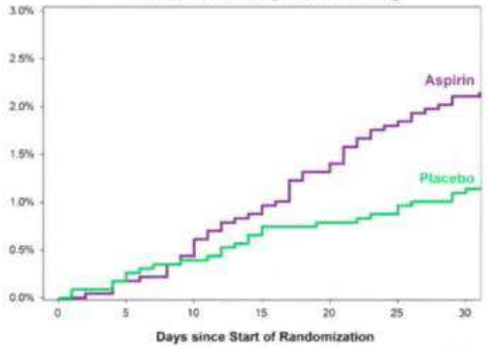
ASPECTOS CONTROVERTIDOS

TRIPLE O DOBLE TERAPIA?: EVENTOS TEMPRANOS Y TARDÍOS

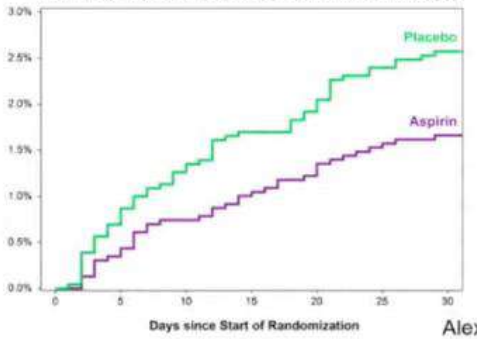
Severe Bleeding and Ischemic Outcomes

Randomization to 30 Days

Fatal, ICH, Major Bleeding



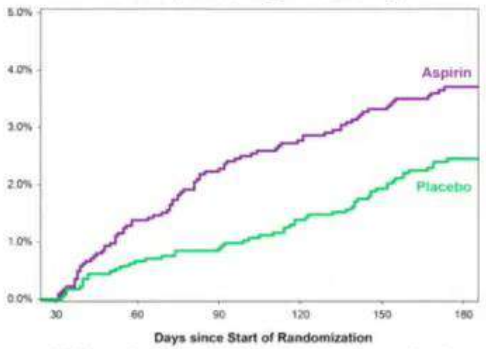
CV Death, Stroke, MI, Stent Thrombosis



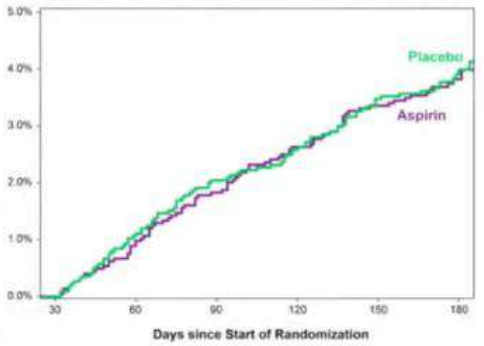
Severe Bleeding and Ischemic Outcomes

30 Days to 6 Months

Fatal, ICH, Major Bleeding



CV Death, Stroke, MI, Stent Thrombosis



Alexander JH et al. Circulation. 2020;141:1618-27

EVITAR TRATAMIENTO ANTIPLAQUETARIO PROLONGADO?

Atrial Fibrillation and Ischemic events with Rivaroxaban AFIRE in patiEnts with stable coronary artery disease: AFIRE Study

A multicenter, prospective, randomized, open-label, parallel-group trial [1]

2200 patients with AF ($CHADS_2 \geq 1$) and stable CAD

Key inclusion criteria
- Underwent PCI or CABG more than 1 year earlier
- Angiographically confirmed CAD (with stenosis of ≥50%) not requiring revascularization

Key exclusion criteria
- A history of stent thrombosis
- Coexisting active tumor
- Poorly controlled hypertension

RANDOMIZE

Rivaroxaban Monotherapy
- **Rivaroxaban** 10 or 15 mg/day [2]*

*The level of rivaroxaban in blood samples obtained from Japanese patients who were taking rivaroxaban at the 15-mg dose was similar to the level in white patients who were taking the 20-mg dose.

Combination Therapy
- **Rivaroxaban** 10 or 15 mg/day
- **Single antiplatelet**
  Aspirin 81 or 100 mg/day,
  Clopidogrel 50 or 75 mg/day, Prasugrel 2.5 or 3.75 mg/day

UMIN Clinical Trials Registry number, UMIN000016612.
ClinicalTrials.gov number, NCT02642419.

1) Yasuda S, et al. *Int J Cardiol.* 2018. 2) Tanigawa T, et al. *Drug Metab Pharmacokinet.*

EVITAR TRATAMIENTO ANTIPLAQUETARIO PROLONGADO?

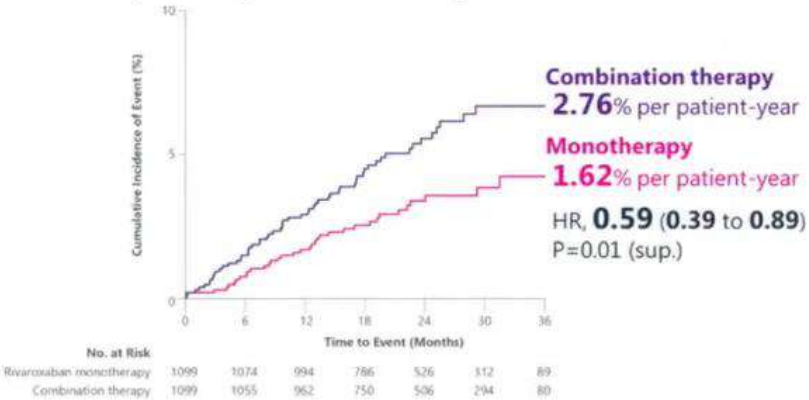
Atrial Fibrillation and Ischemic events with Rivaroxaban in patiEnts with stable coronary artery disease: AFIRE Study

Primary Efficacy End Point

The composite of stroke, systemic embolism, myocardial infarction, unstable angina requiring revascularization, or death from any cause

Primary Safety End Point

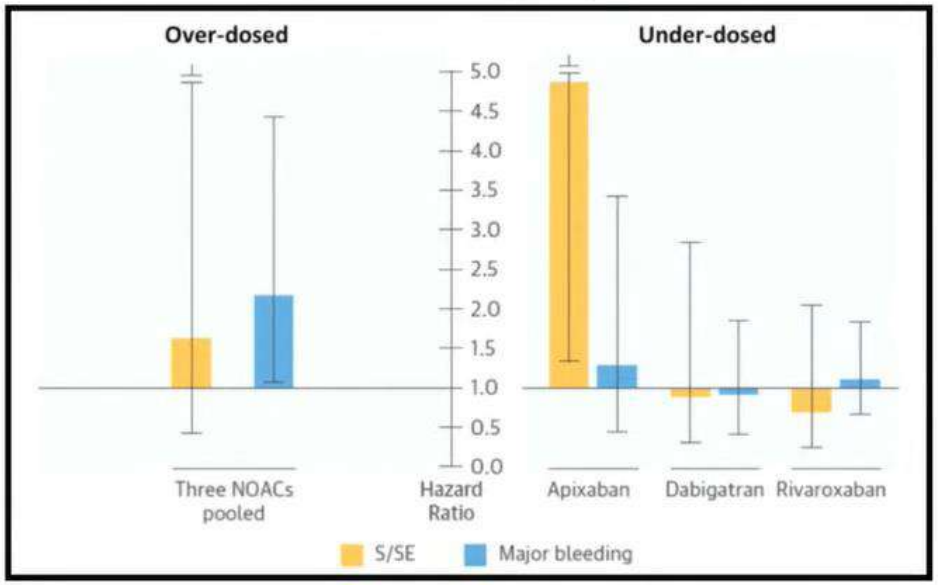
Major bleeding, as defined according to the criteria of the ISTH



Yasuda S et al. N Engl J Med. 2019;381:1103-13

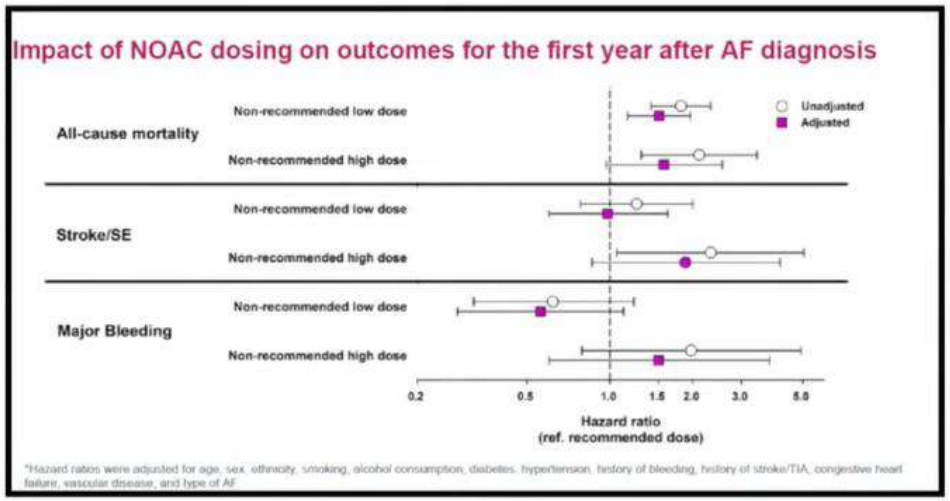
DOSIS DE NOACs Y RESULTADOS

US database: 14,865 patients



Yao X et al. J Am Coll Cardiol. 2017;69:2779-90.

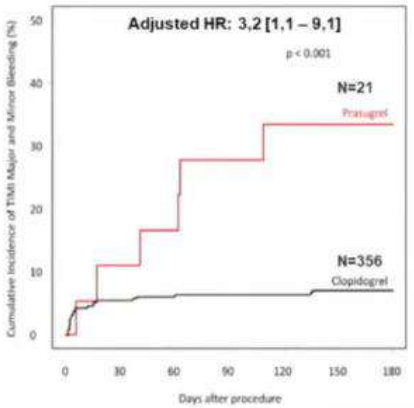
GARFIELD-AF Registry: Newly-diag



Camm AJ et al. Presented at ESC Congress. Munich,2018

USO DE ANTAGONISTAS DE P2Y12

DES patients with chronic OAC



PCI and chronic OAC

Table 3. Outcomes According to $P2Y_{12}$ Inhibitor Group.[a]

	Ticagrelor or Prasugrel (n = 42)	Clopidogrel (n = 126)	*P* Value
Any bleeding	12 (28.6)	16 (12.7)	.017
MACCE	8 (19)	23 (18.3)	.91
Cardiac death	3 (7.1)	4 (3.2)	.37
Myocardial infarction	7 (16.7)	20 (15.9)	.90
Ischemic stroke	1 (2.4)	4 (3.2)	1.00

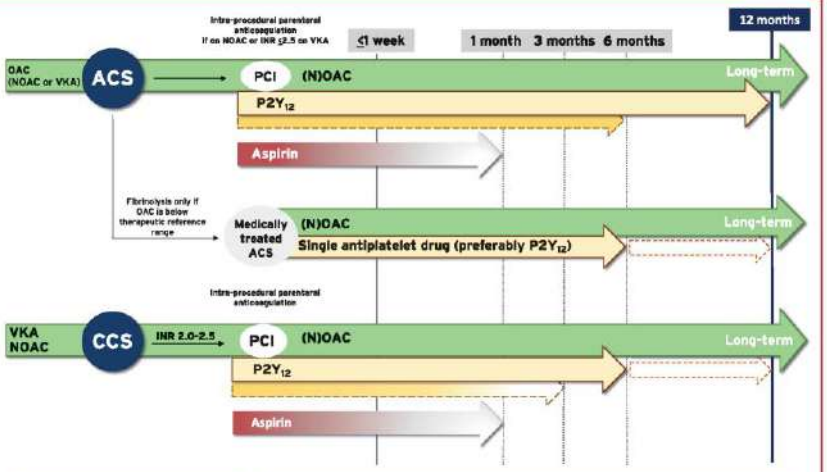
ESC 2020 NSTEACS Guidelines

DAT (with an OAC and either ticagrelor or prasugrel) may be considered as an alternative to TAT (with an OAC, aspirin, and clopidogrel) in patients with a moderate or high risk of stent thrombosis, irrespective of the type of stent used.	IIb	C

Sarafoff N et al. J Am Coll Cardiol 2013

Collet JP et al. Eur Heart J. 2020
Hindricks G et al. Eur Heart J. 2020
Angiolillo DJ et al. Circulation. 2021

Verlinden NJ et al. J Cardiovasc Pharmacol Ther. 2017



THROMBOTIC RISK FACTORS

- Diabetes mellitus requiring therapy
- Prior ACS/recurrent myocardial infarction
- Multivessel CAD
- Concomitant PAD
- Premature CAD (occurring at age of <45 y) or accelerated CAD (new lesion within 2 years)
- CKD (eGFR <60 mL/min)
- Clinical presentation (ACS)
- Multivessel stenting
- Complex revascularisation (left main stenting, bifurcation lesion stenting, chronic total occlusion intervention, last patent vessel stenting)
- Prior stent thrombosis on antiplatelet treatment
- Procedural factors (stent expansion, residual dissection, stent length, etc.)

BLEEDING RISK FACTORS

- Hypertension
- Abnormal renal or liver function
- Stroke or ICH history
- Bleeding history or bleeding diathesis (e.g., anaemia with haemoglobin <110 g/L)
- Labile INR (if on VKA)
- Elderly (>65 years)
- Drugs (concomitant OAC and antiplatelet therapy, NSAIDs), excessive alcohol consumption

STRATEGIES TO REDUCE BLEEDING ASSOCIATED WITH PCI

- Radial artery access
- PPIs in patients taking DAPT who are at increased risk of bleeding (e.g., the elderly, dyspepsia, gastro-oesophageal reflux disease, Helicobacter pylori infection, chronic alcohol use)
- Non-administration of unfractionated heparin in patients on VKA with INR >2.5
- Pre-treatment with aspirin only, add a $P2Y_{12}$ inhibitor when coronary anatomy is known or if STEMI
- GP IIb/IIIa inhibitors only for bailout or periprocedural complications
- Shorter duration of combined antithrombotic therapy

AF patients undergoing PCI—2021 North American Consensus

Time from PCI	Default strategy	Patients at high ischemic/thrombotic and low bleeding risk	Patients at low ischemic/thrombotic or high bleeding risk
Peri-PCI	Triple Therapy (OAC + DAPT)	Triple Therapy (OAC + DAPT)	Triple Therapy (OAC + DAPT)
1 month	Double Therapy up to 12 months (OAC + $P2Y_{12}$ inhibitor)	Triple Therapy up to 1 month (OAC + DAPT)	Double Therapy up to 6 months (OAC + $P2Y_{12}$ inhibitor)
3 months		Double Therapy up to 12 months (OAC + $P2Y_{12}$ inhibitor)	
6 months			
12 months			OAC alone
>12 months	OAC alone	OAC alone	

Peri-PCI period: inpatient stay until time of discharge or a few days longer, up to 1 week post-PCI.

OAC: prefer a NOAC over VKA if no contraindications.

Clopidogrel is the $P2Y_{12}$ inhibitor of choice; ticagrelor may be considered in patients at high thrombotic and acceptable bleeding risks; avoid prasugrel.

Continuation of antiplatelet therapy in adjunct to OAC beyond one-year should be considered only for select patients with high risk for ischemic recurrences and low bleeding risk.

Recommendations for patients with AF and an ACS, PCI, or CCS[1068]

General recommendations for patients with AF and an indication for concomitant antiplatelet therapy	Class[a]	Level[b]
In AF patients eligible for NOACs, it is recommended to use a NOAC[c] in preference to a VKA in combination with antiplatelet therapy.[1079,1081]	I	A
In patients at high bleeding risk (HAS-BLED ≥3), rivaroxaban 15 mg o.d. should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk.[1080]	IIa	B
In patients at high bleeding risk (HAS-BLED ≥3), dabigatran 110 mg b.i.d. should be considered in preference to dabigatran 150 mg b.i.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk.[1079]	IIa	B
In AF patients with an indication for a VKA in combination with antiplatelet therapy, the VKA dosing should be carefully regulated with a target INR of 2.0 - 2.5 and TTR>70%.[1094,1095,1104,1105]	IIa	B
Recommendations for AF patients with ACS		
In AF patients with ACS undergoing an uncomplicated PCI, early cessation (≤1 week) of aspirin and continuation of dual therapy with an OAC and a $P2Y_{12}$ inhibitor (preferably clopidogrel) for up to 12 months is recommended if the risk of stent thrombosis[d] is low or if concerns about bleeding risk[e] prevail over concerns about risk of stent thrombosis,[d] irrespective of the type of stent used.[1090,1092–1095]	I	B
Triple therapy with aspirin, clopidogrel, and an OAC[f] for longer than 1 week after an ACS should be considered when risk of stent thrombosis[d] outweighs the bleeding risk,[e] with the total duration (≤1 month) decided according to assessment of these risks, and the treatment plan should be clearly specified at hospital discharge.	IIa	C
Recommendations in AF patients with a CCS undergoing PCI		
After uncomplicated PCI, early cessation (≤1 week) of aspirin and continuation of dual therapy with OAC for up to 6 months and clopidogrel is recommended if the risk of stent thrombosis[d] is low or if concerns about bleeding risk[e] prevail over concerns about risk of stent thrombosis,[d] irrespective of the type of stent used.[1076,1078–1081]	I	B
Triple therapy with aspirin, clopidogrel, and an OAC[f] for longer than 1 week should be considered when risk of stent thrombosis[d] outweighs the bleeding risk,[e] with the total duration (≤1 month) decided according to assessment of these risks, and the treatment plan should be clearly specified at hospital discharge.	IIa	C

CONCLUSIONES

- Aspectos más claros
  - Individualizar con balance cuidadoso de riesgos: isquémico, tromboembólico y hemorrágico
  - **NOACs** son más seguros que AVKs tanto en triple como en doble terapia antitrombótica
    - Diseño del ensayo AUGUSTUS (apixabán)
    - Importante: dosis adecuadas
  - Triple terapia: el mínimo tiempo estrictamente necesario
- Aspectos menos claros
  - Duración **triple terapia**: entre 1 semana (según guías) y **1 mes** (p.ej. SCA)
    - Doble terapia inmediatamente tras ICP si muy alto riesgo de sangrado
  - Uso de inhibidores potentes $P2Y_{12}$: evitar generalmente como parte de triple terapia
    - Falta evidencia sobre uso en doble terapia
  - Doble terapia antitrombótica: ACO + ¿AAS o clopidogrel?
  - Necesidad de antiagregante además de ACO 1 año tras el ICP: individualizar

- MUCHAS GRACIAS!!!