L'Acadèmia
FUNDACIÓ ACADÈMIA DE CIÈNCIES MÈDIQUES I DE LA SALUT DE CATALUNYA I DE BALEARS

SOCIETAT CATALANA DE CARDIOLOGIA

www.catcardio.cat

Programa

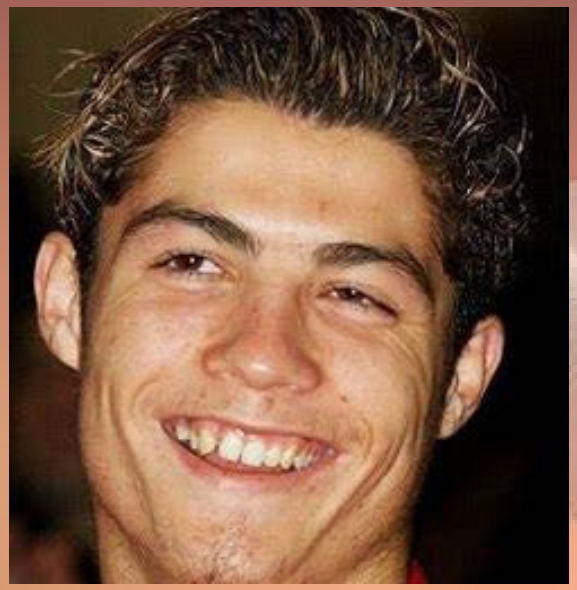
IV JORNADA D'ACTUALITZACIÓ

GRUP D'UNITATS DE CURES AGUDES CARDIOLÒGIQUES

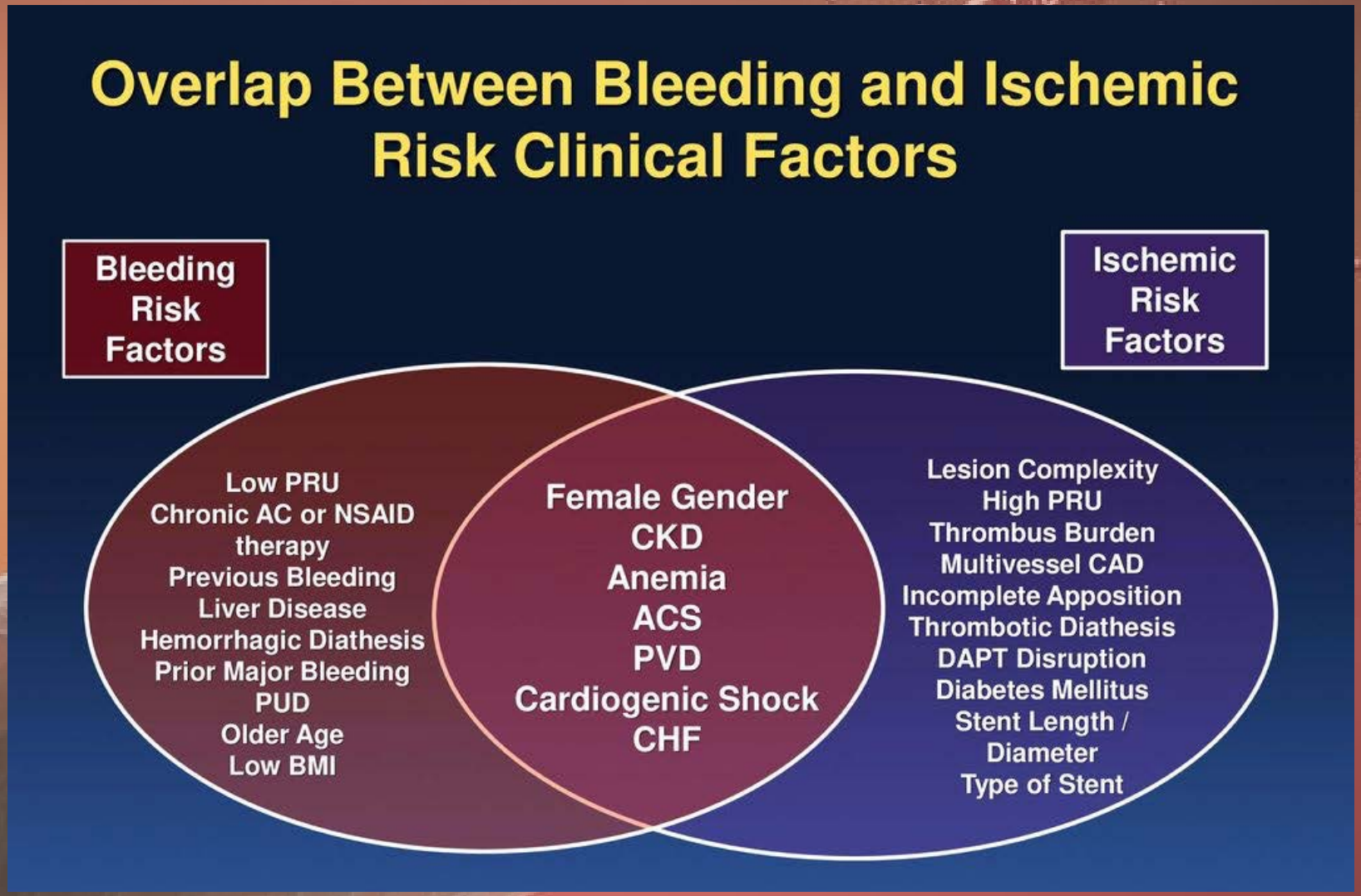
Hemorragia en el paciente bajo tratamiento antitrombótico

Pablo Pastor Pueyo

Hospital Universitari Arnau de Vilanova, Lleida

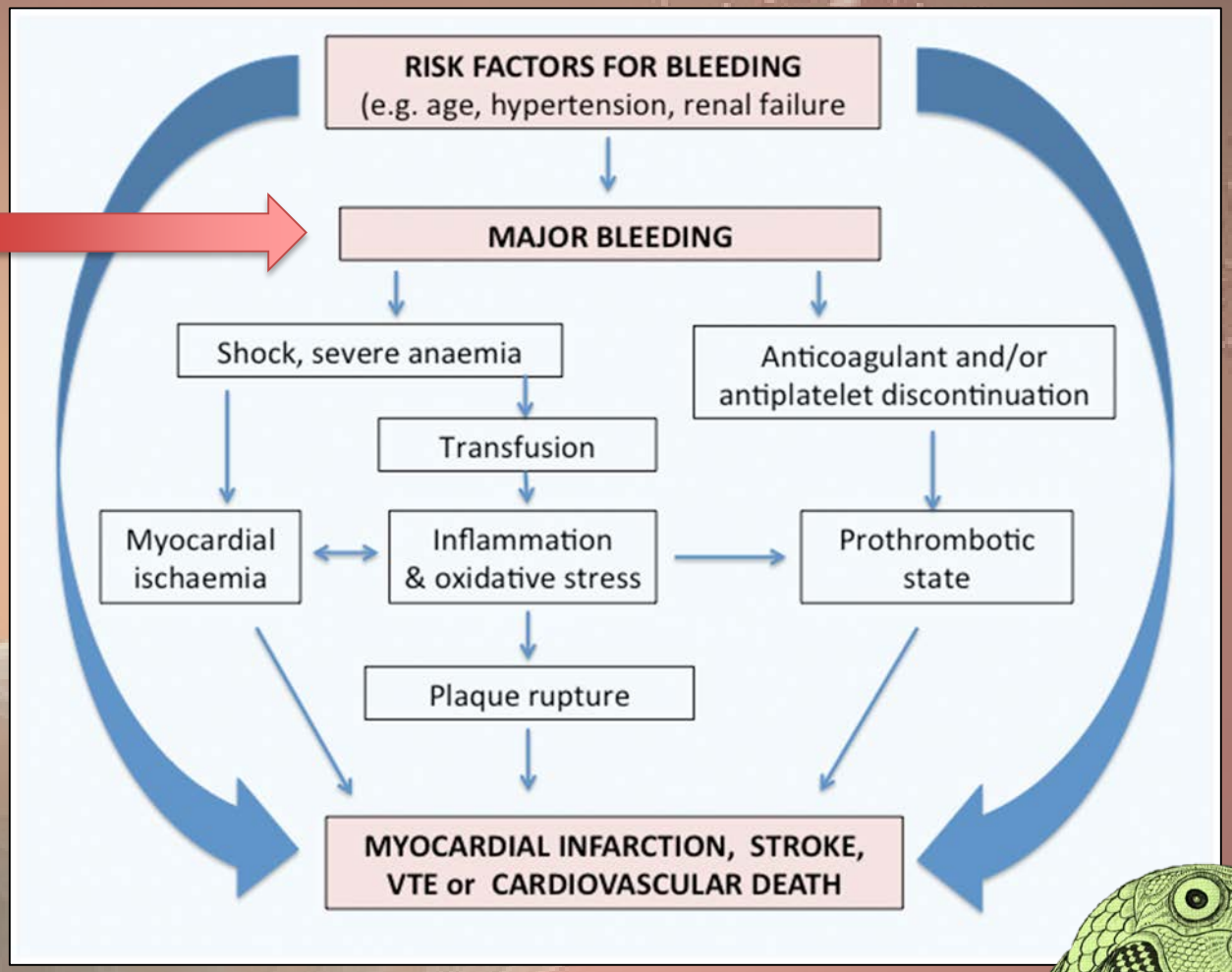


En busca del *sweet spot*

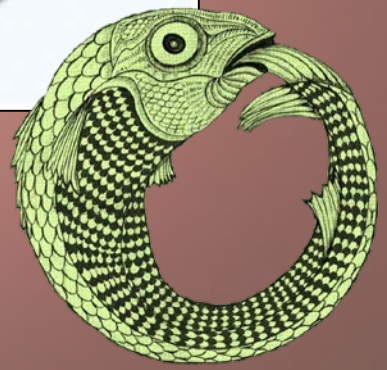


Ferreiro, J. L., Sibbing, D., & Angiolillo, D. (2010). Platelet function testing and risk of bleeding complications. Thrombosis and Haemostasis, 103(06), 1128–1135.

Más anti-trombóticos

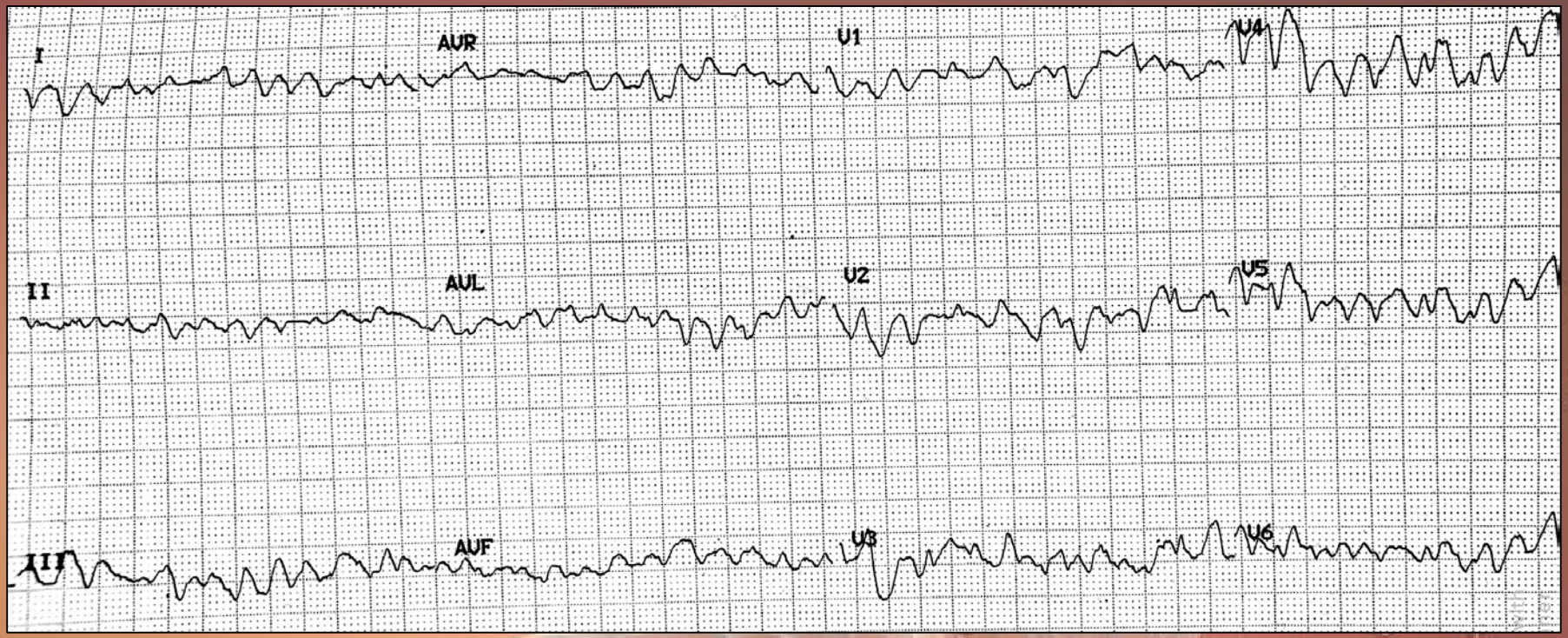


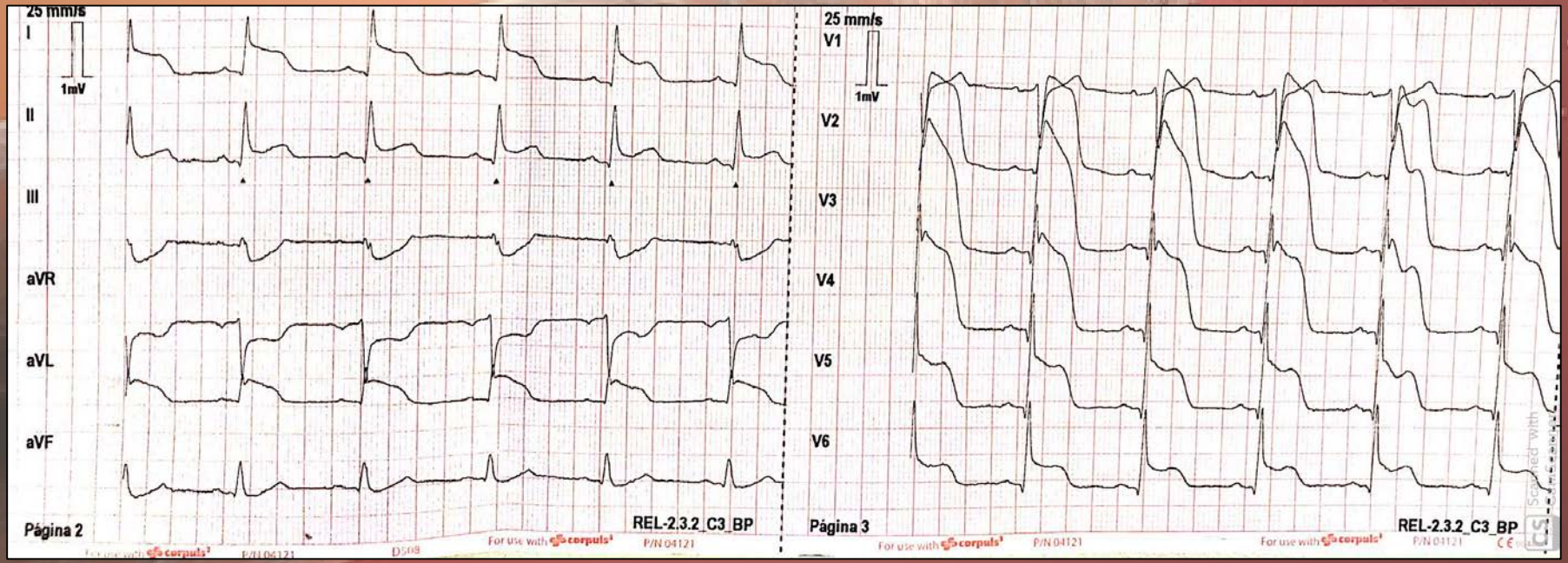
Evento isquémico

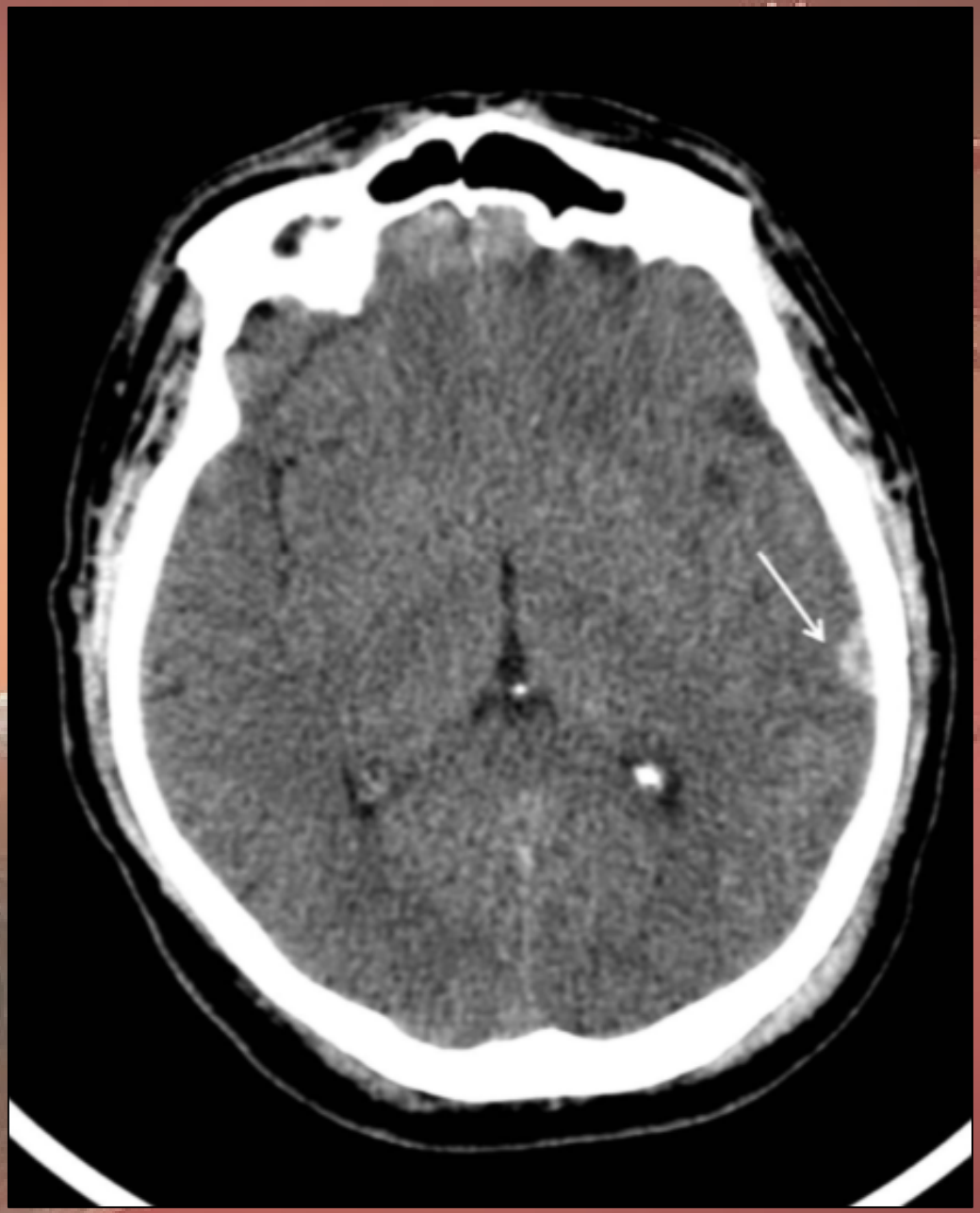


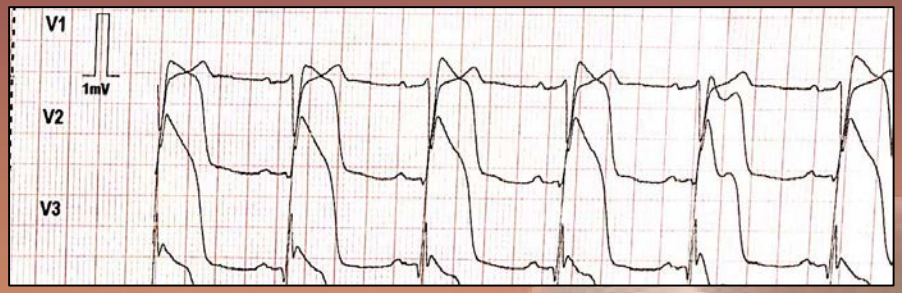
Un caso para comenzar:

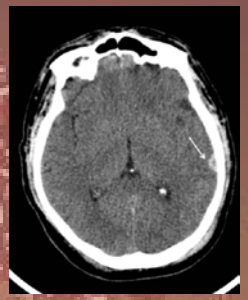
Dilemas en el filo de la navaja

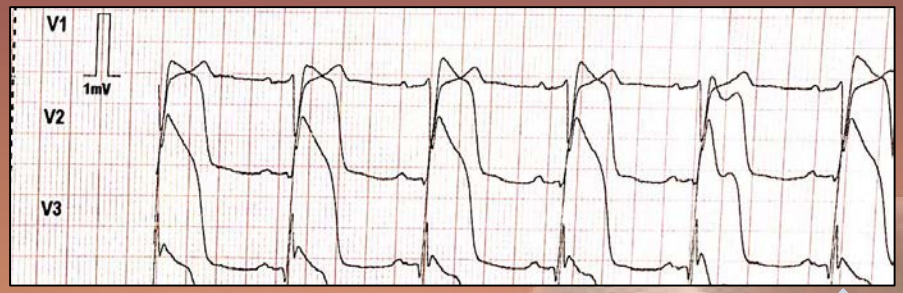

I
AUR
U1
U4
II
AUL
U2
U5
III
AUF
U3
U6

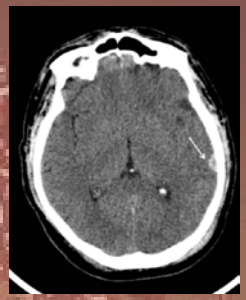

25 mm/s
I
1mV
II
III
aVR
aVL
aVF
Página 2
REL-2.3.2_C3_BP
25 mm/s
V1
1mV
V2
V3
V4
V5
V6
Página 3
REL-2.3.2_C3_BP




V1
1mV
V2
V3







Hemorragia cerebral aguda -> contraindicado tratamiento antitrombótico y por tanto también la ICP y el soporte circulatorio mecánico.

Control Tª y soporte HD farmacológico

Hemorragia cerebral sí, pero IAM anterior extenso y shock cardiogénico…

ICPP a la DA + BIAC/Impella. AAS + inh. P2Y12 + Heparina y crucemos los dedos

Hemorragia cerebral sí, pero IAM anterior extenso y shock cardiogénico…

ICPP a la DA (hep. Sódica/bivalirudina) + BIAC. Monoantiagregación con AAS o P2Y12 y sin anticoagulación.

Cualquier otra combinación

Recomendaciones ESC

European Heart Journal (2017) **38**, 1455–1462
doi:10.1093/eurheartj/ehw454

CURRENT OPINION

Management of antithrombotic therapy after bleeding in patients with coronary artery disease and/or atrial fibrillation: expert consensus paper of the European Society of Cardiology Working Group on Thrombosis

Sigrun Halvorsen[1]*, Robert F. Storey[2], Bianca Rocca[3], Dirk Sibbing[4], Jurrien ten Berg[5], Erik Lerkevang Grove[6], Thomas W. Weiss[7], Jean-Philippe Collet[8], Felicita Andreotti[9], Dietrich C. Gulba[10], Gregory Y.H. Lip[11], Steen Husted[12], Gemma Vilahur[13], Joao Morais[14], Freek W.A. Verheugt[15], Angel Lanas[16], Rustam Al-Shahi Salman[17], Philippe Gabriel Steg[18], and Kurt Huber[7] on behalf of the ESC Working Group on Thrombosis

Recomendaciones ESC
Riesgo trombótico

Table I Consensus definitions of thrombotic risk categories

Risk category	Risk of athero-thrombotic events (stable CAD, ACS or after PCI)	Risk of cardio-embolic events (AF or mechanical valves)
Very high	ACS or PCI with newer generation DES <8 days BVS <30 days	AF with CHA_2DS_2-VASc > =6 Mechanical mitral valves Cardiac assist devices.
High	ACS or PCI with newer generation DES 8–30 days ago. BVS 1–12 months ago	AF with CHA_2DS_2-VASc 4–5 Mechanical aortic valves (bileaflet)
Moderate	ACS or PCI with newer generation DES 1–12 months ago	AF with CHA_2DS_2-VASc 2–3
Low-to-moderate	Stable CAD (>12 months after ACS or PCI with newer generation DES), but complex cases (left main, bifurcations, recurrent ACS)	AF with CHA_2DS_2-VASc 1 (male) or 2 (female)
Low	Stable CAD (>12 months after ACS or PCI with newer generation DES) without additional risk factors	AF with CHA_2DS_2-VASc 0 (male) or 1 (female)

ACS, acute coronary syndrome; AF, atrial fibrillation; BVS, biovascular scaffolds; CAD, coronary artery disease; CHA_2DS_2-VASc, Cardiac failure, Hypertension, Age ≥75 (2 points), Diabetes, Stroke (2 points)—Vascular disease, Age 65–74, Sex category; DES, drug eluting stent; PCI, percutaneous coronary intervention.

Recomendaciones ESC
Riesgo hemorrágico

Table 2 Consensus definitions of recurrent bleeding risk categories

Risk category	Bleeding source and severity	Clinical setting	Patients clinical risk factors for bleeding
Very high	Intracranial bleeding where no treatment is possible or effective. Life-threatening extracranial bleeding where the source is either not identified or identified but not treated effectively	No precipitating or reversible factor identified (e.g. trauma, invasive procedure, hypertension, drug overdosing) Cessation of antithrombotic therapy discouraged because of very high-thrombotic risk, e.g. mechanical heart valve	HAS-BLED ≥5
High	Major extracranial bleeding where the source is identified but not treated effectively.	No reversible factor identified. Cessation of antithrombotic therapy discouraged because of very high thrombotic risk.	HAS-BLED 3–4
Moderate	Intracranial bleeding where cause of bleeding and relevant risk factors have been treated. Extracranial major bleeding where the source has been identified and treated effectively.		HAS-BLED =2
Low-to-moderate	Extracranial minor bleeding	Bleeding caused by antithrombotic drugs which can be discontinued	HAS BLED = 1
Low	Extracranial minimal bleeding	Bleeding caused by antithrombotic drugs which can be discontinued	HAS BLED = 0

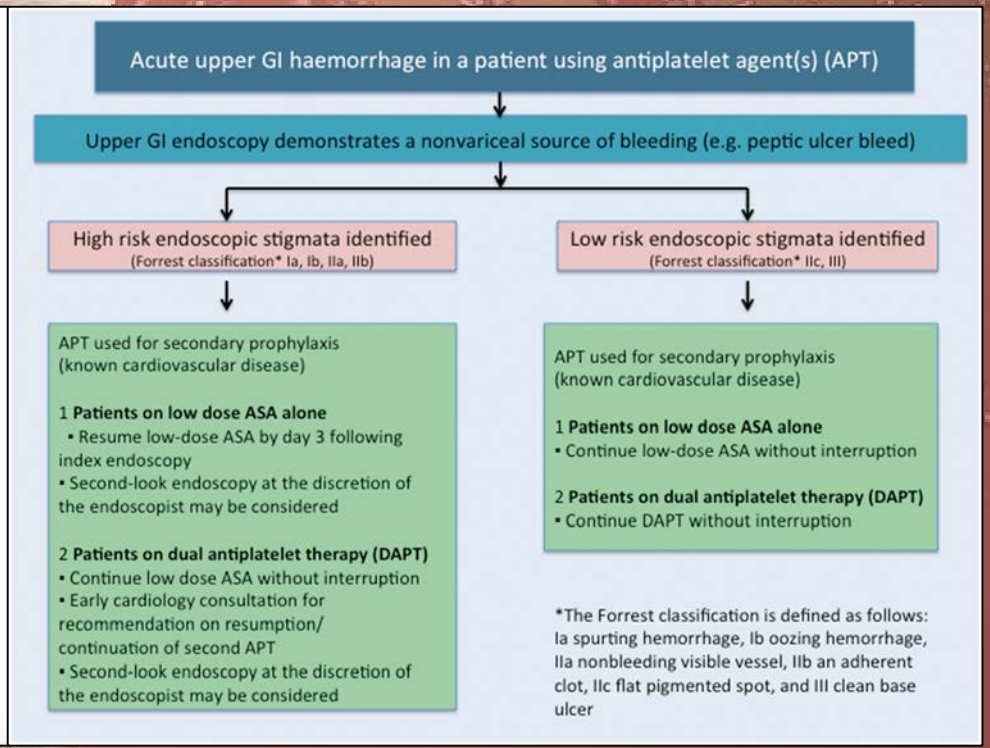
To be in the low-risk category for recurrent bleeding, both bleeding source/severity, clinical setting and patient risk factors for bleeding must be low. To be in the high-risk category, it is sufficient that one variable is high risk.
HAS-BLED, Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly (>65), Drugs/alcohol concomitantly; PCI, percutaneous coronary intervention.

Recomendaciones ESC: antiplaquetarios y sangrado extracraneal

Consensus summary on antiplatelet therapy after extracranial bleed

i. For patients at high or very high thrombotic risk (see *Table 1*: ACS or coronary stenting <30 days) who develop minor or major bleeding, we suggest continuation of low-dose aspirin without interruption. Restarting of the second antiplatelet agent should be considered as soon as possible after stabilization.

ii. For patients at moderate thrombotic risk (see *Table 1*: ACS or PCI with a second generation DES 1–12 months ago) who develop minor or major bleeding, we suggest resumption of low-dose aspirin as soon as bleeding is controlled, preferably within 3 days. Restarting a second antiplatelet agent should be considered if thrombotic risk outweighs recurrent bleeding risk. For patients who develop bleeding while on DAPT within 3 months of new generation DES implantation, we suggest resuming DAPT up to 3 months. If patients develop bleeding more than 3 months after new generation DES implantation and remain at risk of recurrent bleeding, we suggest resumption of only one antiplatelet agent (either aspirin or clopidogrel).



Otras:

- En caso de prasugrel/ticagrelor -> clopidogrel
- Si SCA bajo tratamiento médico -> monoantiagregación

Recomendaciones ESC: anticoagulantes y sangrado extracraneal

Consensus summary on anticoagulant therapy after extracranial bleed

i. After extracranial bleeding, OAC should be reinitiated as soon as the cardiovascular thrombotic risks associated with discontinuation are thought to outweigh the risk of re-bleeding with reinitiation, in most cases within 1 week.

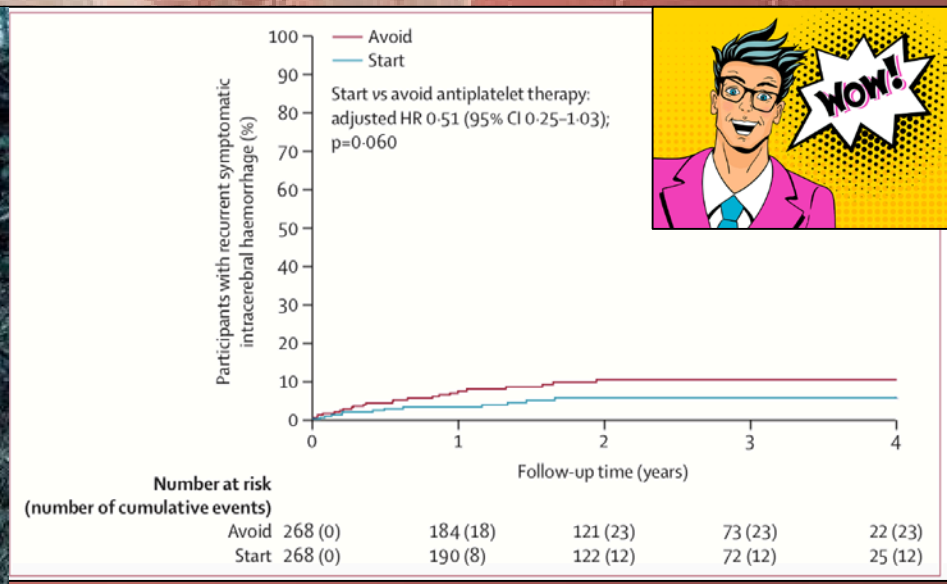
ii. When (re)starting a NOAC, renal function should be carefully assessed and monitored to avoid drug accumulation.

iii. If an antidote (idaruzicumab) has been used to reverse the anticoagulant effect of a NOAC, it is suggested to restart OAC as soon as possible, preferably within 3–4 days if the individual bleeding risk allows.

iv. In patients with mechanical heart valves, discontinuation of VKA is associated with a high risk of thrombosis and is discouraged, particularly for valves in the mitral position. NOACs are currently contraindicated for patients with mechanical heart valves.

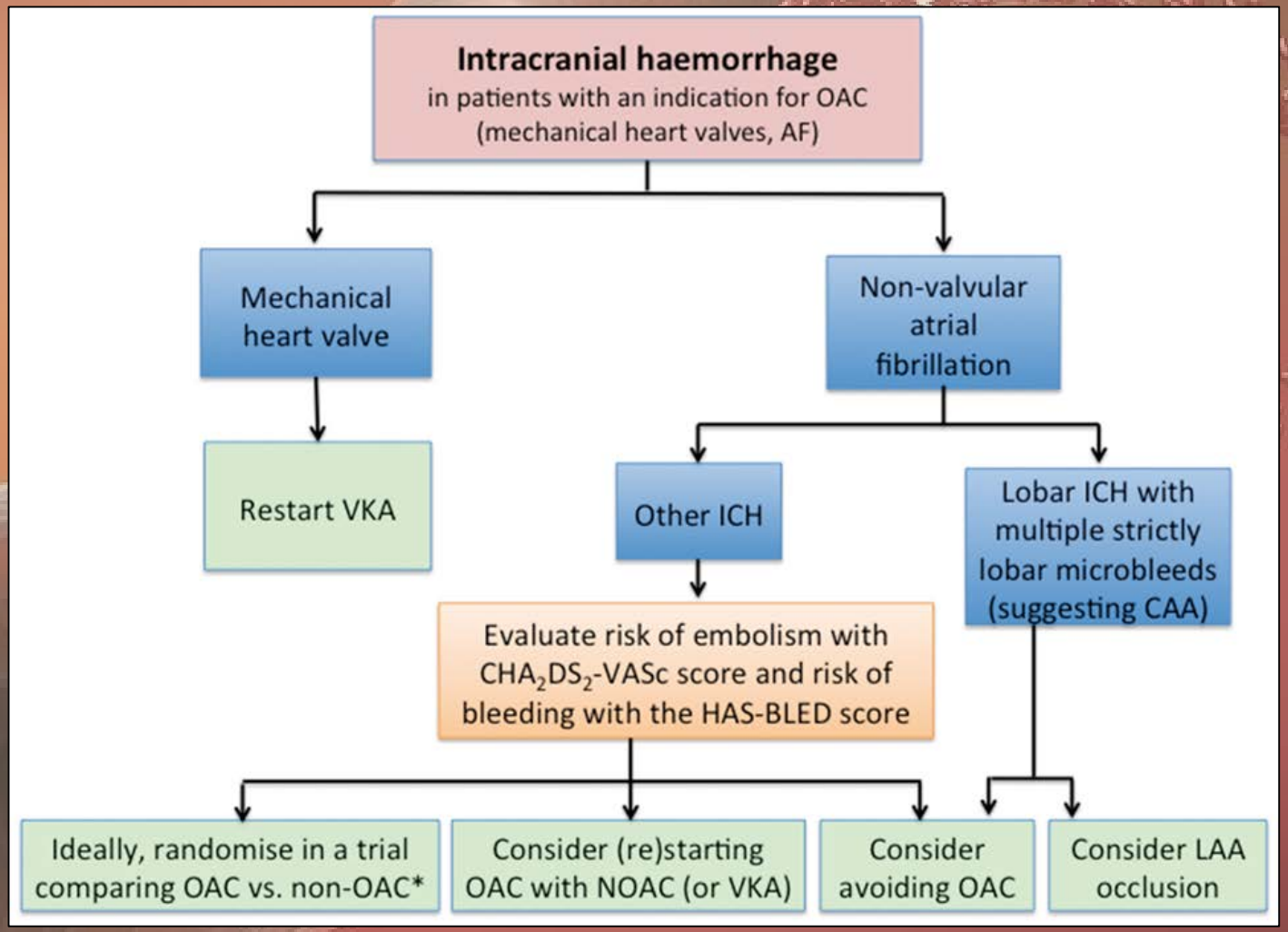
Recomendaciones ESC: antiplaquetarios y sangrado intracraneal

Careful consideration of thrombotic and bleeding risk is needed. In general, restarting therapy after temporary discontinuation should be considered if thrombotic risk, as defined in *Table 1*, is very high or high. One randomized controlled trial of restarting vs. avoiding antiplatelet drugs after antithrombotic-associated ICH is ongoing (ISRCTN71907627).



The Restart Collaboration. Lancet. 2019 Jun 29;393(10191):2613-2623

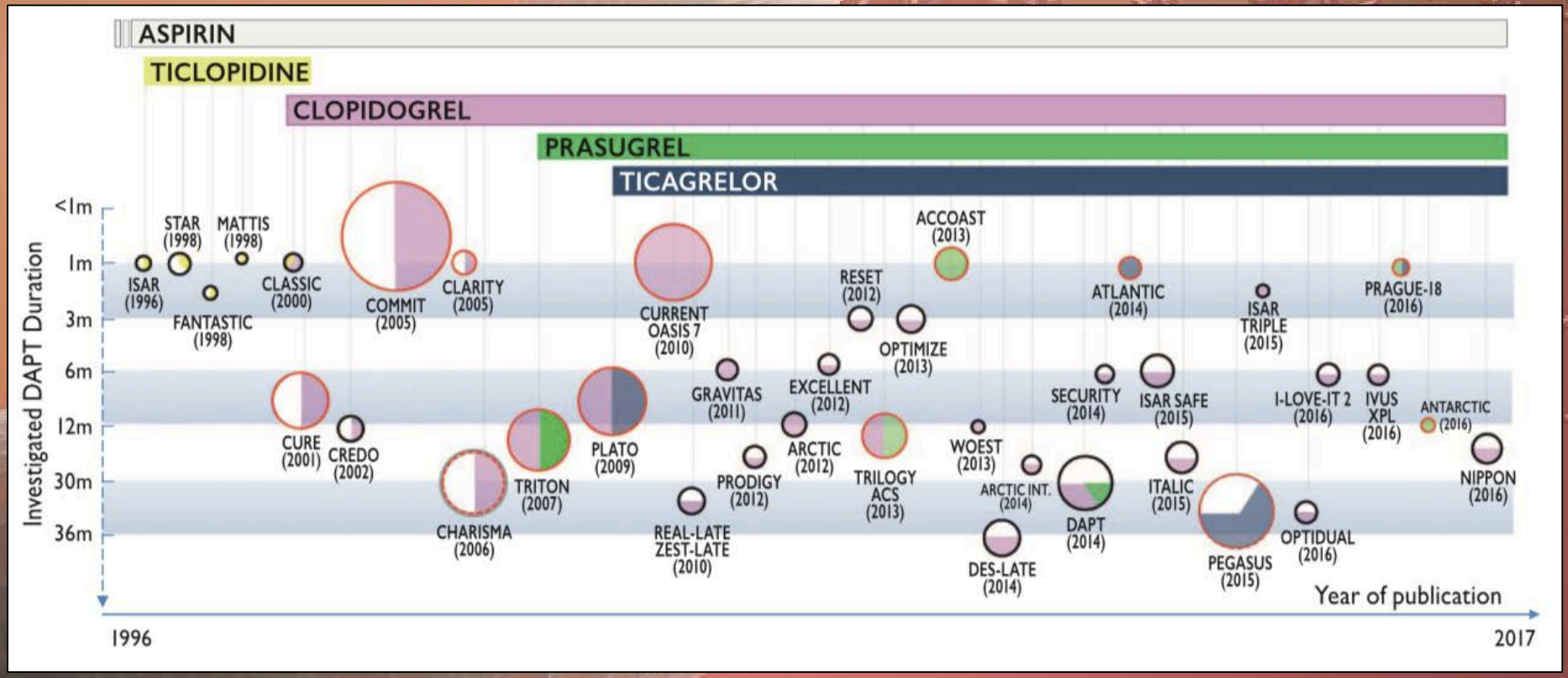
Recomendaciones ESC: anticoaguantes y sangrado intracraneal



Reflexiones sobre dogmas en cardiología:

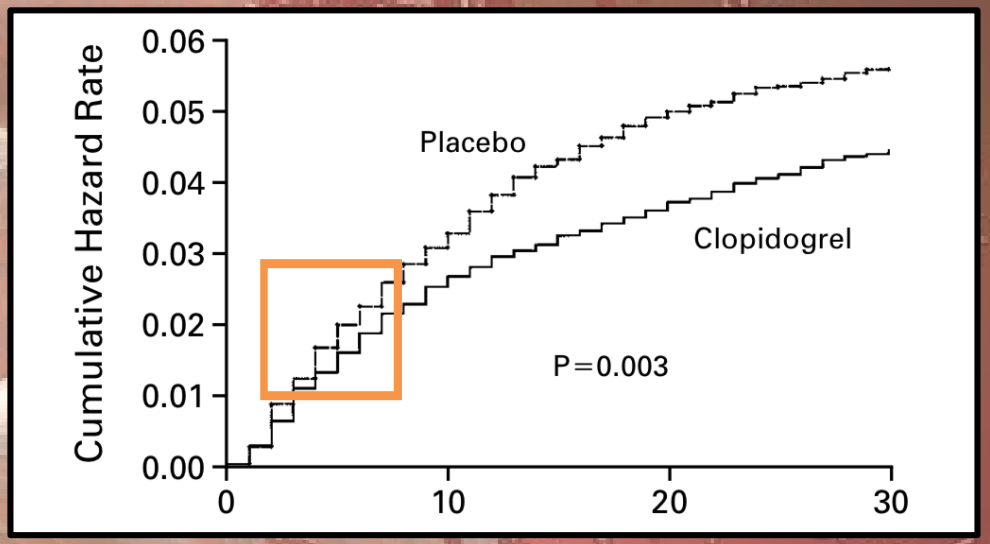
El efecto real del tratamiento antitrombótico

El universo de los antitrombóticos



Escenario SCASEST: CURE Trial (2001)

Outcome	Clopidogrel Group (N=6259)	Placebo Group (N=6303)	Relative Risk (95% CI)	P Value
	no. (%)			
First primary outcome: nonfatal myocardial infarction, stroke, or death from cardiovascular causes	582 (9.3)	719 (11.4)	0.80 (0.72–0.90)	<0.001
Second primary outcome: first primary outcome or refractory ischemia	1035 (16.5)	1187 (18.8)	0.86 (0.79–0.94)	<0.001
Death from cardiovascular causes	318 (5.1)	345 (5.5)	0.93 (0.79–1.08)	
Myocardial infarction†	324 (5.2)	419 (6.7)	0.77 (0.67–0.89)	
Q-wave	116 (1.9)	193 (3.1)	0.60 (0.48–0.76)	
Non–Q-wave	216 (3.5)	242 (3.8)	0.89 (0.74–1.07)	
Stroke	75 (1.2)	87 (1.4)	0.86 (0.63–1.18)	
Refractory ischemia‡	544 (8.7)	587 (9.3)	0.93 (0.82–1.04)	
During initial hospitalization	85 (1.4)	126 (2.0)	0.68 (0.52–0.90)	
After discharge	459 (7.6)	461 (7.6)	0.99 (0.87–1.13)	
Death from noncardiovascular causes	41 (0.7)	45 (0.7)	0.91 (0.60–1.39)	



Effects of Clopidogrel in Addition to Aspirin in Patients with Acute Coronary Syndromes without ST-Segment Elevation. (2001). *New England Journal of Medicine, 345(7), 494–502.*

Evento primario combinado a 12 meses

- Grupo AAS+clopidogrel 9.3%
- Grupo solo AAS: 11.4%.

➢ RAR: 2.1%, NNT 47.

Escenario SCA: COMMIT Trial (2005)

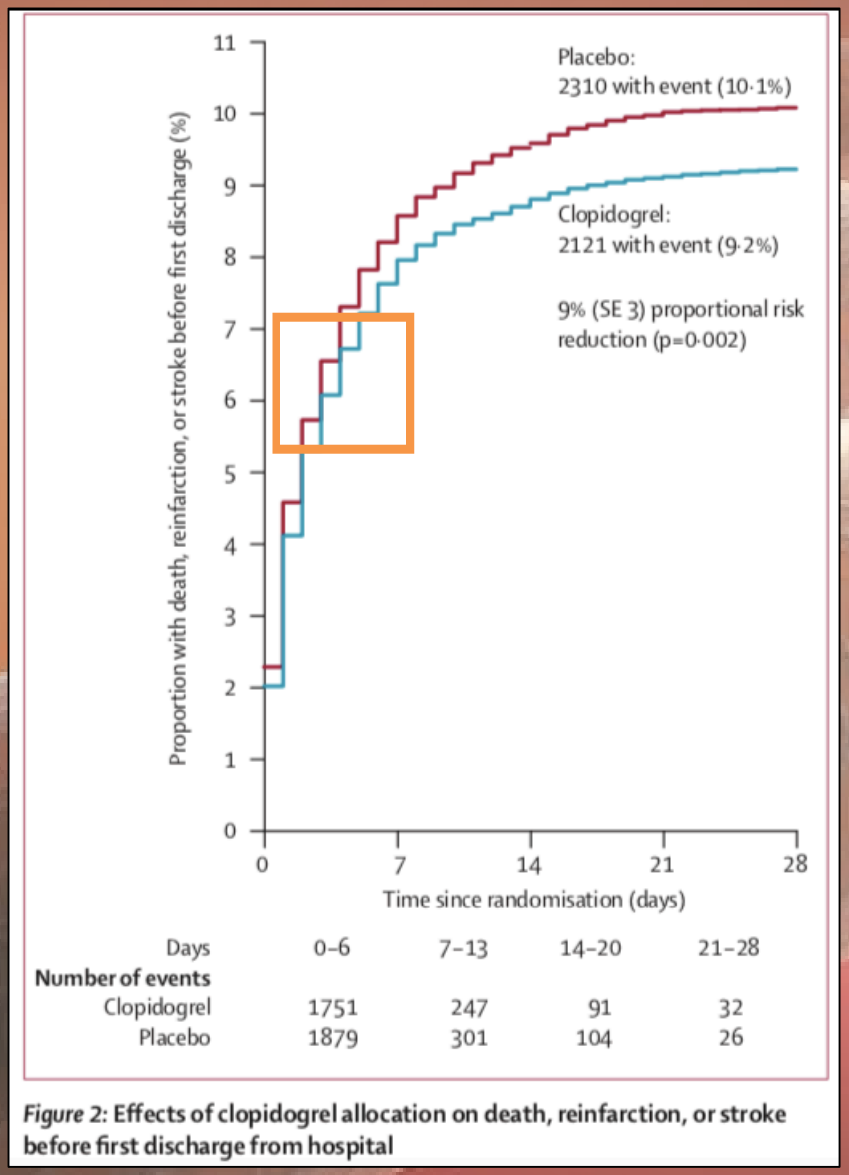
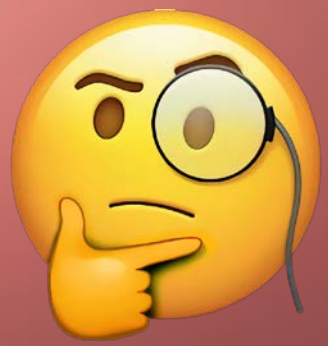


Figure 2: Effects of clopidogrel allocation on death, reinfarction, or stroke before first discharge from hospital

Evento primario combinado a 1 mes

- Grupo AAS+clopidogrel 9.2%
- Grupo solo AAS: 10.1%.
  - RAR: 0.9%
  - NNT 111.



Escenario FibA: ¿cuán alto es el riesgo?

Table 6—*Stroke or Other TE at 1 Year Based on the 2009 Birmingham (CHA_2DS_2-VASc) Scoring System*

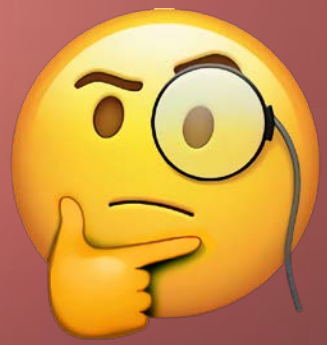
CHA_2DS_2-VASc Score	No.	Number of TE Events	TE Rate During 1 y (95% CI)	TE Rate During 1 y, Adjusted for Aspirin Prescription,[a] %
0	103	0	0% (0-0)	0
1	162	1	0.6% (0.0-3.4)	0.7
2	184	3	1.6% (0.3-4.7)	1.9
3	203	8	3.9% (1.7-7.6)	4.7
4	208	4	1.9% (0.5-4.9)	2.3
5	95	3	3.2% (0.7-9.0)	3.9
6	57	2	3.6% (0.4-12.3)	4.5
7	25	2	8.0% (1.0-26.0)	10.1
8	9	1	11.1% (0.3-48.3)	14.2
9	1	1	100% (2.5-100)	100
Total	1,084	25	*P* Value for trend 0.003	

Lip, Gregory Y.H. et al. Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach. CHEST, Volume 137, Issue 2, 263 - 272

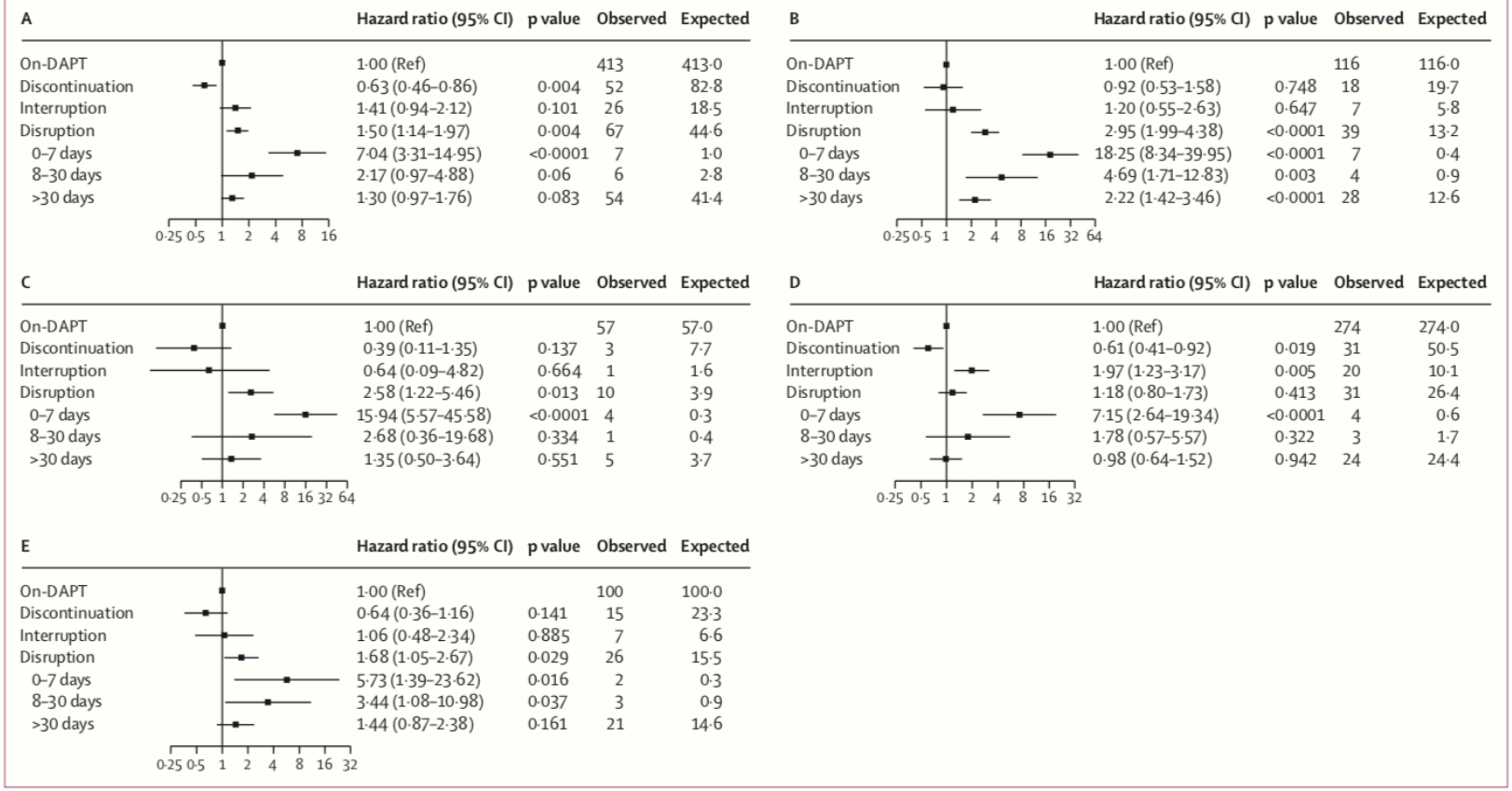
Ejemplo: CHA_2DS_2-VASC 4:

97-98% Probabilidad de NO tener un evento embólico a 12 meses

2% Evento embólico anual -> 0.16% mensual -> 0.04% semanal



Estudio PARIS (2013): interrupción de DAPT post-ICP y eventos cardiovasculares



A	Hazard ratio (95% CI)	p value	Observed	Expected
On-DAPT	1·00 (Ref)		413	413·0
Discontinuation	0·63 (0·46–0·86)	0·004	52	82·8
Interruption	1·41 (0·94–2·12)	0·101	26	18·5
Disruption	1·50 (1·14–1·97)	0·004	67	44·6
0–7 days	7·04 (3·31–14·95)	<0·0001	7	1·0
8–30 days	2·17 (0·97–4·88)	0·06	6	2·8
>30 days	1·30 (0·97–1·76)	0·083	54	41·4

0·25 0·5 1 2 4 8 16

B	Hazard ratio (95% CI)	p value	Observed	Expected
On-DAPT	1·00 (Ref)		116	116·0
Discontinuation	0·92 (0·53–1·58)	0·748	18	19·7
Interruption	1·20 (0·55–2·63)	0·647	7	5·8
Disruption	2·95 (1·99–4·38)	<0·0001	39	13·2
0–7 days	18·25 (8·34–39·95)	<0·0001	7	0·4
8–30 days	4·69 (1·71–12·83)	0·003	4	0·9
>30 days	2·22 (1·42–3·46)	<0·0001	28	12·6

0·25 0·5 1 2 4 8 16 32 64

C	Hazard ratio (95% CI)	p value	Observed	Expected
On-DAPT	1·00 (Ref)		57	57·0
Discontinuation	0·39 (0·11–1·35)	0·137	3	7·7
Interruption	0·64 (0·09–4·82)	0·664	1	1·6
Disruption	2·58 (1·22–5·46)	0·013	10	3·9
0–7 days	15·94 (5·57–45·58)	<0·0001	4	0·3
8–30 days	2·68 (0·36–19·68)	0·334	1	0·4
>30 days	1·35 (0·50–3·64)	0·551	5	3·7

0·25 0·5 1 2 4 8 16 32 64

D	Hazard ratio (95% CI)	p value	Observed	Expected
On-DAPT	1·00 (Ref)		274	274·0
Discontinuation	0·61 (0·41–0·92)	0·019	31	50·5
Interruption	1·97 (1·23–3·17)	0·005	20	10·1
Disruption	1·18 (0·80–1·73)	0·413	31	26·4
0–7 days	7·15 (2·64–19·34)	<0·0001	4	0·6
8–30 days	1·78 (0·57–5·57)	0·322	3	1·7
>30 days	0·98 (0·64–1·52)	0·942	24	24·4

0·25 0·5 1 2 4 8 16 32

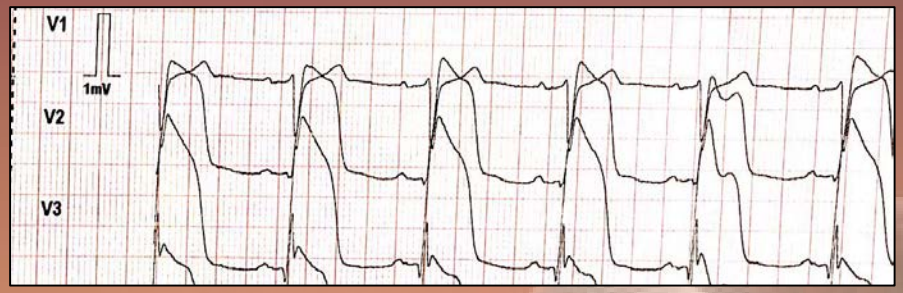
E	Hazard ratio (95% CI)	p value	Observed	Expected
On-DAPT	1·00 (Ref)		100	100·0
Discontinuation	0·64 (0·36–1·16)	0·141	15	23·3
Interruption	1·06 (0·48–2·34)	0·885	7	6·6
Disruption	1·68 (1·05–2·67)	0·029	26	15·5
0–7 days	5·73 (1·39–23·62)	0·016	2	0·3
8–30 days	3·44 (1·08–10·98)	0·037	3	0·9
>30 days	1·44 (0·87–2·38)	0·161	21	14·6

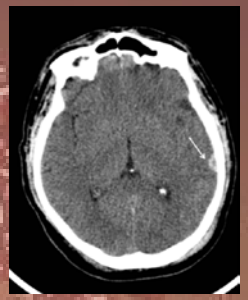
0·25 0·5 1 2 4 8 16 32

Figure 3: **Risk of ischaemic endpoints**

Results of Cox model analyses for risk of major adverse cardiovascular event (MACE; A), spontaneous myocardial infarction (B), definite or probable stent thrombosis (C), target lesion revascularisation (D), and cardiac death (E). Boxes are hazard ratio point estimates and error bars are 95% CIs. DAPT=dual antiplatelet therapy.

Mehran, R., Baber, et al. Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. The Lancet 2013, 382(9906), 1714–1722





Evidencia científica y niveles de recomendación en IAMEST + shock cardiogénico + sangrado intracraneal agudo

1A++	SIEMPRE SE HA HECHO ASÍ
2	A MÍ ME GUSTA ASÍ
2 A	HE OBSERVADO QUE ASÍ SUELE IR BIEN
2 B	NUNCA ME HA DADO NINGÚN PROBLEMA
3 A	TÚ PÓNSELO QUE NO PASA NADA
3 B	TÚ PRUEBA A VER QUÉ PASA
4	NO HAY HUEVOS

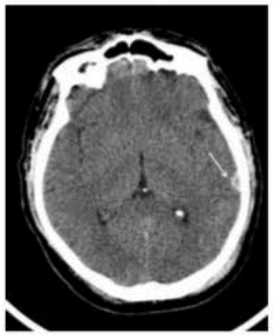
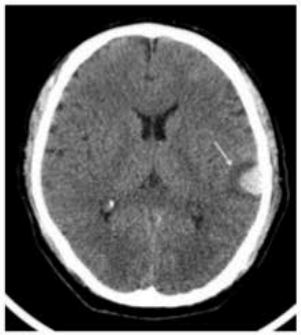
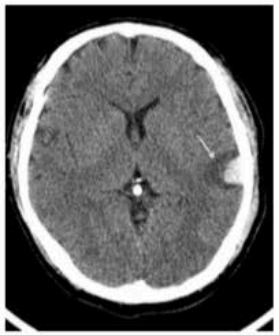
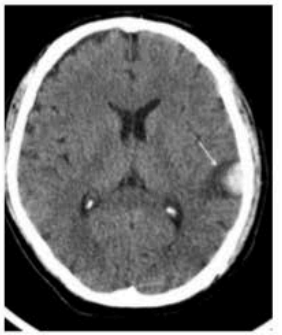
1. Implante BIAC
2. ICP primaria a DAp (heparina sódica IV). Clopidogrel en monoterapia.
3. Soporte con BIAC 1:1 y sin heparina adicional.
4. Controles radiográficos del sangrado -> ligero aumento y posterior estabilidad
5. A las 72h, switch a ticagrelor en monoterapia
6. Día 10 (hematoma en resolución) inicio de AAS

Anticoagulation therapy in intra-aortic balloon counterpulsation: Does IABP really need anti-coagulation ?

JIANG Chen-yang(蒋晨阳)[1], ZHAO Li-li(赵莉莉)[2], WANG Jian-an(王建安)[1]
SAN Jiang(单 江)[1], MOHAMMOD Balgaith[3]
([1]Department of Cardiology, Sir Run Run Shaw Hospital, Zhejiang University, Hangzhou 310016, China)
([2]Department of Cardiology, First Affilicated Hospital, Zhejiang University, Hangzhou 310006, China)
([3]King Abdulaziz Cardiac Center, Riyadh, Kindom of Saudi Arabia)

Table 3 IABP vascular complications

	GroupA (N = 71)	GroupB (N = 82)	P
Major limb ischemia(%)	0	0	
Minor limb ischemia(%)	3(4.2)	2(2.4)	>0.05
Bleeding(%)	10(14.1)	2(2.4)	<0.05
Major bleeding(%)	2(2.8)	0	>0.05
Minor bleeding(%)	8(11.3)	2(2.4)	<0.05

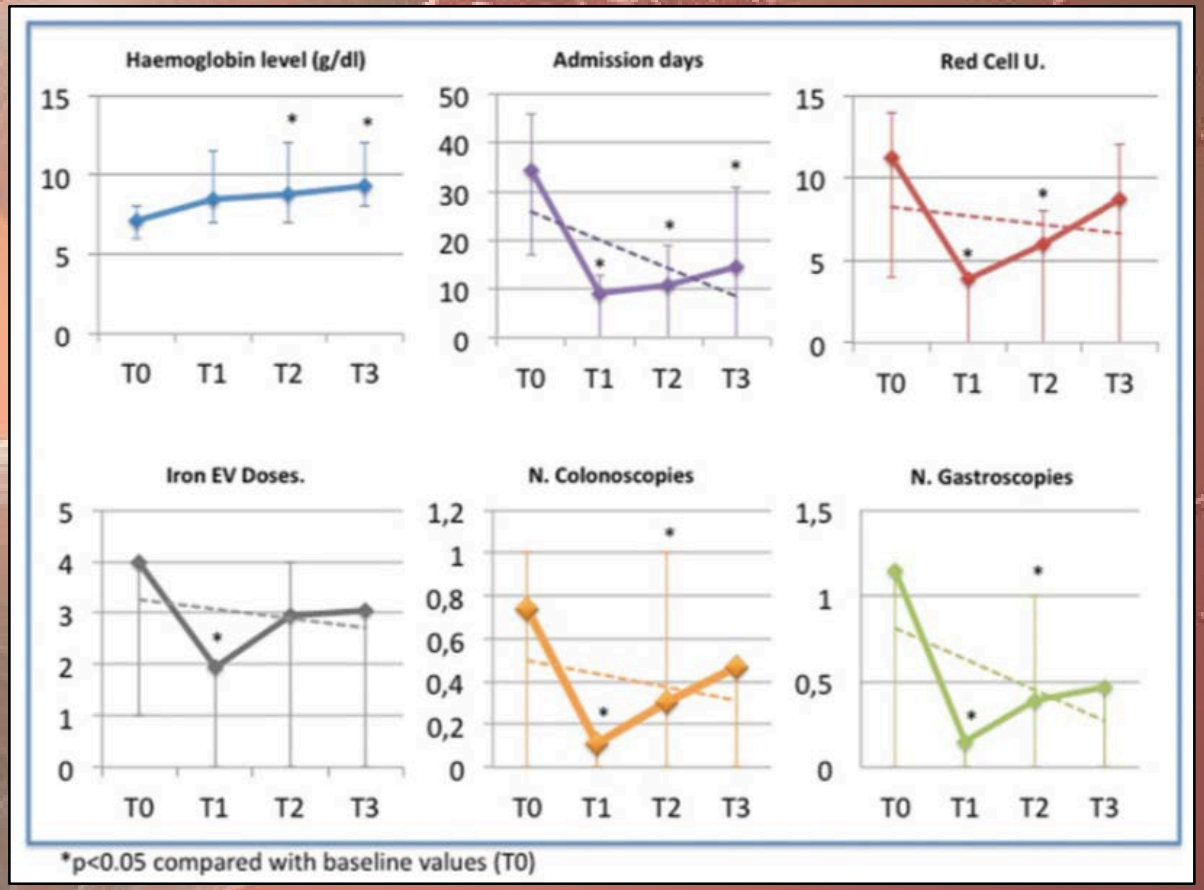





Novedades en el tratamiento de la hemorragia en paciente bajo terapia antitrombótica

Lanreótido (análogo somatostatina) sc mensual, en pacientes con hemorragia digestiva de origen incierto.
60% anticoagulantes
20% antitrombóticos.

↑ hemoglobina
↓ reingresos, endoscopias y necesidad transfusional.

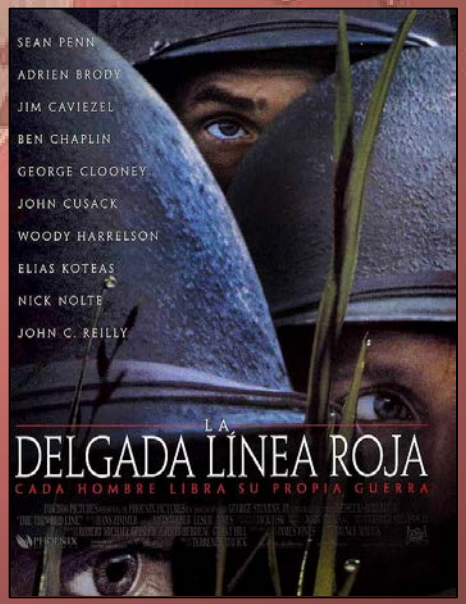
Potenciales aplicaciones:
- Síndrome Heyde
- VADs



Santiago Frago, Javier Alcedo, et al (2019): Long-term results with lanreotide in patients with recurrent gastrointestinal angiodysplasias bleeding or obscure gastrointestinal bleeding. Benefits in efficacy and procedures consumption, Scandinavian Journal of Gastroenterology. DOI: 10.1080/00365521.2018.1547921

Mensajes para llevar a casa

1. **Variedad** de situaciones clínicas complejas: manejo multidisciplinar –digestivo, neuro- y **sentido común**.
2. **PREVENCIÓN**: Evitar triple terapia. Aplicar escalas de riesgo hemorrágico.
3. **Abandonar dogmas en decisiones difíciles**.
   - ✓ ¿ICP solo con monoterapia?
   - ✓ ¿BIAC sin heparina?
4. **Recomendaciones ESC**:
   - ✓ Alto/muy alto riesgo isquémico + sangrado leve: mantener antitrombóticos.
   - ✓ Alto/muy alto riesgo isquémico y sangrado grave: retirar un antiplaquetario peri-sangrado, reintroducir pre-alta.
   - ✓ Moderado/bajo riesgo isquémico + sangrado: retirar un antiplaquetario.
   - ✓ Sangrado intracraneal: seguridad en reiniciar un antiplaquetario o anticoagulante a largo plazo



SOCIETAT CATALANA DE CARDIOLOGIA