Consell Català de Formació Continuada Professions Sanitàries

Societat Catalana d'Hematologia i Hemoteràpia

TROMBOC@T Working Group

WORLD THROMBOSIS DAY
13 OCTOBER

DIA MUNDIAL DE LA TROMBOSIS
16 OCTUBRE 2018

Acadèmia de Ciencies Mèdiques
18:00 a 20:00h

1. **Benvinguda** (5 min)
   Dra. Mireia Constans. Fundació Althaia . Barcelona
   Dra. Amparo Santamaria. H.U. Vall d´Hebrón . Barcelona

2. **Escales de risc hemorràgic. Són vàlides?** (20min)
   Dra. Mireia Constans
   Xarxa Assistencial de Manresa. Fundació Althaia.

3. **Pacient Fràgil i ACODs.** (20 min)
   Juan josé López Núñez. Servei Medicina Interna.
   Hospital Universitari Germans Trias i Pujol. Badalona

4. **Trombosi Portal (20 min)**
   Dr. Joan Carles Garcia Pagán.
   Cap de Secció d'Hemodinàmica Hepàtica. ICMDM.
   IDIBAPS. CIBEREHD. Hospital Clínic Barcelona.

5. **ACODs a Primària. La realitat en el dia a dia.** (30 min)
   Dra. Elisenda Sant . CAPSBE
   Dra Rosa Saladich. Ambulatori de Vinyets. Sant Boi de Llobregat
   Dr. German Las Heras. Hospital General Parc Sanitari Sant Joan de Déu Sant Boi del Llobregat

6. **Preguntes i discussió** (15 min)

Bayer HealthCare
Bayer Schering Pharma

Boehringer Ingelheim

Bristol-Myers Squibb

LEO Pharma

WORLD THROMBOSIS DAY
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Escales de risc hemorràgic:

Són vàlides?

Dra. Mireia Constans
Servei d´Hematologia
Fundació Althaia, Xarxa Assistencial de Manresa

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Introducció

- Actualment disposem de diferents possibilitats de tractament anticoagulant (anti-vit K i ACODs) per reduir el risc trombòtic del pacients amb FA, però hem de valorar el risc hemorràgic pero poder decidir el millor tractament.
- Els anticoagulants están en el “top 10” de fàrmacs amb efectes adversos greus reportats en la FDA
- El risc hemorràgic descrit és del 1-5% per persona/any. Hemorragia intracraneal.

WORLD THROMBOSIS DAY
13 OCTOBER

Factors de risc mes importants [1,2,3,4]

- Edat
- Sexe femení
- DM
- HTA
- Neoplasies
- Enolisme, hepatopatia
- Insuf renal crònica
- Anemia
- Ictus o HIC previa
- Presència de lesions sagnants previes

- Tractament concomitant amb AAS, AINEs, AAG, ATB, amiodarona, estatines o fibrats
- INR irregulars o INR >3.0
- INR >1.2 abans d´iniciar el tractament
- Hemorràgies greus amb INR correcte
- Poca adherència al tractament o a les visites

1,2,3,4 Delaney JA, et al. CMAJ 2007;177(4):347;Schelleman H, et al. Am J Med.2010;123(2):151;Limbdi NA, et al. J Am Soc Nephrol 2009;20(4):912;Fitzmaurice DA, et al. BMJ 2002;325 (7368):828.

HEMORR2HAGES risk index

Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF).

Gage BF, Yan Y, Milligan PE, Waterman AD, Culverhouse R, Rich MW, Radford MJ
Am Heart J. 2006;151(3):713.

BACKGROUND: Although warfarin and other anticoagulants can prevent ischemic events, they can cause hemorrhage. Quantifying the rate of hemorrhage is crucial for determining the risks and net benefits of prescribing antithrombotic therapy. Our objective was to find a bleeding classification scheme that could quantify the risk of hemorrhage in elderly patients with atrial fibrillation.

METHODS: We combined bleeding risk factors from existing classification schemes into a new scheme, HEMORR2HAGES, and validated all bleeding classification schemes. **We scored HEMORR2HAGES by adding 2 points for a prior bleed and 1 point for each of the other risk factors:** hepatic or renal disease, ethanol abuse, malignancy, older (age>75 years), reduced platelet count or function, hypertension (uncontrolled), anemia, genetic factors, excessive fall risk, and stroke. We used data from quality improvement organizations representing 7 states to assemble a registry of 3791 Medicare beneficiaries with atrial fibrillation.

RESULTS: There were 162 hospital admissions with an International Classification of Diseases, Ninth Revision, Clinical Modification code for hemorrhage. With each additional point, the rate of bleeding per 100 patient-years of warfarin increased: 1.9 for 0, 2.5 for 1, 5.3 for 2, 8.4 for 3, 10.4 for 4, and 12.3 for>or =5 points. In patients prescribed warfarin, **HEMORR2HAGES had greater predictive accuracy (c statistic 0.67) than other bleed prediction schemes (P<.001).**

CONCLUSIONS: Adaptations of existing classification schemes, especially a new bleeding risk scheme, HEMORR2HAGES, can quantify the risk of hemorrhage and aid in the management of antithrombotic therapy.

HEMORR$_2$HAGES

Letter	Clinical Characteristic	Points
H	Hepatic or Renal Disease	1
E	Ethanol Abuse	1
M	Malignancy	1
O	Older Age	1
R	Reduced Platelet Count or Function	1
R	Rebleeding Risk	2
H	Hypertension	1
A	Anemia	1
G	Genetic Factors	1
E	Excessive Fall Risk	1
S	Stroke	1
Maximum Score		12

HEMORR2HAGES risk index

- L´estudi més extens en seguiment i factors de risc
- 2/3 parts dels sagnats majors que es van descriure eren gastro-intestinals i un 15% intracraneals.
- Util per identificar subgrups de risc hemorràgic
- Poc utilitzada a la pràctica per número massa extens de factors de risc i es necessiten estudis genètics

HAS-BLED

A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey.

Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY
Chest. 2010;138(5):1093.

OBJECTIVE: Despite extensive use of oral anticoagulation (OAC) in patients with atrial fibrillation (AF) and the increased bleeding risk associated with such OAC use, no handy quantification tool for assessing this risk exists. We aimed to develop a practical risk score to estimate the 1-year risk for major bleeding (intracranial, hospitalization, hemoglobin decrease> 2 g/L, and/or transfusion) in a cohort of real-world patients with AF.

METHODS: Based on **3,978 patients** in the Euro Heart Survey on AF with complete follow-up, all univariate bleeding risk factors in this cohort were used in a multivariate analysis along with historical bleeding risk factors. A new bleeding risk score termed HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (> 65 years), Drugs/alcohol concomitantly) was calculated, incorporating risk factors from the derivation cohort.

RESULTS: Fifty-three (1.5%) major bleeds occurred during 1-year follow-up. The annual bleeding rate increased with increasing risk factors. The predictive accuracy in the overall population using significant risk factors in the derivation cohort (C statistic 0.72) was consistent when applied in several subgroups. Application of the new bleeding risk score (HAS-BLED) gave similar C statistics except where patients were receiving antiplatelet agents alone or no antithrombotic therapy, with C statistics of 0.91 and 0.85, respectively.

CONCLUSION: This **simple, novel bleeding risk score (HAS-BLED) provides a practical tool to assess the individual bleeding risk of real-world patients with AF,** potentially supporting clinical decision making regarding antithrombotic therapy in patients with AF.

HAS-BLED

Letter	Clinical Characteristic	Points
H	Hypertension	1
A	Abnormal Liver or Renal Function	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly (age > 65)	1
D	Drugs or Alcohol	1 or 2
Maximum Score		9

HAS-BLED

- Escala fàcil de recordar
- Identifica factors modificables (HTA, antiagregants) que poden reduir el risc hemorràgic.
- Major valor predictiu per la HIC
- S´ha validat per valorar risc hemorràgic en ACODs
- S´ha validat per predir el risc hemorràgic en teràpies pont durant l´intervencionisme coronari percutani en pacients en ACXFA

ATRIA

A new risk scheme to predict warfarin-associated hemorrhage:
The ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) Study.
Fang MC, Go AS, Chang Y, Borowsky LH, Pomernacki NK, Udaltsova N, Singer DE
J Am Coll Cardiol. 2011;58(4):395.

OBJECTIVES: The purpose of this study was to develop a risk stratification score to predict warfarin-associated hemorrhage. BACKGROUND: Optimal decision making regarding warfarin use for atrial fibrillation requires estimation of hemorrhage risk.

METHODS: We followed up **9,186 patients** with atrial fibrillation contributing 32,888 person-years of follow-up on warfarin, obtaining data from clinical databases and validating hemorrhage events using medical record review. We used Cox regression mode bility of to develop a hemorrhage risk stratification score, selecting candidate variables using bootstrapping approaches. The final model was internally validated by split-sample testing and compared with 6 published hemorrhage risk schemes.

RESULTS: We observed 461 first major hemorrhages during follow-up (1.4% annually). Five independent variables were included in the final model and weighted by regression coefficients: anemia (3 points), severe renal disease (e.g., glomerular filtration rate<30 ml/min or dialysis-dependent, 3 points), age≥75 years (2 points), prior bleeding (1 point), and hypertension (1 point). Major hemorrhage rates ranged from 0.4% (0 points) to 17.3% per year (10 points). Collapsed into a 3-category risk score, major hemorrhage rates were 0.8% for low risk (0 to 3 points), 2.6% for intermediate risk (4 points), and 5.8% for high risk (5 to 10 points). The c-index for the continuous risk score was 0.74 and 0.69 for the 3-category score, higher than in the other risk schemes. There was net reclassification improvement versus all 6 comparators (from 27% to 56%).

CONCLUSIONS: **A simple 5-variable risk score was effective in quantifying the risk of warfarin-associated hemorrhage in a large community-based cohort of patients with atrial fibrillation.**

ATRIA

Clinical Characteristic	Points
Anemia	3
Severe Renal Disease	3
Age ≥75 Years	2
Prior Bleeding	1
Hypertension	1
Maximum Score	10

Low risk	Intermediate Risk	High Risk
0-3 puntos	4 puntos	5-10 puntos
0,76 e/100p-years	2,62	5,76

ATRIA

- Estudi amb el número més extens de pacients
- Poques variables
- Senzill i fàcil d´utilitzar a la pràctica clínica diaria
- Bon poder predictiu de sagnat major a la seva cohort
- No obstant s´ha posat de manifest en diferents estudis poc poder predictiu de HIC


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journal homepage: www.

Letter to the Editor

Comparative evaluation of HAS-BLED and /

the

atria

Rami

Alfre

Carlo

CHEST

Original Research

CARDIOVASCULAR DISEASE

Predictive Value of the HAS-BLED and

- HAS-BLED va resultar superior al HEMORR2AGES i al ATRIA per preveure el risc hemorràgic major.
- El HAS-BLED va ser l´únic que va demostrar una predicció significativa en HIC
- Senzilla d´utilitzar
- El HAS-BLED es recomana en la majoria de les guies clíniques per valorar el risc hemorràgic.

J Am Coll Cardiol. 2012;60(9):861.

ORBIT

European Heart Journal Advance Access published September 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv476

CLINICAL RESEARCH
Atrial fibrillation

The ORBIT bleeding score: a simple bedside score to assess bleeding risk in atrial fibrillation

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Received 17 March 2015; revised 13 July 2015; accepted 24 August 2015

Background Therapeutic decisions in atrial fibrillation (AF) are often influenced by assessment of bleeding risk. However, existing bleeding risk scores have limitations.

Objectives We sought to develop and validate a novel bleeding risk score using routinely available clinical information to predict major bleeding in a large, community-based AF population.

Methods We analysed data from Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF), a prospective registry that enrolled incident and prevalent AF patients at 176 US sites. Using Cox proportional hazards regression, we identified factors independently associated with major bleeding among patients taking oral anticoagulation (OAC) over a median follow-up of 2 years (interquartile range 1.6–2.5). We also created a numerical bedside risk score that included the five most predictive risk factors weighted according to their strength of association with major bleeding. The predictive performance of the full model, the simple five-item score, and two existing risk scores (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly, drugs/alcohol concomitantly, HAS-BLED, and anticoagulation and risk factors in atrial fibrillation, ATRIA) were then assessed in both the ORBIT-AF cohort and a separate clinical trial population, Rivaroxaban Once-daily oral direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and embolism trial in atrial fibrillation (ROCKET-AF).

Results Among 7411 ORBIT-AF patients taking OAC, the rate of major bleeding was 4.0/100 person-years. The full continuous model (12 variables) and five-factor ORBIT risk score (older age [75+ years], reduced haemoglobin/haematocrit/history of anaemia, bleeding history, insufficient kidney function, and treatment with antiplatelet) both had good ability to identify those who bled vs. not (C-index 0.69 and 0.67, respectively). These scores both had similar discrimination, but markedly better calibration when compared with the HAS-BLED and ATRIA scores in an external validation population from the ROCKET-AF trial.

Conclusions The five-element ORBIT bleeding risk score had better ability to predict major bleeding in AF patients when compared with HAS-BLED and ATRIA risk scores. The ORBIT risk score can provide a simple, easily remembered tool to support clinical decision making.

Keywords Atrial fibrillation • Anticoagulants • Major bleeding • Risk prediction

Riesgo hemorrágico: nunca impide la ACO

HEMORR$_2$HAGES		ATRIA		HAS-BLED		ORBIT	
H	Disfunción hepática o renal 1	Anemia	3	H	Hipertensión 1	O	Edad > 74 años 1
E	Alcohol 1	Disfunción renal severa (ClCr<30 ml/min)	3	A	Disfunción hepática o renal 1 ó 2	R	Reducción Hb Anemia 2
M	Enfermedad maligna 1	Edad > 75 años	2	S	Ictus 1	B	Sangrado previo 2
O	Edad > 75 años 1	Sangrado previo	1	B	Sangrado previo 1	I	Insuficiencia renal 1
R	Reducción recuento plaquetas 1	Hipertensión	1	L	Labilidad INR 1	T	Tratamiento antiagregantes 1
R	Resangrado 2			E	Edad > 65 años 1		
H	Hipertensión 1			D	Fármacos/Alcohol 1 ó 2		
A							
G	Anemia 1						
E	Genética 1						
S	Excesivo riesgo de caídas 1						
	Ictus 1						
	Puntuación máxima 12	Puntuación máxima	10		Puntuación máxima 9		Puntuación máxima 7
	Categorías de riesgo	Categorías de riesgo			Categorías de riesgo		Categorías de riesgo
	Bajo riesgo: 1-2 p Intermedio:2-3 p Alto: ≥ 4 p	Bajo riesgo: 2-3 p Moderado: 4 p Alto: ≥ 5 p			Bajo riesgo: 0-1 p Moderado:2 p Alto: ≥ 3 p		Bajo riesgo: 0-2 p Moderado: 3 p Alto: ≥ 4 p

Kirchhof P et al. Rev Esp Cardiol 2017;70:43.e1-e84.

ORBIT

- Estudi realitzat amb població amb ACODs
- Poques variables, senzilla
- Factors de risc poc modificables en la práctica diaria

CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Evaluation of the HAS-BLED, ATRIA, and ORBIT Bleeding Risk Scores in Patients with Atrial Fibrillation Taking Warfarin

Keitaro Senoo, MD,[a] Marco Proietti, MD,[a] Deirdre A. Lane, PhD,[a] Gregory Y.H. Lip, MD[a,b]

[a]*University of Birmingham Institute of Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom;* [b]*Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark.*

Les 3 escales van demostrar un valor predictiu modest del sagnat major, pero el HAS-BLED va ser superior.

bleeding: hazard ratio, 1.85; 95% confidence interval, 1.43-2.40, $P < .001$; major bleeding: hazard ratio, 2.40; 95% confidence interval, 1.28-4.52; $P = .007$). There were strong inverse correlations of ATRIA and ORBIT scores to time in therapeutic range as a continuous variable (low risk ATRIA, $r = -0.96$; $P = .003$; ORBIT, $r = -0.96$; $P = .003$). Improvement in the predictive performance for both ATRIA and ORBIT scores for any clinically relevant bleeding was achieved by adding time in therapeutic range to both scores, with significant differences in c-indexes ($P = .001$ and $P = .002$, respectively), net reclassification improvement, and integrated discriminant improvement (both $P < .001$).

CONCLUSIONS: All 3 bleeding risk prediction scores demonstrated modest predictive ability for bleeding outcomes, although the HAS-BLED score performed better than the ATRIA or ORBIT score. Significant improvements in both ATRIA and ORBIT score prediction performances were achieved by adding time in therapeutic range to both scores.

KEYWORDS: Anticoagulation; ATRIA; Bleeding; HAS-BLED; ORBIT; Risk assessment

ABC

El paper dels biomarcadors per valorar el risc dels pacients en ACXFA. Podrien millorar el valor predictiu en el risc hemorràgic?

The novel biomarker-based ABC (age, biomarkers, clinical history)-bleeding risk score for patients with atrial fibrillation: a derivation and validation study

Ziad Hijazi, Jonas Oldgren, Johan Lindbäck, John H Alexander, Stuart J Connolly, John W Eikelboom, Michael D Ezekowitz, Claes Held, Elaine M Hylek, Renato D Lopes, Agneta Siegbahn, Salim Yusuf, Christopher B Granger, Lars Wallentin, on behalf of the ARISTOTLE and RE-LY Investigators

Summary

Background The benefit of oral anticoagulation in atrial fibrillation is based on a balance between reduction in ischaemic stroke and increase in major bleeding. We aimed to develop and validate a new biomarker-based risk score to improve the prognostication of major bleeding in patients with atrial fibrillation.

Methods We developed and internally validated a new biomarker-based risk score for major bleeding in 14 537 patients with atrial fibrillation randomised to apixaban versus warfarin in the ARISTOTLE trial and externally validated it in 8468 patients with atrial fibrillation randomised to dabigatran versus warfarin in the RE-LY trial. Plasma samples for determination of candidate biomarker concentrations were obtained at randomisation. Major bleeding events were centrally adjudicated. The predictive values of biomarkers and clinical variables were assessed with Cox regression models. The most important variables were included in the score with weights proportional to the model coefficients. NCT00412984 and NCT

Findings The most imp differentiation factor-15 (bleeding. The ABC-blee [previous bleeding]) scor major bleeding in both respectively; ABC-bleedi yielded a higher c-index HAS-BLED *vs* 0·68 [0·6 p=0·0016). A modified creatinine clearance) also

Interpretation The ABC-b GDF-15 or cystatin C/CK atrial fibrillation receivin ORBIT scores and should

Funding BMS, Pfizer, Bo

- Analiza la edad (A); como biomarcadores (B) de sangrado (troponina T, NT-proBNP y GDF-15) ultrasensible y el hematocrito, y como variable clínica (C), el antecedente de sangrado.
- El esquema ABC presenta mayor poder predictivo que el HAS-BLED recomendado por las guías clínicas
- Incluye pocas variables
- El papel de los biomarcadores presentes en la práctica clínica diaria con la finalidad de individualizar
- El esquema ABC no está ampliamente validado, por lo que no se lo puede considerar herramienta de referencia en la práctica clínica diaria.

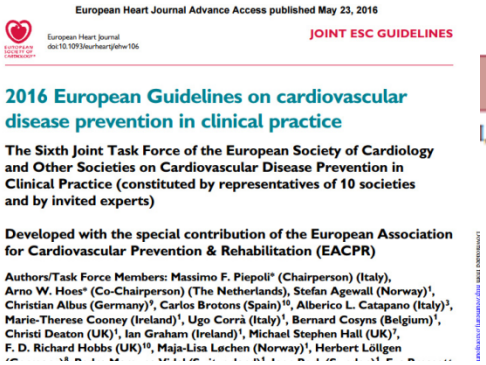
Scores to predict major bleeding risk during oral anticoagulation therapy: a prospective validation study.

Donzé J, Rodondi N, Waeber G, Monney P, Cornuz J, Aujesky D
Am J Med. 2012 Nov;125(11):1095-102. Epub 2012 Aug 30. .

- Estudi per pacients anticoagulats per diferents diagnòstics
- No hi han diferencies importants entre les escales de risc.
- ATRIA va ser millor que la resta, lleugerament superior en predir el risc hemorragic major. Era l´estudi amb mes pacients.
- No existeixen diferències entre les escales de risc i la valoració subjectiva del metge

Factors in Atrial Fibrillation score performed slightly better than would be expected by chance (C statistic, 0.61; 95% confidence interval, 0.52-0.70). **The performance of the scores was not statistically better than physicians' subjective risk assessments** (C statistic, 0.55; P=.94).

CONCLUSION: The performance of 7 clinical scoring systems in predicting major bleeding events in patients receiving oral anticoagulation therapy was poor and not better than physicians' subjective assessments



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JOINT ESC GUIDELINES

2016 European Guidelines on cardiovascular disease prevention in clinical practice

The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)

Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR)

Authors/Task Force Members: Massimo F. Piepoli* (Chairperson) (Italy), Arno W. Hoes* (Co-Chairperson) (The Netherlands), Stefan Agewall (Norway)[1], Christian Albus (Germany)[2], Carlos Brotons (Spain)[10], Alberico L. Catapano (Italy)[3], Marie-Therese Cooney (Ireland)[1], Ugo Corrà (Italy)[1], Bernard Cosyns (Belgium)[1], Christi Deaton (UK)[1], Ian Graham (Ireland)[1], Michael Stephen Hall (UK)[7], F. D. Richard Hobbs (UK)[10], Maja-Lisa Løchen (Norway)[1], Herbert Löllgen

Recomendaci

			Guía estadounidense AHA/ACC 2014		Guía NICE (Reino Unido)
Riesgo troml		I, nivel A	Se recomienda el esquema CHA_2DS_2-VASc para la evaluación del riesgo trombótico de pacientes con fibrilación auricular no valvular	Clase I, nivel B	Se recomienda la utilización del esquema de riesgo CHA_2DS_2-VASc para evaluar el riesgo trombótico de pacientes con: • Fibrilación auricular persistente, permanente o paroxística tanto sintomática como asintomática • *Flutter* auricular • Recurrencia de fibrilación auricular
Riesgo hemorrágico	Se recomienda evaluar el riesgo hemorrágico al iniciar la terapia antitrombótica, ya sea con antagonistas de la vitamina K o anticoagulantes orales directos	Clase I, nivel A	Se recomienda revaluar periódicamente la necesidad y el tipo de terapia antitrombótica, evaluando riesgo trombótico y hemorrágico	Clase I, nivel C	Se recomienda la utilización del esquema HAS-BLED para evaluar el riesgo hemorrágico de pacientes que empiezan anticoagulación o están anticoagulados. Es necesario monitorizar y realizar una modificación frecuente de: • Hipertensión incontrolada • Labilidad de la INR • Uso concomitante de AINE o AAS • Alto consumo de alcohol
	Se debe considerar HAS-BLED como her[illegible] para evaluar [illegible]angrado. HAS-BLED [illegible] usar para identifi[illegible]e riesgo modificab[illegible]s, pe[illegible] no para excluir a pacientes de la terapia anticoagulante	Clase IIa, nivel A			

AAS: ácido acetilsalicílico; ACC: *American College of Cardiology*; AHA: *American Heart Association*; AINE: antiinflamatorios no esteroideos; ESC: Sociedad Europea de Cardiología; NICE: *National Institute for Health and Care Excellence*.

Take to home

- Existeixen múltiples estudis retrospectius i prospectius per estimar el risc hemorràgic en el pacient anticoagulat però no existeix cap realment fiable.
- No està clar quin és el millor mètode per preveure el risc hemorràgic individual en el pacient anticoagulat
- Necessitem nous mètodes clinics que puguin preveure de forma més acurada i real el risc d´hemorragia major en el pacient anticoagulat.
- El HAS-BLED es el risk score que es recomana en mes guies per valorar el risc hemorràgic en els pacients en la practica clinica real.
- Recordar que una puntuació elevada de risc hemorràgic no es motiu per no iniciar anticoagulació, pero si es una alerta per evaluar i corretgir els factors que generen aquesta puntuació elevada i control mes estricte.

Moltes gràcies!