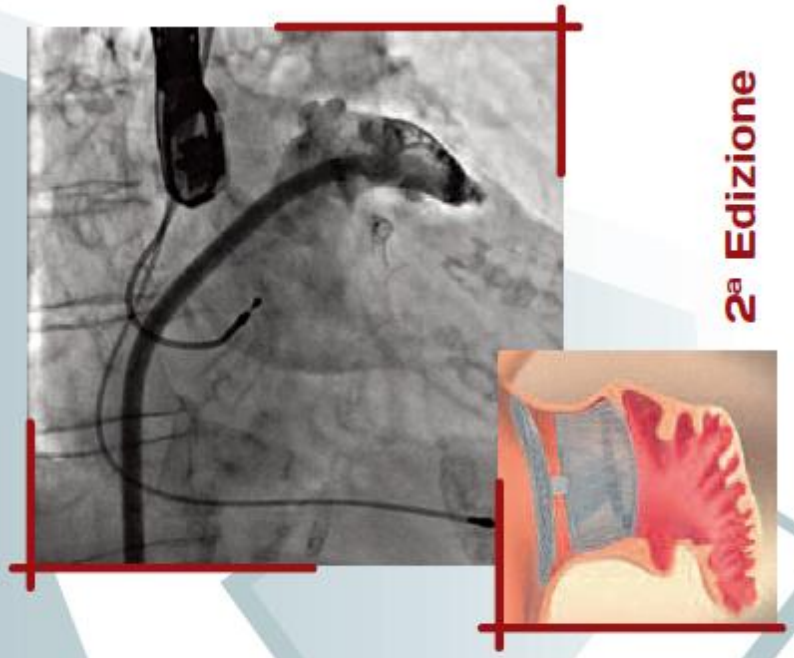

2ª Edizione

CHIUSURA PERCUTANEA DELL'AURICOLA SINISTRA: dalle linee guida alla pratica clinica

MARTEDI 8 MAGGIO 2018
Ospedale San Giovanni Bosco
Torino

Torino 08 Maggio 2018

I limiti degli score di rischio trombotico ed emorragico nel paziente fragile con fibrillazione atriale

Fabrizio UGO

Ospedale San Giovanni Bosco
Torino

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European Heart Journal (2016) **37**, 2893–2962
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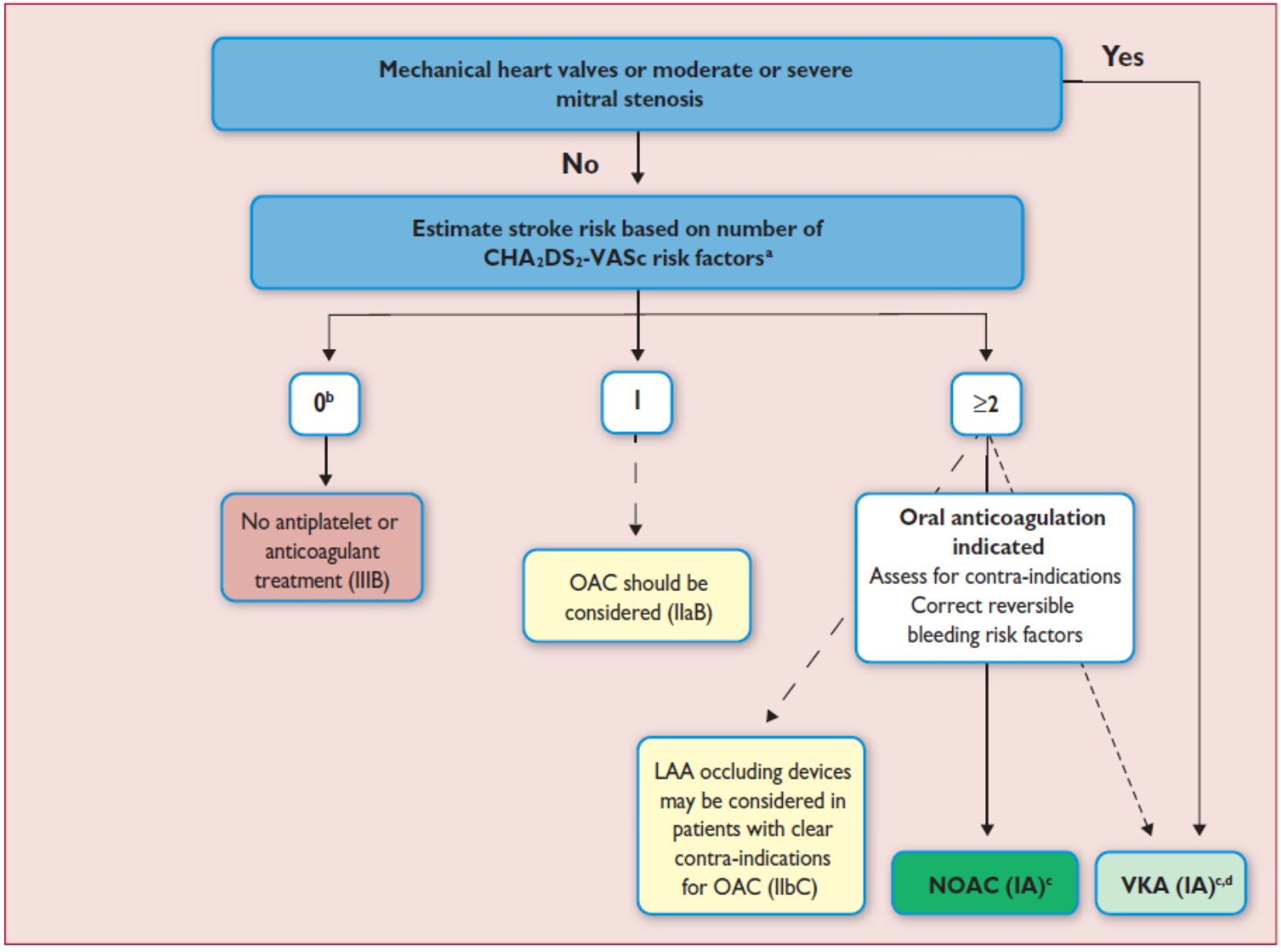

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Lo Score di rischio

- Lo Score è uno “ Strumento”
- Si basa su un campione di derivazione ed uno di validazione.
- Valore predittivo (performance = C statistics)
- Miglior definizione del profilo di rischio.
- Uniformità di linguaggio (indispensabile)
- Strategia terapeutica.

Stoke Stratification Scores

Main stroke stratification schemas

Schema	Low risk†	Intermediate risk†	High risk†	Ref.
$CHADS_2$	Score 0	Score 1–2	Score 3–6	[10]
$CHADS_2$‡	Score 0	Score 1–5	Score >6	[47]
Framingham	Score 0–7	Score 8–15	Score 16–31	[11]
AHA/ACC/ESC	No risk factors	Age ≥75 years, HT, HF, or LVEF ≤35%, or DM	Previous stroke, TIA or TE, or ≥2 moderate risk factors (age ≥75 years, HT, HF, LVEF ≤35% or DM)	[7]
ACCP-8	No risk factors	Age >75 years, HT, moderate or severe LV impairment and/or HF, or DM	Previous stroke, TIA or embolism, or ≥2 moderate risk factors (age ≥75 years, HT, moderate/severe LV impairment and/or HF, or DM)	[8]
ESC 2010	CHA_2DS_2-VASc = 0 No clinically relevant non-major risk factors§	CHA_2DS_2-VASc = 1 One 'clinically relevant non-major' risk factor§	CHA_2DS_2-VASc ≥2 One 'major' risk factor or ≥2 'clinically relevant non-major' risk factors§	[9]
CHA_2DS_2-VASc	No risk factors	One clinically relevant non-major risk factor (HF/LVEF ≤40%, HT, DM, vascular disease, female gender, or age 65–74 years)	Previous stroke, TIA or TE, or age ≥75 years, or ≥2 clinically relevant non-major risk factors (HF/LVEF ≤40%, HT, DM, vascular disease, female gender, or age 65–74 years)	[15]

Pamukcu B and Lip G Expert Rev. Cardiovasc Ther. 2010; 8: 1703-1710

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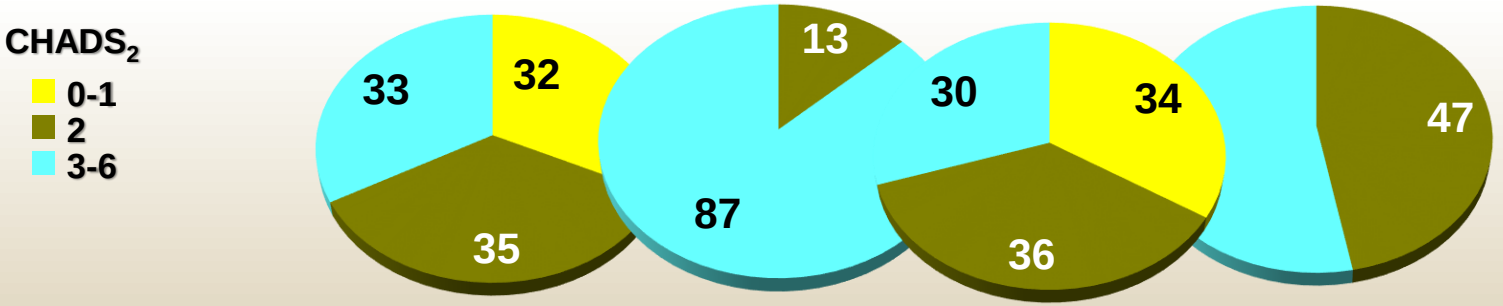
Baseline characteristics in AF trial

	RE-LY (Dabigatran)	ROCKET-AF (Rivaroxaban)	ARISTOTLE (Apixaban)	ENGAGE AF (Edoxaban)
Randomized, n	18,113	14,264	18,201	21,105
Age, years	72 ± 9	73 [65-78]	70 [63-76]	72 [64-78]
Female, %	37	40	36	39
$CHADS_2$ score	2.1	3.5	2.1	2.8
Paroxysmal AF, %	32	18	15	25
Prior stroke/TIA, %	20	55	19	28
VKA naïve, %	50	38	43	41
Aspirin use, %	40	36	31	29
Median follow-up, years	2.0	1.9	1.8	2.8
Median TTR, %	66	58	66	68



1. Connolly SJ et al. N Engl J Med 2009;361:1139-1151; 2. Patel MR et al. N Engl J Med 2011;365:883-891;
3. Granger CB et al. N Engl J Med 2011;365:981-992; 4. Giugliano RP et al. N Engl J Med 2013;369:2093-2104.

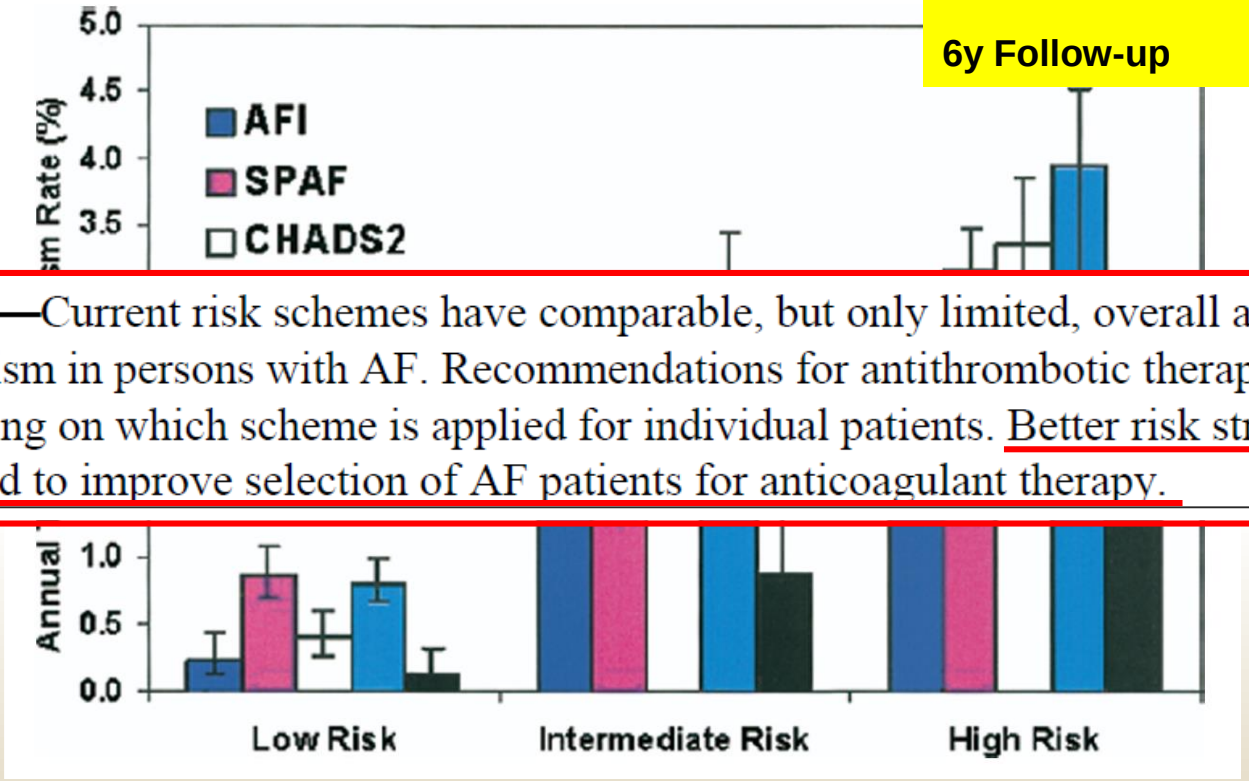
Comparison of Risk Stratification Schemes to Predict Thromboembolism in People With Nonvalvular Atrial Fibrillation

Margaret C. Fang, MD, MPH[*], Alan S. Go, MD[*,†], Yuchiao Chang, PhD[‡], Leila Borowsky, MPH[‡], Niela K. Pomernacki, RD[†], Daniel E. Singer, MD[‡], and for the ATRIA Study Group

J Am Coll Cardiol. 2008 February 26; 51(8): 810–815. doi:10.1016/j.jacc.2007.09.065.

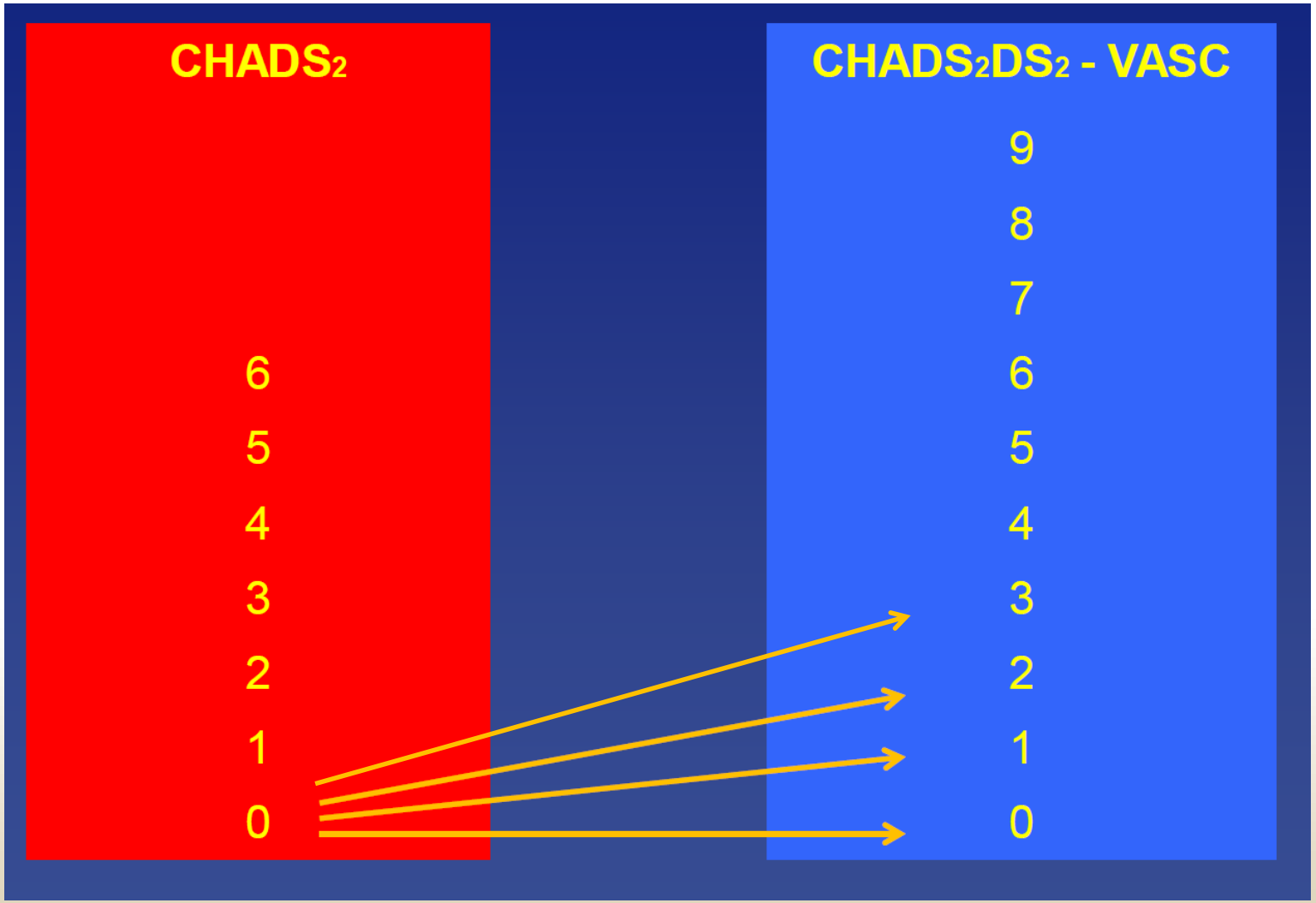
> 13,500 cohort pts

6y Follow-up



Conclusions—Current risk schemes have comparable, but only limited, overall ability to predict thromboembolism in persons with AF. Recommendations for antithrombotic therapy may vary widely depending on which scheme is applied for individual patients. Better risk stratification is crucially needed to improve selection of AF patients for anticoagulant therapy.

$CHADS_2$ vs CHA_2DS_2-VASc Score



$CHADS_2$ vs CHA_2DS_2-VASc Score

$CHADS_2$ punteggio attribuito a ciascun fattore di rischio	
Pregresso ictus/TIA	2
Ipertensione arteriosa	1
Età ≥75 anni	1
Scompenso cardiaco recente	1
Diabete	1
Nessuno dei precedenti	0

Punteggio $CHADS_2$ totale	Rischio di eventi cardioembolici per i diversi punteggi % paz. per anno (IC)
0	1.9 (1.2-3.0)
1	2.8 (2.0-3.8)
2	4.0 (3.1-5.1)
3	5.9 (4.6-7.3)
4	8.5 (6.3-11.1)
5	12.5 (8.2-17.5)
6	18.2 (10.5-27.4)

CHA_2DS_2-VASc punteggio attribuito a ciascun fattore di rischio	
Pregresso ictus/TIA	2
Età ≥75 anni	2
Età 65-74 anni	1
Sesso femminile	1
Scompenso cardiaco recente	1
Ipertensione arteriosa	1
Diabete	1
Vasculopatia	1
Nessuno dei precedenti	0

Punteggio CHA_2DS_2-VASc totale	Rischio di eventi cardioembolici per i diversi punteggi % paz. per anno (IC)
0	0.78 (0.58 - 1.04)
1	2.01 (1.70 - 2.36)
2	3.71 (3.36 - 4.09)
3	5.92 (5.53 - 6.34)
4	9.27 (8.71 - 9.86)
5	15.26 (14.35 - 16.24)
6	19.74 (18.21 - 21.41)
7	21.50 (18.75 - 24.64)
8	22.38 (16.29 - 30.76)
9	23.64 (10.62 - 52.61)

Età 68 aa con FA
Pregresso infarto del miocardio

$CHADS_2$ = 0

CHA_2DS_2-VASc = 3

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Event rate of stroke/TE in AF patients

	1 year follow-up					
	Person-years	Events	Stroke rate (95%CI)			
$CHADS_2$ score 0–1	40,272	1,405	3.49 (3.31–3.68)			
CHA_2DS_2-VASc = 0	6,919	58	0.84 (0.65–1.08)			
CHA_2DS_2-VASc = 1	8,880	159	1.79 (1.53–2.09)			
CHA_2DS_2-VASc = 2	11,863	435	3.67 (3.34–4.03)			
CHA_2DS_2-VASc = 3	11,473	660	5.75 (5.33–6.21)			
CHA_2DS_2-VASc = 4	1,137	93	8.18 (6.68–10.02)			
$CHADS_2$ score = 0	17,327	275	1.59 (1.41–1.79)			
CHA_2DS_2-VASc = 0	6,919	58	0.84 (0.65–1.08)			
CHA_2DS_2-VASc = 1	6,811	119	1.75 (1.46–2.09)			
CHA_2DS_2-VASc = 2	3,347	90	2.69 (2.19–3.31)			
CHA_2DS_2-VASc = 3	250	8	3.20 (1.60–6.40)			
$CHADS_2$ score = 1	22,945	1,130	4.92 (4.65–5.22)			
CHA_2DS_2-VASc = 1	2,069	40	1.93 (1.42–2.64)			
CHA_2DS_2-VASc = 2	8,516	345	4.05 (3.65–4.50)			
CHA_2DS_2-VASc = 3	11,223	652	5.81 (5.38–6.27)	44,557	1907	4.28 (4.09–4.48)
CHA_2DS_2-VASc = 4	1,137	93	8.18 (6.68–10.02)	4,380	216	4.93 (4.32–5.64)
$CHADS_2$ and CHA_2DS_2-VASc: see text						

What is known about this topic?

- North American and European guidelines on atrial fibrillation (AF) are conflicting regarding the classification of patients at low/intermediate risk of stroke.
- Those with $CHADS_2$ score=0 are often described as 'low risk'.

What does this paper add?

- Patients with a $CHADS_2$ score=0 were not all 'low risk', with 1-year event rates ranging from 0.84 (CHA_2DS_2-VASc score=0) to 3.2 (CHA_2DS_2-VASc score=3).
- The CHA_2DS_2-VASc score improved stroke risk reduction in the AF patients who have a $CHADS_2$ score of 0–1.
- Even in patients categorised as 'low risk' using a $CHADS_2$ score=0, the CHA_2DS_2-VASc score significantly improved the predictive value of the $CHADS_2$ score alone and a CHA_2DS_2-VASc score=0 could clearly identify 'truly low risk' subjects.
- Use of the CHA_2DS_2-VASc score would significantly improve classification of AF patients at low and intermediate risk of stroke, compared to the commonly used $CHADS_2$ score.

Olesen JB et al. Throm. Haemost. 2012; 107: 1172- 79

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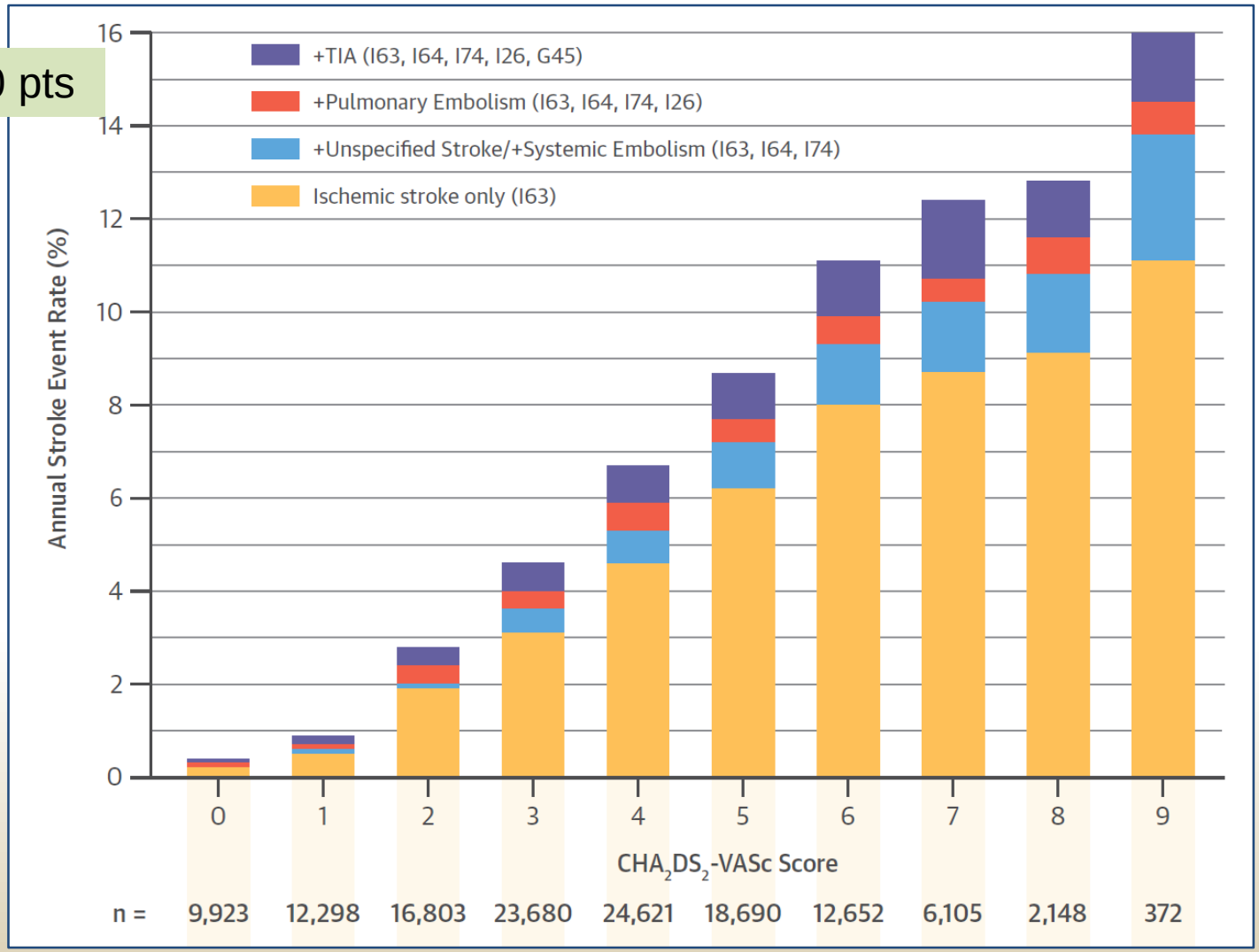
Annual Event Rate

Swedish National Patient Register

> 140000 pts



Friberg L. et al. JACC 2015; 65: 225 - 32

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Recommendation for prediction of stroke and bleeding risk

Recommendations	Class[a]	Level[b]	Ref[c]
The CHA_2DS_2-VASc score is recommended for stroke risk prediction in patients with AF.	I	A	368, 371, 386
Bleeding risk scores should be considered in AF patients on oral anticoagulation to identify modifiable risk factors for major bleeding.	IIa	B	384, 386, 387, 389–392
Biomarkers such as high-sensitivity troponin and natriuretic peptide may be considered to further refine stroke and bleeding risk in AF patients.	IIb	B	380–382, 387, 393

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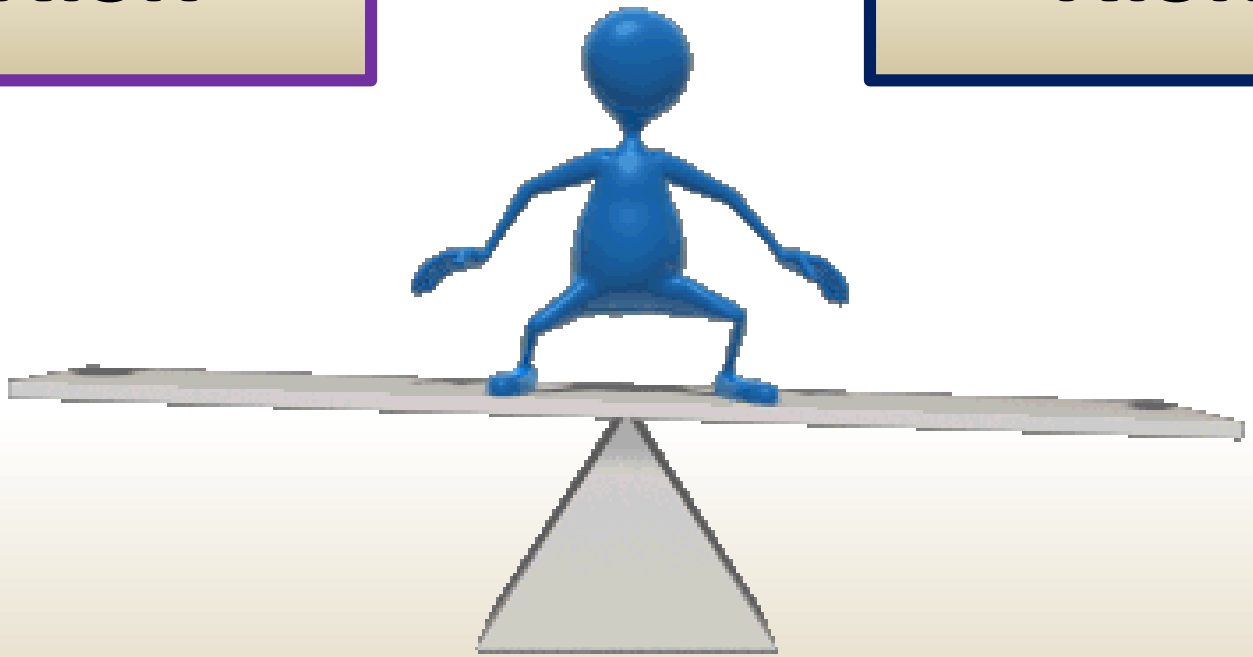
ISCHEMIC Risk

BLEEDING Risk



Risk factors for stroke and bleeding

Risk factors for stroke	Risk factors for bleeding
Age ≥75 or 65–74 years	Advanced age (>75 years)
Previous stroke, TIA or thromboembolism	Cerebrovascular disease
Hypertension	History of bleeding (gastrointestinal or intracranial)
Diabetes mellitus	Prior MI or ischemic heart disease
Mitral stenosis, prosthetic heart valve	Uncontrolled hypertension
Congestive heart failure or LV dysfunction (EF ≤35%)	Anemia
Vascular disease (prior MI, peripheral artery disease or aortic plaque)	Polypharmacy (aspirin or NSAIDs)
Female gender	Poorly controlled international normalized ratio
	Renal dysfunction

EF: Ejection fraction; LV: Left ventricle; MI: Myocardial infarction; TIA: Transient ischemic attack.

Pamukcu B and Lip G Expert Rev. Cardiovasc Ther. 2010; 8: 1703-1710

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Bleeding Risk Scores

Main bleeding risk schemas in AF pts

Schema (year)	Risk factors recruited in score calculation	Ref.
Kuijer *et al.* (1999)	Risk score = (1.6 × age) + (1.3 × sex) + (2.2 × malignancy). 1 point for being ≥60 years old, being female or having malignancy; 0 if none of those	[26]
Beyth *et al.* (1998)	OBRI: age ≥65 years, GI bleeding in last 2 weeks, previous stroke, comorbidities (≥1 of the following; recent MI, hematocrit <30%, diabetes mellitus or creatinine >1.5 mg/dl; 1 point for each existing risk factor)	[27]
Gage *et al.* (2006)	HEMORR$_2$HAGES: hepatic and/or renal disease, ethanol abuse, malignancy, older (age >75 years), low platelet count or function, rebleeding risk, uncontrolled hypertension, anemia, genetic factor(s) (e.g., CYP2C9 single-nucleotide polymorphisms), excessive fall risk and stroke (1 point for each risk factor; 2 points for previous bleeding)	[28]
Shireman *et al.* (2006)	Risk score = (0.49 × aged >70 years) + (0.32 × female) + (0.58 × remote bleed) + (0.62 × recent bleed) + (0.71 × alcohol/drug abuse) + (0.27 × diabetes) + (0.86 × anemia) + (0.32 × antiplatelet drug use); 1 point for each existing condition; 0 if absent	[29]
Pisters *et al.* (2010)	HAS-BLED: hypertension (systolic blood pressure >160 mmHg; 1 point), abnormal renal and liver function (presence of chronic dialysis or renal transplantation or serum creatinine ≥200 µmol/l, chronic hepatic disease [cirrhosis] or bilirubin >2× upper limit of normal, AST/ALT/ALP >3× upper limit of normal; 1 point each), stroke (1 point), previous bleeding history or bleeding diathesis or anemia (1 point), labile INRs (high INRs and poor time in therapeutic range; 1 point), elderly (e.g., age >65 years; 1 point), drugs (concomitant use of antiplatelet agents or NSAID) or alcohol (1 point each)	[30]

ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CYP: Cytochrome P; GI: Gastrointestinal; HAS-BLED: Hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly (e.g., >65), drugs/alcohol concomitantly; INR: International normalized ratio; MI: Myocardial infarction; OBRI: Outpatient bleeding risk index.

Pamukcu B and Lip G Expert Rev. Cardiovasc Ther. 2010; 8: 1703-1710

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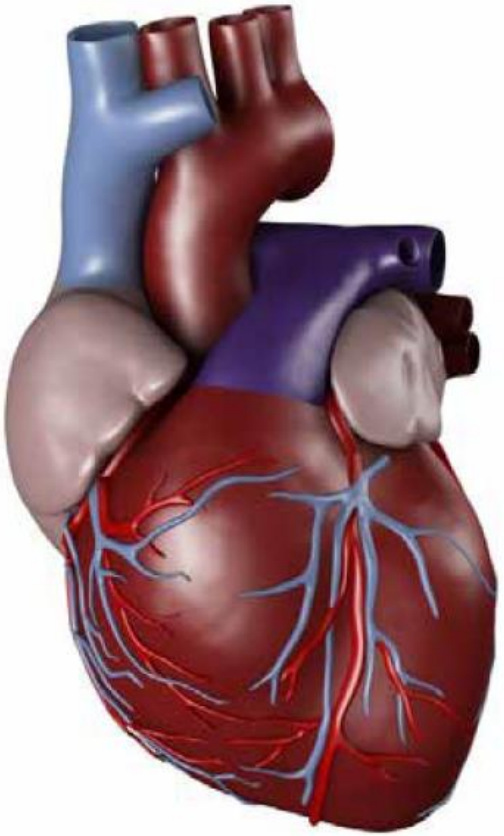
Bleeding Risk Scores widely used in AF pts

- HAEMORRHAGES[1]
- HASBLED[2]
- ATRIA Score[3]



1. Gage BF, et al. Am Heart J. 2006 Mar;151(3):713-9. PMID: 16504638. Pub Med PMID:16504638.
2. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. Chest. 2010 Nov;138(5):1093-100. PMID:20299623.
3. Fang MC, et al. J Am Coll Cardiol. 2011 Jul 19;58(4):395-401. Pub Med PMID:21757117.

Bleeding risk scores in AF

ATRIA		HAS-BLED		HEMORR$_2$HAGES	
Anemia[1]	3	Hypertension[4]	1	Hepatic[10] or Renal disease[2]	1 1
Severe renal disease[2]	3	Abnormal Renal[5] or Liver function[6]	1 1	Ethanol abuse	1
Age ≥75 yrs	2	Stroke	1	Malignancy	1
Any prior hemorrhage	1	Bleeding	1	Older Age (>75 yrs)	1
Hypertension[3]	1	Labile INR[8]	1	Reduced platelet number or function[11]	1
		Elderly (>65 yrs)	1	Rebleeding[12]	2
		Drugs[9] or Alcohol	1 1	Hypertension[4]	1
				Anemia[13]	1
				Genetic factors[14]	1
				Excessive fall risk[15]	1
				Stroke	1

1. Hemoglobin <13 g/dl men; <12 g/dl women
2. Estimated glomerular filtration rate <30 ml/min or dialysis-dependent
3. Diagnosed hypertension
4. Systolic blood pressure >160 mmHg
5. Presence of chronic dialysis or renal transplantation or serum creatinine ≥200 mmol/L
6. Chronic hepatic disease (eg cirrhosis) or biochemical evidence of significant hepatic derangement (eg bilirubin 2 x upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase >3 x upper limit normal, etc.)
8. Unstable/high INRs or poor time in therapeutic range (eg <60%)
9. Concomitant use of drugs, such as antiplatelet agents, non-steroidal anti-inflammatory drugs, or alcohol abuse etc.
10. Cirrhosis, two-fold or greater elevation of AST or APT, or albumin <3.6 g/dl
11. Platelets <75,000, use of antiplatelet therapy (eg daily aspirin) or NSAID therapy; or blood dyscrasia
12. Prior hospitalization for bleeding
13. Most recent hematocrit <30 or hemoglobin <10 g/dl
14. CYP2C9*2 and/or CYP2C9*3
15. Alzheimer's dementia, Parkinson's disease, schizophrenia, or any condition predisposing to repeated falls

Apostolakis S, Lane DA, Guo Y, Buller H, Lip GY. J Am Coll Cardiol 2012;60:000–000. 2012 Jul 24. [Epub ahead of print] Online Appendix. PMID: 22858389.

AMADEUS Cohort

Stratified by the HEMORR$_2$HAGES, HAS-BLED, and ATRIA Schemes

Scheme	All Patients	Clinically Relevant Bleeding	Major Bleeding
HEMORR$_2$HAGES			
Low (≤1) Risk	1,738 (76.6)	182 (10.5)	25 (1.4)
Intermediate Risk (2–3)	517 (22.8)	63 (12.2)	13 (2.5)
High Risk (>3)	13 (0.5)	3 (23.1)	1 (7.7)
TOTAL	**2,268**	**248 (10.9)**	**39 (1.7)**
HAS-BLED			
Low Risk (<3)	1,739 (75.9)	159 (9.1)	22 (1.3)
High Risk (≥3)	553 (24.1)	92 (16.6)	17 (3.1)
TOTAL	**2,292**	**251 (11.0)**	**39 (1.7)**
ATRIA			
Low Risk (<4)	2,038 (90)	220 (10.8)	31 (1.5)
Intermediate Risk (4)	102 (4.4)	13 (12.7)	3 (2.9)
High Risk (>4)	128 (5.6)	18 (14.1)	5 (3.9)
TOTAL	**2,268**	**248 (10.9)**	**39 (1.7)**

Apostolakis S. et al. JACC 2012; 60: 861 - 867

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Performance of the HEMORR$_2$HAGES, ATRIA, and HAS-BLED Bleeding Risk–Prediction Scores in Patients With Atrial Fibrillation Undergoing Anticoagulation

The AMADEUS (Evaluating the Use of SR34006 Compared to Warfarin or Acenocoumarol in Patients With Atrial Fibrillation) Study

2,293 pts

251 (11%) Any clinical relevant bleeding

39 (1,7) major bleeding

Conclusions All 3 tested bleeding risk–prediction scores demonstrated only modest performance in predicting any clinically relevant bleeding……

HAS-BLED was the only score that demonstrated a significant predictive performance for intracranial hemorrhage (c-index: 0.75; p 0.03).

Apostolakis S. et al. JACC 2012; 60: 861 - 867

The HAS-BLED Score

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

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Bleeding risk by HAS-BLED Score

HAS-BLED Score	1 year Bleeding risk	Bleeds/100 pt-years
0	0.9%	1.13
1	3.4%	1.02
2	4.1%	1.88
3	5.8%	3.72
4	8.9%	8.70
5	9.1%	12.50
6 – 9	Insufficient data	Insufficient data

Pister R. et al. Chest 2010; 138: 1093 - 1100

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Limitation of HAS-BLED Score

- **Potential selection bias**
- **25% missing data regarding the occurrence of major bleeding during the follow-up**
- **Underestimation of the overall bleeding rate**
- **Limited number of major bleeding**
- **Short follow-up**
- **Modest number of very elderly pts and low rate of comorbidities.**

Pister R. et al. Chest 2010; 138: 1093 - 1100

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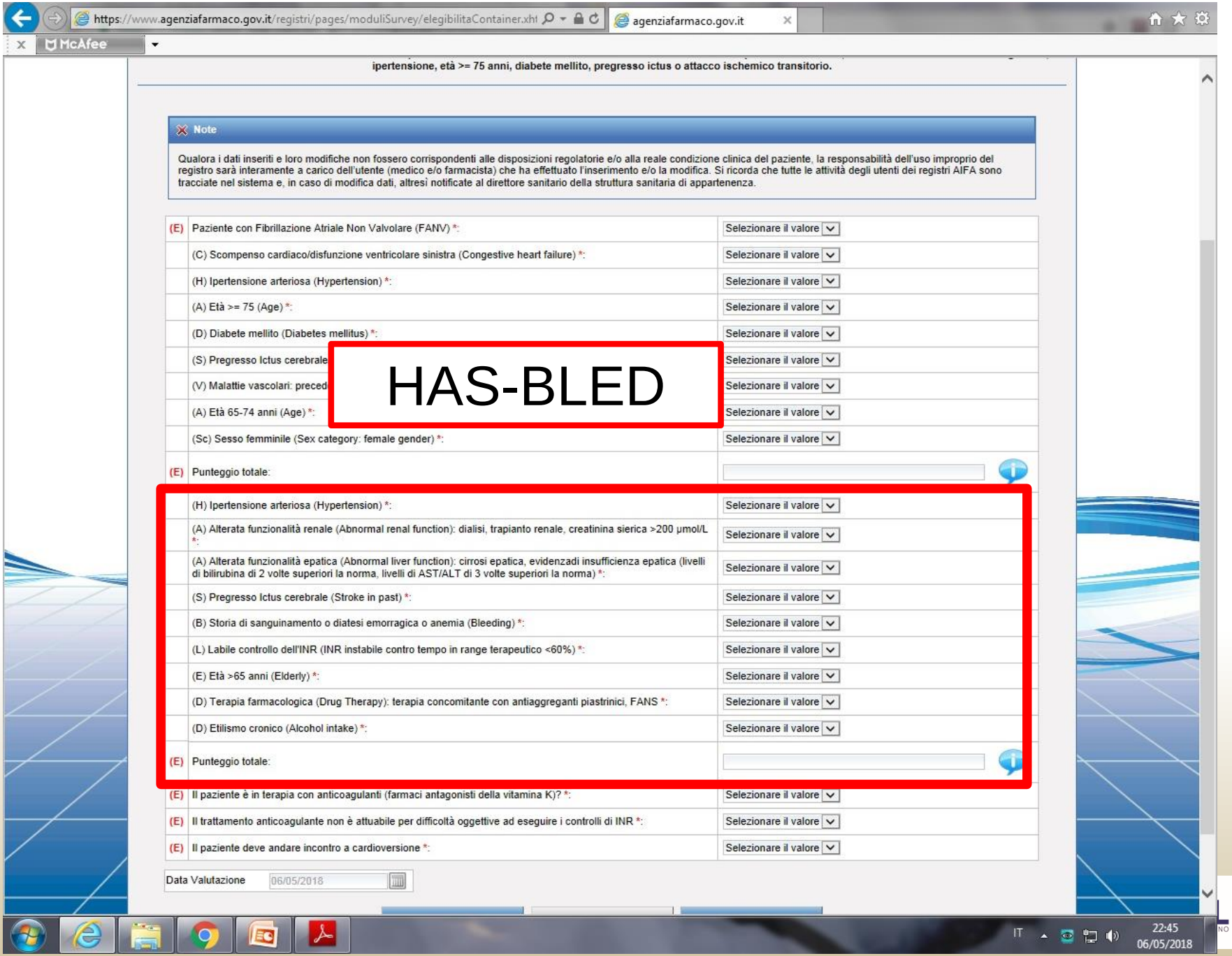
9.1.3 Clinical risk scores for bleeding

Several bleeding risk scores have been developed, mainly in patients on VKAs. These include HAS-BLED [hypertension, abnormal renal/liver function (1 point each), stroke, bleeding history or predisposition, labile INR, elderly (>65 years), drugs/alcohol concomitantly (1 point each)], ORBIT (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation), and more recently, the ABC (age, biomarkers, clinical history) bleeding score, which also makes use of selected biomarkers.[383–385] Stroke and bleeding risk factors overlap (compare *Tables 11* and *12*). For example, older age is one of the most important predictors of both ischaemic stroke and bleeding in AF patients.[386,387] A high bleeding risk score should generally not result in withholding OAC. Rather, bleeding risk factors should be identified and treatable factors corrected (see chapter 8.5). *Table 12* provides details of modifiable bleeding risk factors.


https://www.agenziafarmaco.gov.it/registri/pages/moduliSurvey/elegibilitaContainer.xht
agenziafarmaco.gov.it
McAfee
ipertensione, età >= 75 anni, diabete mellito, pregresso ictus o attacco ischemico transitorio.
Note
Qualora i dati inseriti e loro modifiche non fossero corrispondenti alle disposizioni regolatorie e/o alla reale condizione clinica del paziente, la responsabilità dell'uso improprio del registro sarà interamente a carico dell'utente (medico e/o farmacista) che ha effettuato l'inserimento e/o la modifica. Si ricorda che tutte le attività degli utenti dei registri AIFA sono tracciate nel sistema e, in caso di modifica dati, altresì notificate al direttore sanitario della struttura sanitaria di appartenenza.
(E) Paziente con Fibrillazione Atriale Non Valvolare (FANV) *:
(C) Scompenso cardiaco/disfunzione ventricolare sinistra (Congestive heart failure) *:
(H) Ipertensione arteriosa (Hypertension) *:
(A) Età >= 75 (Age) *:
(D) Diabete mellito (Diabetes mellitus) *:
(S) Pregresso Ictus cerebrale
(V) Malattie vascolari: preced
(A) Età 65-74 anni (Age) *:
(Sc) Sesso femminile (Sex category: female gender) *:
Selezionare il valore
(E) Punteggio totale:
HAS-BLED
(H) Ipertensione arteriosa (Hypertension) *:
(A) Alterata funzionalità renale (Abnormal renal function): dialisi, trapianto renale, creatinina sierica >200 µmol/L *:
(A) Alterata funzionalità epatica (Abnormal liver function): cirrosi epatica, evidenzadi insufficienza epatica (livelli di bilirubina di 2 volte superiori la norma, livelli di AST/ALT di 3 volte superiori la norma) *:
(S) Pregresso Ictus cerebrale (Stroke in past) *:
(B) Storia di sanguinamento o diatesi emorragica o anemia (Bleeding) *:
(L) Labile controllo dell'INR (INR instabile contro tempo in range terapeutico <60%) *:
(E) Età >65 anni (Elderly) *:
(D) Terapia farmacologica (Drug Therapy): terapia concomitante con antiaggreganti piastrinici, FANS *:
(D) Etilismo cronico (Alcohol intake) *:
(E) Punteggio totale:
(E) Il paziente è in terapia con anticoagulanti (farmaci antagonisti della vitamina K)? *:
(E) Il trattamento anticoagulante non è attuabile per difficoltà oggettive ad eseguire i controlli di INR *:
(E) Il paziente deve andare incontro a cardioversione *:
Data Valutazione 06/05/2018
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22:45
06/05/2018

Situazioni cliniche particolari associate ad elevato rischio emorragico

Casu G, et al. Giornale Italiano Cardiologia 2016; 17: 594-613

Situazioni cliniche particolari associate ad elevato rischio emorragico

- Paziente anziano
- Storia di sanguinamenti maggiori soprattutto intracranici
- Patologie gastrointestinali (epatopatie, angiodisplasie)
- Insufficienza renale cronica severa
- Coagulopatie
- Coronaropatia con recente impianto di stent in alto rischio emorragico
- disabilità psichica o rischio di frequenti cadute
- Paziente fragile

Casu G, et al. Giornale Italiano Cardiologia 2016; 17: 594-613

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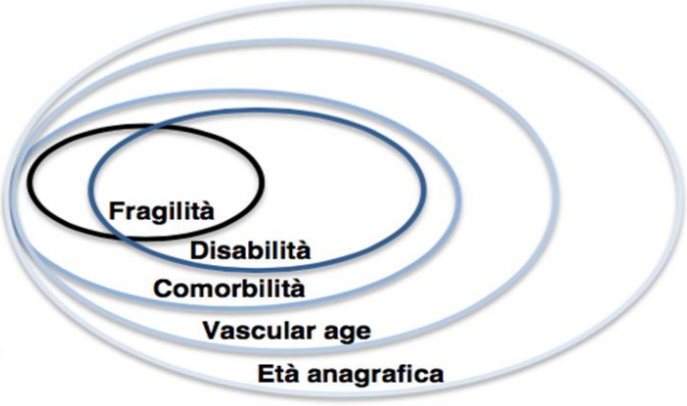
Casu G, et al. Giornale Italiano Cardiologia 2016; 17: 594-613

Fragilita’

termine proposto in geriatria 30 anni fa per identificare

Soggetti in cui il processo di invecchiamento si manifesta in modo rapido ed intenso, esponendoli ad una elevato rischio di manifestazioni cliniche quali :

- Cadute
- Frequenti ospedalizzazioni
- Perdita dell’autonomia funzionale
- Istituzionalizzazione e morte.



anche se non confinata alla popolazione anziana , si osserva prevalentemente negli ultra80enni

=>65 anni → 10% **80-84 → 16%** **> 85→26%**

ASL
CITTÀ DI TORINO

Criteri di FRIED per la fragilita' fisica

se presenti => 3

1. Perdita di peso non intenzionale
2. Facile affaticabilita' e senso di debolezza
3. Marcata riduzione dell'attivita' fisica
4. Cammino a bassa velocita'
5. Debolezza muscolare agli arti superiori

FRAGILITA' diversa da COMORBILITA'

FRAGILITA' diversa da DISABILITA'

ASL CITTÀ DI TORINO

Real-world characteristics of hospitalized frail elderly patients with atrial fibrillation: can we improve the current prescription of anticoagulants?

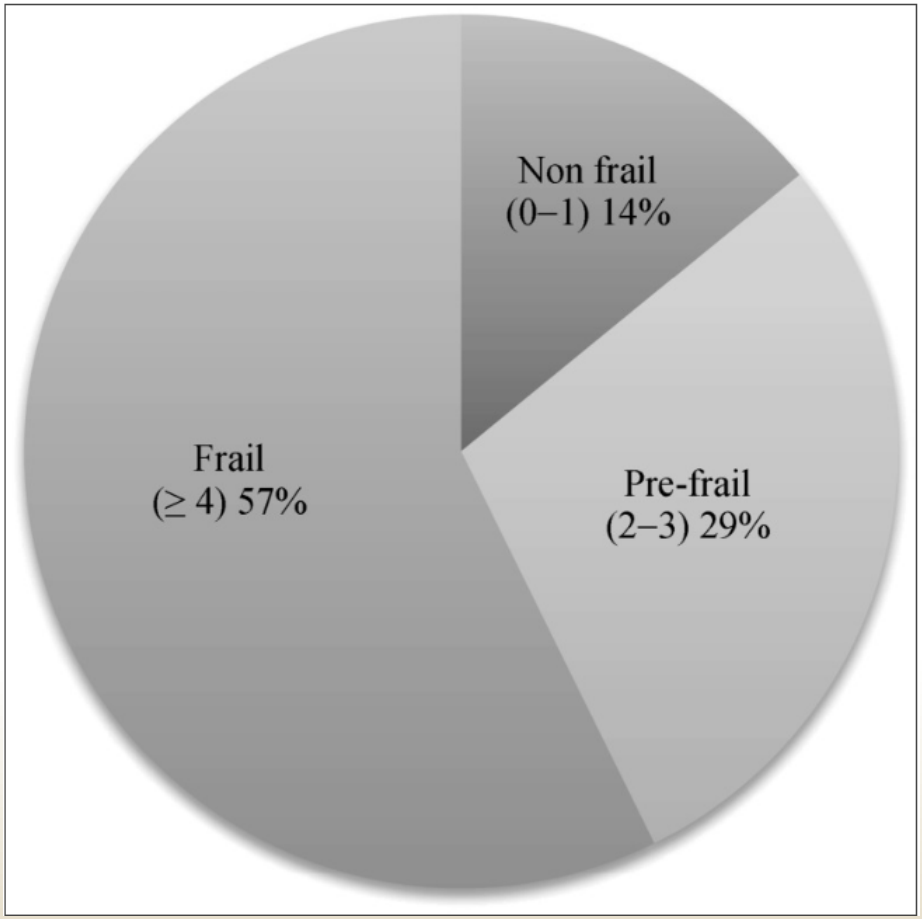
Studio osservazionale retrospettivo : inclusi 1619 pazienti , eta' =>65 aa , provenienti dal DEA nel periodo 2012-2014 e ricoverati in Unita' geriatrica per acuti (Monza)

Obiettivi dello studio :

- analizzare le caratteristiche cliniche dei paz. anziani con /senza FA
- discutere i motivi che riducono la prescrizione e la persistenza della terapia anticoagulante orale negli anziani fragili
- identificare le strategie per ridurre il sottoutilizzo della terapia anticoagulante orale negli anziani

J Geriatr Cardiol. 2016 Mar; 13(3): 226–232.

FRAGILITA’ nei pazienti in fibrillazione atriale



85.9% pazienti frail e pre-frail

J Geriatr Cardiol. 2016 Mar; 13(3): 226–232.

Clinical characteristics of 1619 patient with and without AF.

24%

	Without AF (n = 1216)	With AF (n = 403)	P value
Age, yrs	83.9 ± 6.9	84.6 ± 6.2	0.102
Female	727 (59.8%)	240 (59.6%)	0.934
Charlson comorbidity index	2 (1–4)	3 (2–4)	< 0.001
Comorbidities			
Heart failure	146 (12.0%)	147 (36.5%)	< 0.001
COPD	233 (19.2%)	98 (24.3%)	0.026
CKD (from stage 3A)	160 (13.2%)	83 (20.6%)	< 0.001
Cerebrovascular disease	275 (22.6%)	121 (30.0%)	0.003
Multimorbidity (> 3 diseases)	350 (28.8%)	286 (71.0%)	< 0.001
Number of medications	3 (2–5)	4 (3–6)	< 0.001

J Geriatr Cardiol. 2016 Mar; 13(3): 226–232.

ASL CITTÀ DI TORINO

Conclusioni degli autori ….

- Il trattamento della FA nei pazienti anziani deve sempre prevedere la terapia anticoagulante orale per l'elevato rischio tromboembolico (25%)

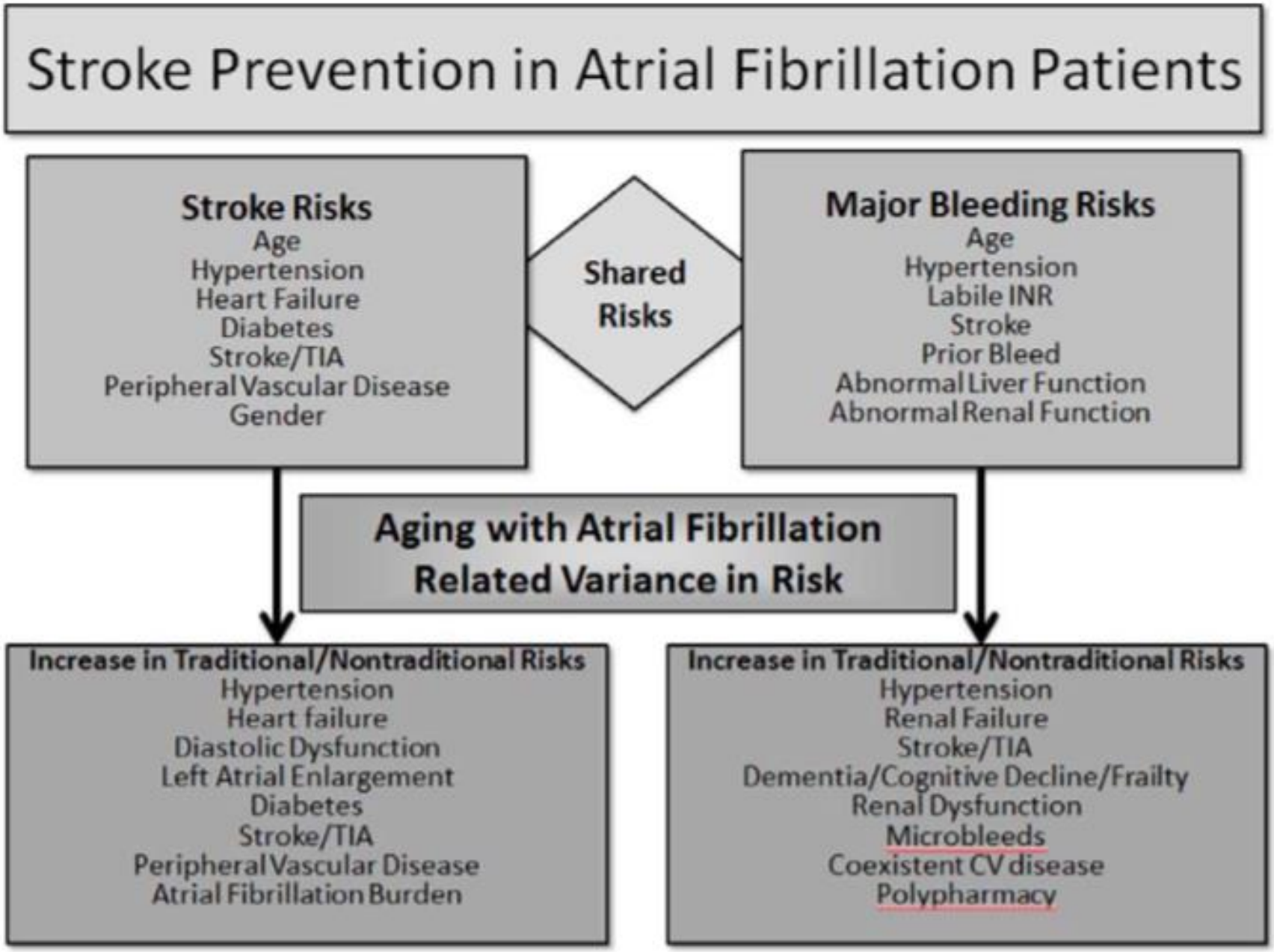
- Nei pazienti di eta' =>80 anni la sospensione del warfarin ad 1 anno e' piu' elevata rispetto ai pazienti < 80 anni . A 5 anni e' > 60% .

- Fattori determinanti la sospensione

➢ Fragilita'
➢ Rischio di cadute - limitazioni fisiche
➢ Elevato rischio emorragico e di ospedalizzazione
➢ Interferenze farmacologiche per politerapia

ASL CITTÀ DI TORINO

Stroke Prevention in Atrial Fibrillation Patients



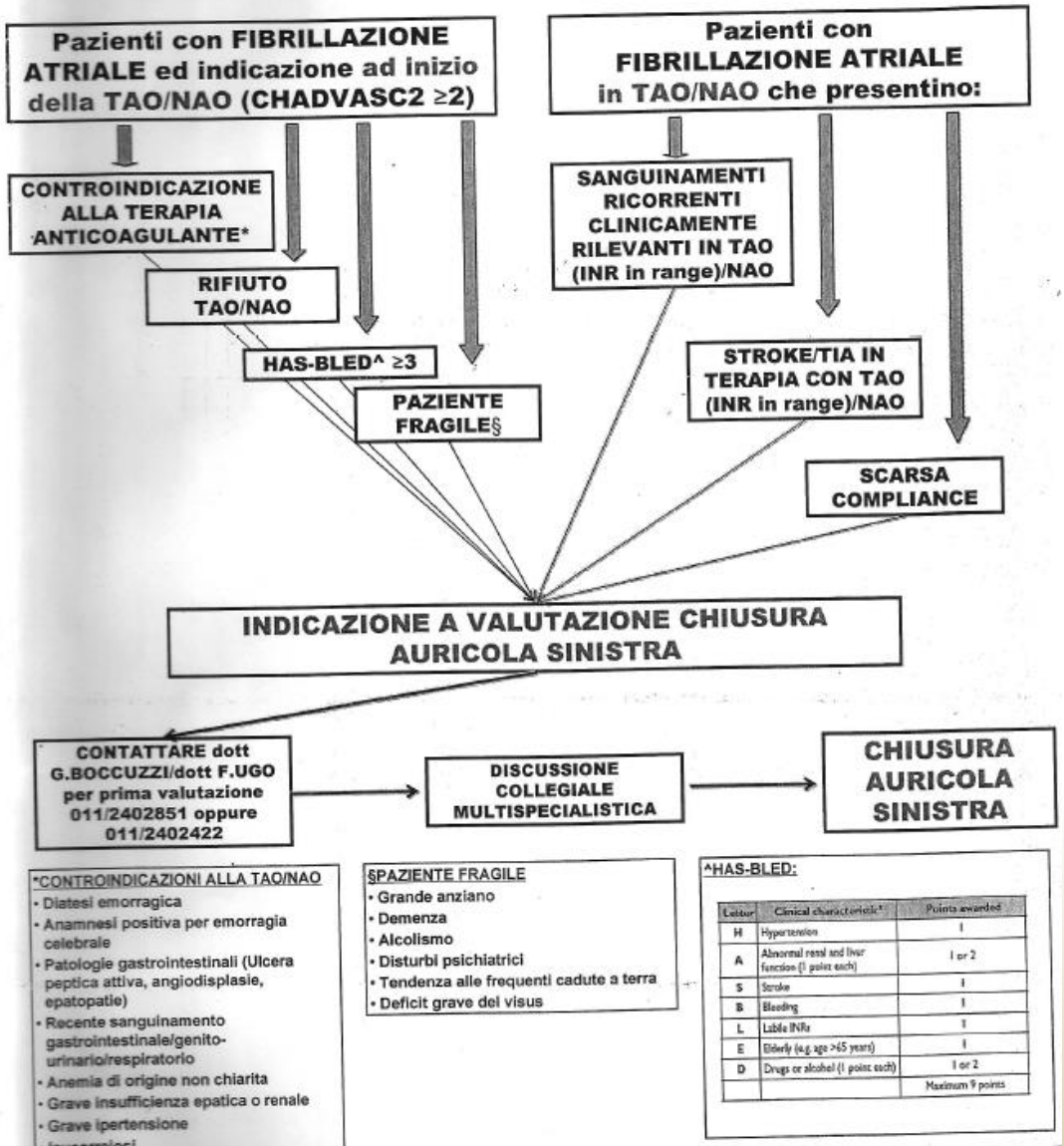
ORBIT-AF

controindicazioni alla terapia anticoagulante nella pratica clinica

Contraindication†	Overall (n = 1330)	Age (y)			ATRIA bleeding score			$CHADS_2$			CHA_2DS_2-VASc		
		<75 (n = 493)	≥75 (n = 837)	P§	<5 (n = 929)	≥5 (n = 400)	P§	<2 (n = 312)	≥2 (n = 1018)	P§	<2 (n = 81)	≥2 (n = 1249)	P§
Prior bleed	27.7	21.1	31.7	<.0001	21.6	42.0	<.0001	16.7	31.1	<.0001	13.6	28.7	.003
Patient refusal	27.5	31.6	23.1	.01	30.6	20.5	.0002	42	23.1	<.0001	48.2	26.2	<.0001
High bleeding risk	18.0	15.4	19.5	.06	13.7	27.8	<.0001	10.3	20.3	<.0001	6.2	18.7	.004
Frequent falls/frailty	17.6	5.9	24.5	<.0001	14.8	24.0	<.0001	7.4	20.7	<.0001	2.5	18.6	.0002
Need for dual APT	10.4	12.0	9.4	.14	12.3	6.0	.001	10.9	10.2	.73	4.9	10.7	.10
Unable to adhere	6.0	7.3	5.3	.13	6.9	4.0	.04	5.1	6.3	.45	6.2	6.0	.95
Comorbid Illness	5.3	6.1	4.8	.30	3.4	9.5	<.0001	3.2	5.9	.06	2.5	5.4	.24
Prior intracranial hemorrhage	5.0	5.1	4.9	.89	5.1	4.8	.81	3.2	5.5	.10	3.7	5.0	.59
Allergy	2.4	3.9	1.6	.01	3.0	1.0	.03	3.5	2.1	.14	3.7	2.3	.43
Occupational risk	0.8	1.4	0.5	.07	1.1	0.3	.13	1.9	0.5	.01	2.4	0.7	.09
Pregnancy	0.2	0.4	0.1	.29	0.2	0.3	.90	0.3	0.2	.69	0.0	0.2	.66
Other	12.6	15.8	10.6	.01	14.5	7.8	.001	18	10.9	.001	24.7	11.8	.001

INDICAZIONI ALLA CHIUSURA DELL'AURICOLA SINISTRA

GIACOMO BOCCUZZI, FABRIZIO UGO



*CONTROINDICAZIONI ALLA TAO/NAO
- Diatesi emorragica
- Anamnesi positiva per emorragia celebrale
- Patologie gastrointestinali (Ulcera peptica attiva, angiodisplasie, epatopatie)
- Recente sanguinamento gastrointestinale/genito-urinario/respiratorio
- Anemia di origine non chiarita
- Grave insufficienza epatica o renale
- Grave ipertensione
- leucorraiosi

§PAZIENTE FRAGILE
- Grande anziano
- Demenza
- Alcolismo
- Disturbi psichiatrici
- Tendenza alle frequenti cadute a terra
- Deficit grave del visus

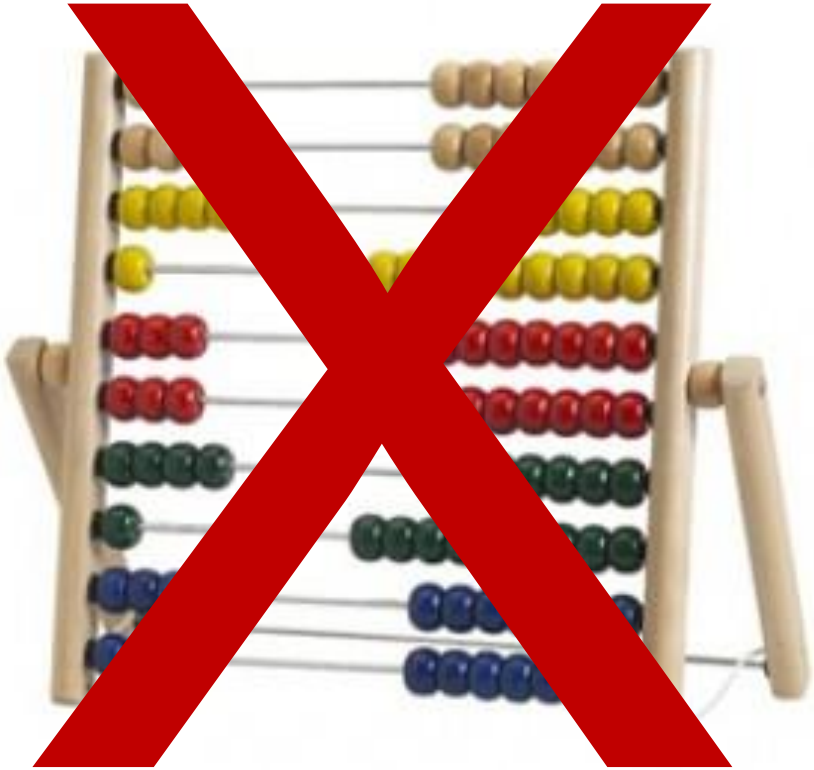
^HAS-BLED:

Letter	Clinical characteristic*	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

BIBLIOGRAFIA:
Casu G et al Documento di consenso ANMCO/AIAC/SICI-GISE/SICCH G ITAL CARDIOL 2016; 17(7-8):597-613
Meier B et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion. Europace 2014;16:1397-416
Camm AJ et al 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. Eur Heart J 2012;33:2719-47

A.S.L. TO2
Azienda Sanitaria Locale Torino Nord

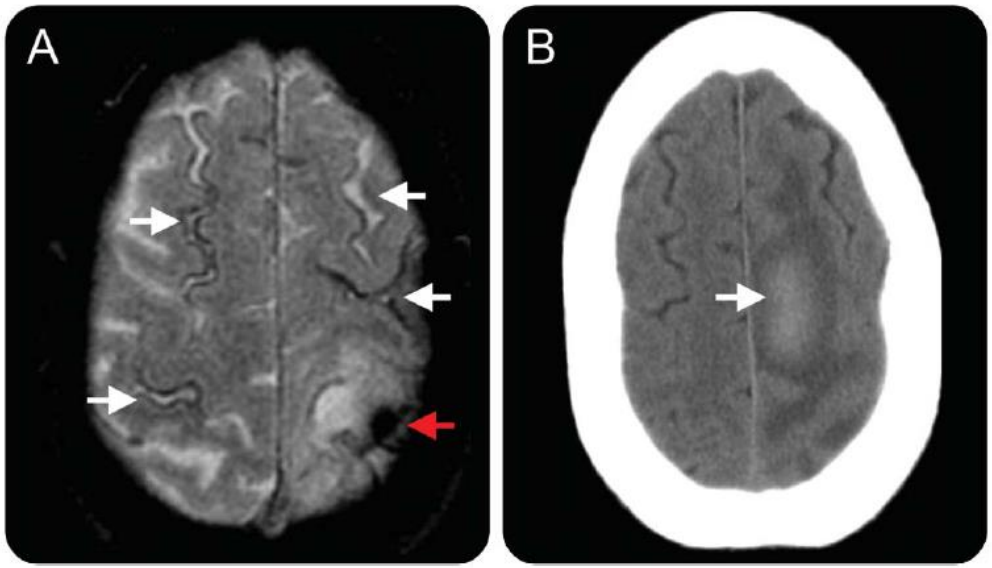
Conclusioni



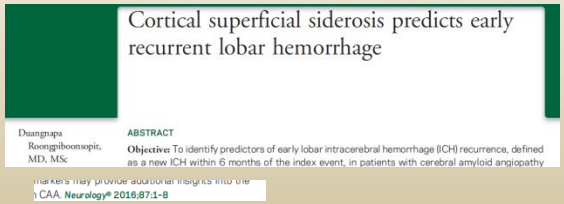

Grazie

L’angiopatia amiloide cerebrale

Figure 2 Disseminated cortical superficial siderosis and early recurrent lobar intracerebral haemorrhage (ICH)



Baseline brain MRI scan and follow-up CT scan of a 79-year-old man who had recurrent symptomatic lobar ICH at 2 months after index ICH. (A) Axial T2*-weighted gradient-recalled echo at baseline demonstrates disseminated cortical superficial siderosis (white arrows) and index ICH in the left posterior frontal parietal area (red arrow). (B) Follow-up axial noncontrast CT scan at 2 months after index ICH demonstrates new subacute lobar intracerebral hemorrhage in the posterior aspect of the left superior frontal gyrus with surrounding edema.


Cortical superficial siderosis predicts early recurrent lobar hemorrhage

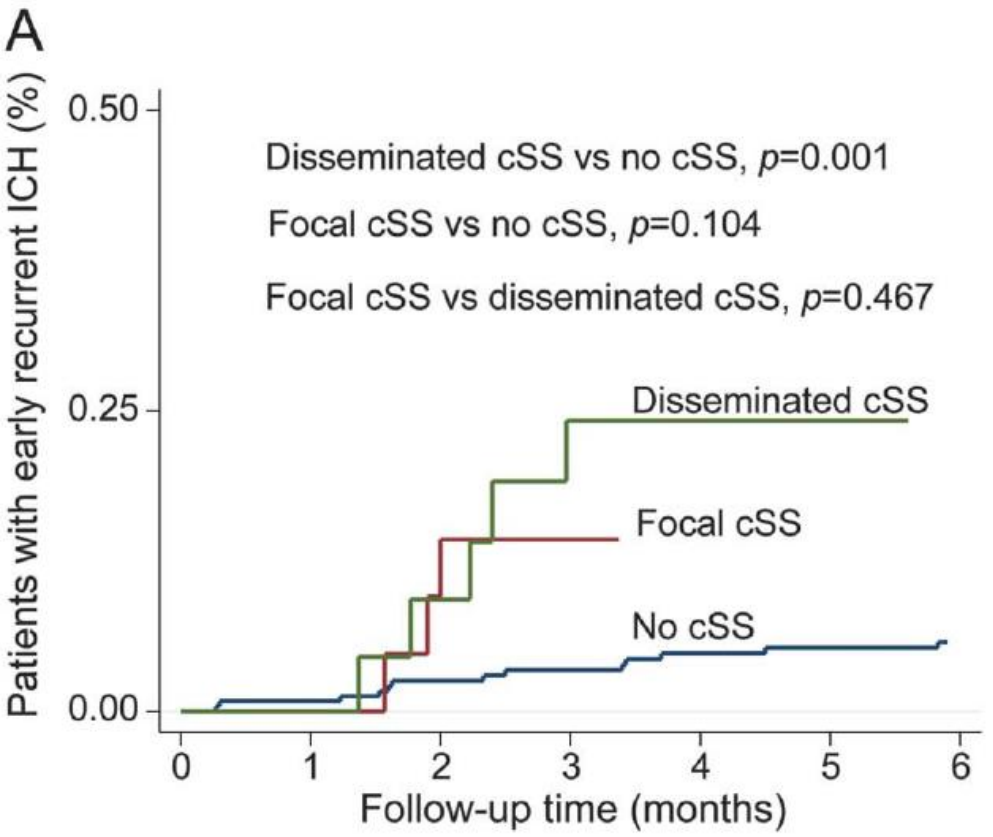
Duangnapa Rooyuthiboonsopit, MD, MSc

ABSTRACT

Objective To identify predictors of early lobar intracerebral hemorrhage (ICH) recurrence, defined as a new ICH within 6 months of the index event, in patients with cerebral amyloid angiopathy

markers may provide additional insights into the CAA. *Neurology*® 2016;87:1-8

Figure 3 Cortical superficial siderosis (cSS), convexity subarachnoid hemorrhage (cSAH), and early recurrent lobar intracerebral hemorrhage (ICH)



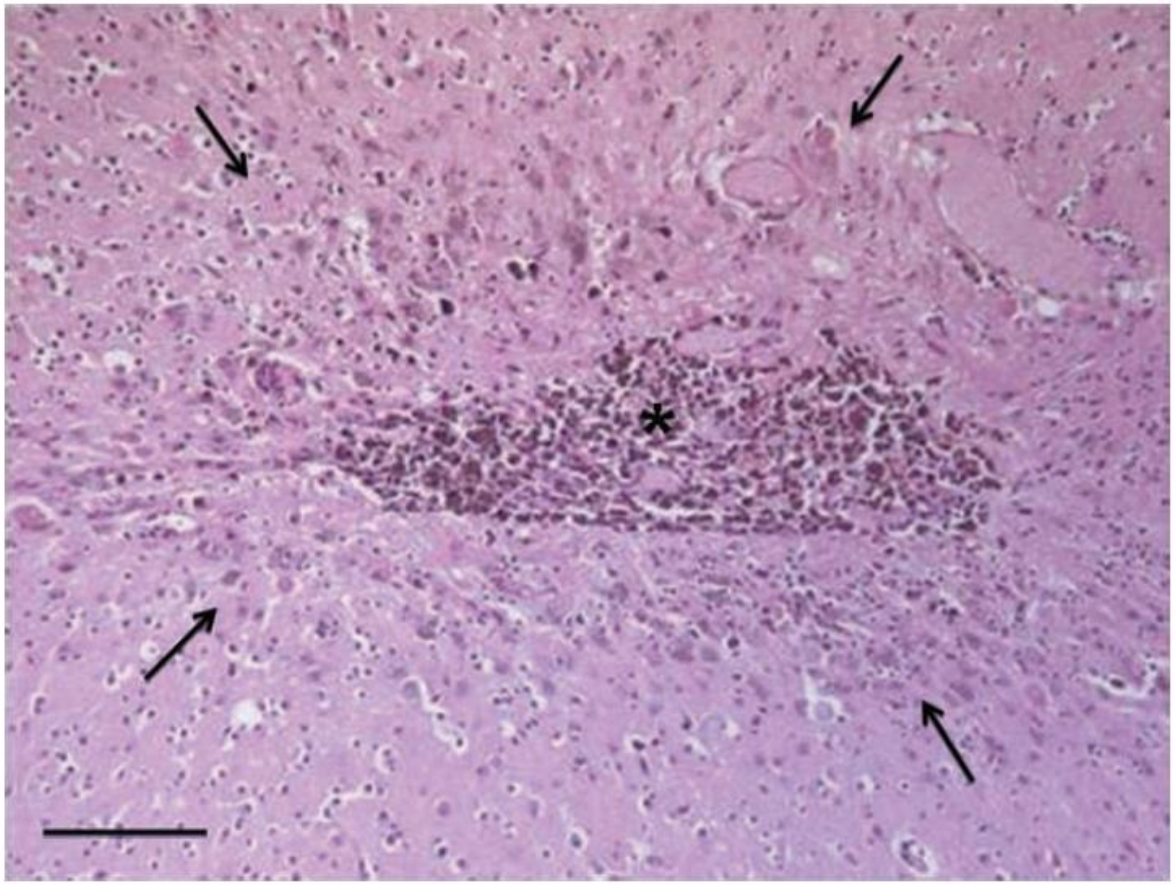


Figure 1

sin stain. The lesion consists of central
ısterisk) surrounded by ring-shaped
aemosiderin resorption. Scale bar=100 µm.

NEUROLOGICAL DILEMMA

Pract Neurol 2010; 10: 94–100

Brain microbleeds

Charlotte Cordonnier

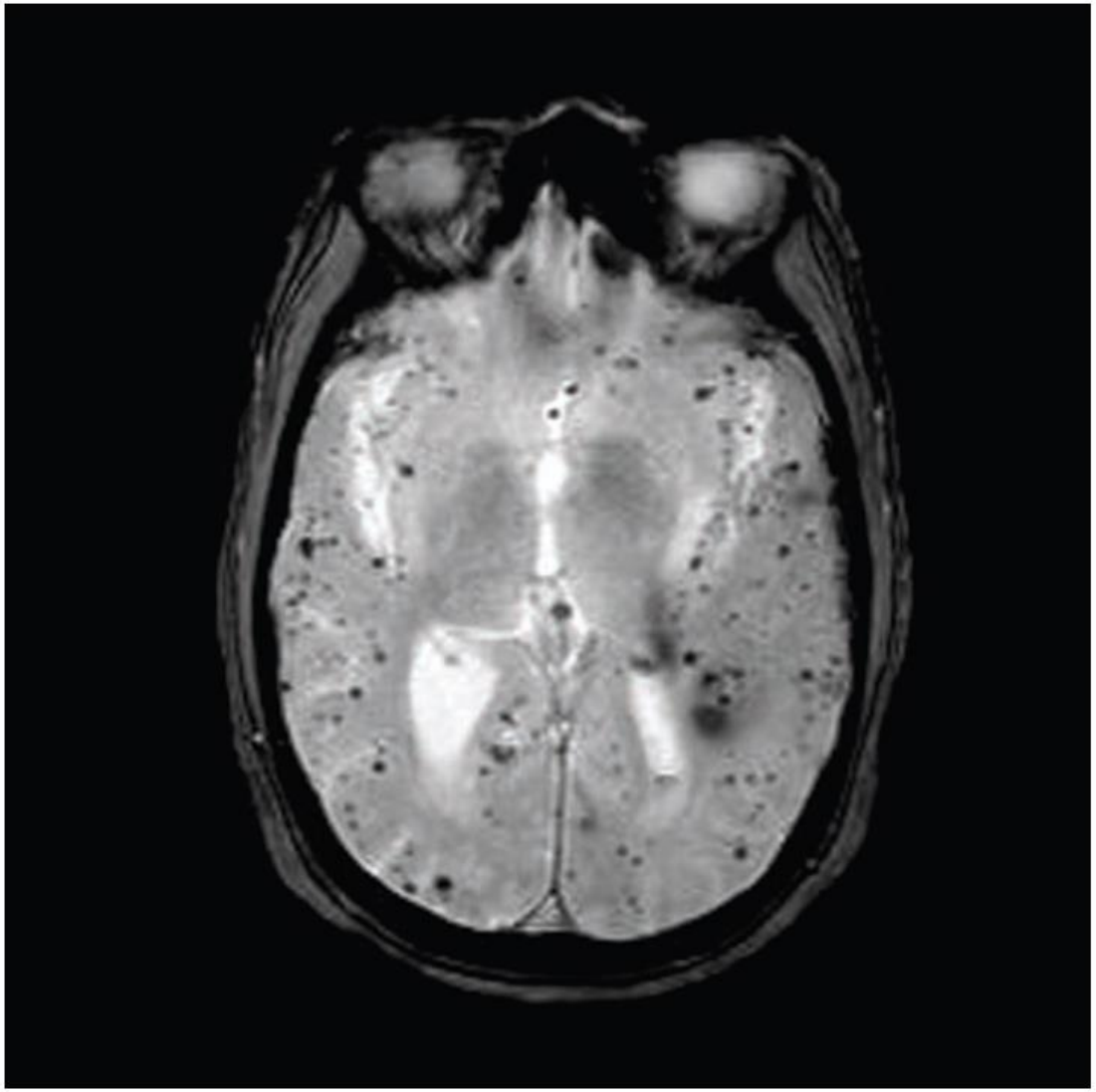


Figure 2
MRI, axial plane, T2* gradient echo sequence showing multiple lobar brain microbleeds as small black dots, without any lesions in the basal ganglia.

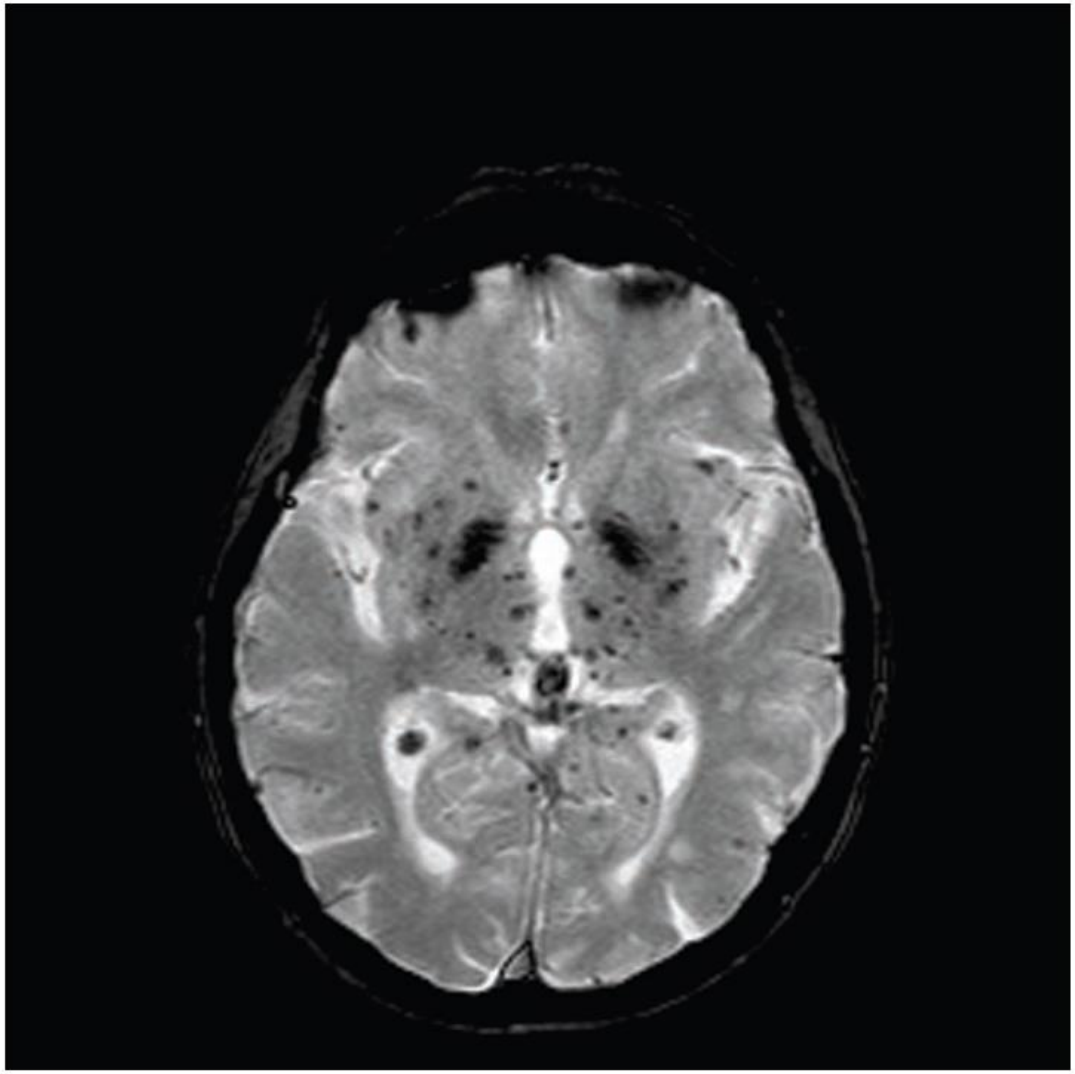


Figure 3
MRI, axial plane, T2* gradient echo sequence showing multiple brain microbleeds predominantly in the basal ganglia region.

DO THEY PREDICT FUTURE INTRACEREBRAL HEMORRHAGE?

Some clinicians have raised obvious concerns about the safety of antithrombotic treat-

Brain microbleeds, anticoagulation, and hemorrhage risk

Meta-analysis in stroke patients with AF

Andreas Charidimou, MD, PhD

ABSTRACT

Objectives: To assess the association between cerebral microbleeds (CMBs) and future sponta
nticoagulation decisions, and in guiding randomi
es. *Neurology*® 2017;89:2317–2326

Table 1 Characteristics of included cohorts

Cohort	Country (study period)	Patients (M), n	Mean age, y	Hypertension, %	CHADS2 score, median (IQR)	Warfarin naive, %	History of ICH, %	WMH, %	Aspirin, %	NOAC, %	MRI parameters				
											Sequence (echo time, ms)	Field strength, T	ST, mm	CMB, %	Mean FU, y
Charidimou et al.[35]	Japan (2008–2014)	72 (60)	74	74	4 (3–4)	93	1	24	19	38	T2*-GRE (ET 26)	1.5	6.5	26	2.1
Srikanth et al.[41]	Australia (2010–2015)	359 (52)	75	79	4 (3–4)	91	1.7	54	8	11	SWI[b]	1.5/3	2/1.7	42	1.7
Haji et al.[36]	US (2008–2014)	90 (58)	80	87	4 (3–4)	80	0	60	67	0	T2*-GRE[a] (ET 20/15/24)	1.5	4–5	22	2.9
Horstmann et al.[6]	Germany (2009–2012)	70 (59)	75	90	4 (3–4)	67	0	71	31	50	SWI	3	3	30	0.6
Song et al.[37]	Korea (2005–2011)	477 (60)	69	76	2 (1–3)	74	1.9	40	45	0	T2*-GRE (ET 16)	1.5	5	29	3.5
Orken et al.[38]	Turkey (2009–2015)	204 (57)	67	16	4 (3–4)	100	0	53	28	0	T2*-GRE (ET 15)	1.5	6	17	3.3
Imaizumi et al.[39]	Japan (2004–2010)	68 (71)	70	69	3 (2–4)	71	2	10	29	0	T2*-GRE (ET 26)	1.5	6.5	32	2.5
Thijs et al.[40]	Belgium (2003–2006)	99 (56)	75	71	2 (1–3)	95	1	41	51	0	T2*-GRE (TE 35/26/16)	1.5/3	7	28	2
Soo et al.[8]	Hong Kong (1999–2004)	60 (55)	72	75	3 (2–4)	63	3	52	32	0	T2*-GRE (ET 30)	1.5	5	35	2.1
Saito et al.[18,c]	Japan (2012–2014)	53 (72)	71	62	2 (2–2)	NA	0	36	17	43	T2*-GRE (ET 18–20)	1.5	5.5	43	2.7

Abbreviations: CHADS2 = congestive heart failure, hypertension, age ≥75 years, diabetes, stroke; CMB = cerebral microbleed; ET = echo time; FU = follow-up; GRE = gradient-recalled echo; ICH = intracerebral hemorrhage; IQR = interquartile range; NA = not applicable; NOAC = non-vitamin K oral anticoagulant; ST = slice thickness; SWI = susceptibility-weighted imaging; WMH = white matter hyperintensities.

[a] More than 90% of the cases.

[b] Ninety-five percent patients had SWI; 20 patients had T2*-GRE (ET 15 milliseconds, slice thickness 7 mm).

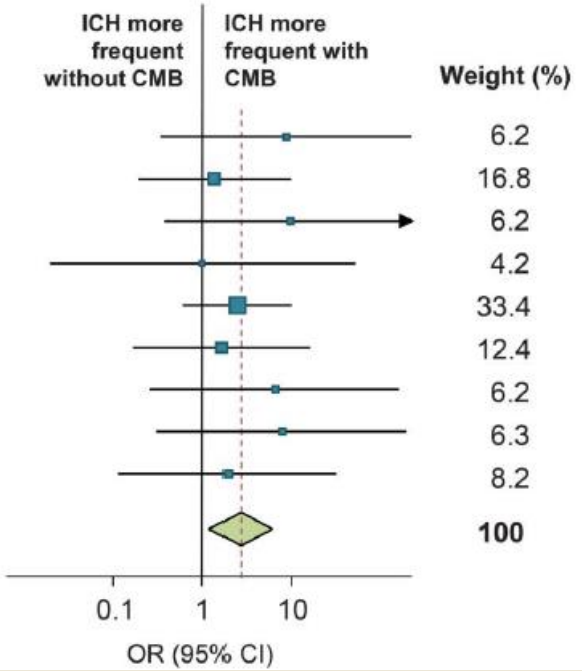
[c] Study including patients with atrial fibrillation without ischemic stroke.

Figure 3 Meta-analyses of CMBs and risk of future ICH in included studies

A

Study	Events, CMBs (n/N)	Events, no CMBs (n/N)	OR (95% CI)
Ref #35	1/19	0/53	8.68 (0.34-222.40)
Ref #41	2/152	2/207	1.37 (0.19-9.81)
Ref #36	1/22	0/68	9.56 (0.38-243.34)
Ref #6	0/21	0/49	1.00 (0.02-52.10)
Ref #37	4/140	4/337	2.45 (0.60-9.93)
Ref #38	1/35	3/169	1.63 (0.16-16.12)
Ref #39	1/22	0/46	6.49 (0.25-165.87)
Ref #40	1/28	0/71	7.80 (0.31-197.32)
Ref #8	1/21	1/39	1.90 (0.11-32.01)
Overall: p=0.017	**12/483**	**10/1069**	**2.68 (1.19-6.01)**

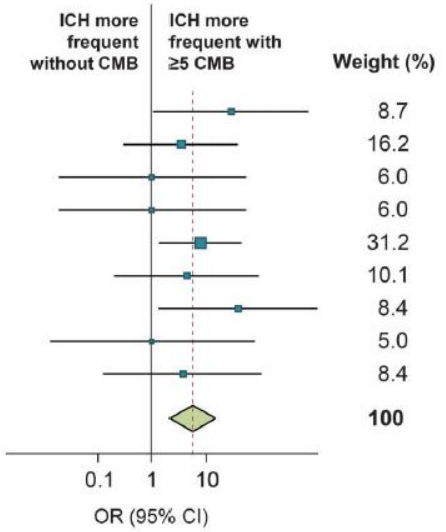
(I^2=0.0%, p=0.949, X^2_{8d}=2.74)



B

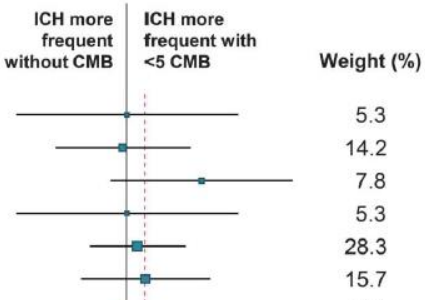
Study	Events, ≥5 CMBs (n/N)	Events, no CMBs (n/N)	OR (95% CI)	Weight (%)
Ref #35	1/6	0/53	29.18 (1.06-806.18)	8.7
Ref #41	1/31	2/207	3.42 (0.30-38.84)	16.2
Ref #36	2/23	4/337	1.00 (0.02-54.40)	6.0
Ref #6	0/5	3/169	1.00 (0.02-54.55)	6.0
Ref #37	1/4	0/46	7.93 (1.37-45.80)	31.2
Ref #38	0/3	1/39	4.32 (0.20-94.34)	10.1
Ref #39	0/7	0/68	39.86 (1.36-1170.58)	8.4
Ref #40	0/7	0/49	1.00 (0.01-80.54)	5.0
Ref #8	0/1	0/71	3.67 (0.12-107.96)	8.4
Overall: *p*=0.001	**5/87**	**10/1039**	**5.50 (2.07-14.66)**	**100**

(I^2=0.0%, p=0.793, X^2_{8d}=4.66)



C

Study	Events, <5 CMBs (n/N)	Events, no CMBs (n/N)	OR (95% CI)	Weight (%)
Ref #35	1/121	2/207	1.00 (0.02-52.80)	5.3
Ref #41	1/15	0/68	0.85 (0.08-9.52)	14.2
Ref #36	2/117	4/337	14.17 (0.55-365.65)	7.8
Ref #6	1/30	3/169	1.00 (0.02-52.70)	5.3
Ref #37	1/27	0/71	1.45 (0.26-8.01)	28.3
Ref #38	1/18	1/39	1.91 (0.19-18.98)	15.7



Forest plots of associations between (A) CMB presence, (B) ≥5 CMBs, and (C) <5 CMBs and the risk of symptomatic ICH (main outcome) during follow-up. Plots show cohort-level and pooled estimates of these associations with no CMBs as the reference group in all analyses. The area of each shaded box is proportional to the weight of the cohort it represents. CI = confidence interval; CMB = cerebral microbleed; ICH = intracerebral hemorrhage; OR = odds ratio.

OR (95% CI)