

Evaluation du risque thromboembolique et hémorragique dans la Fibrillation Atriale

Laurent Fauchier



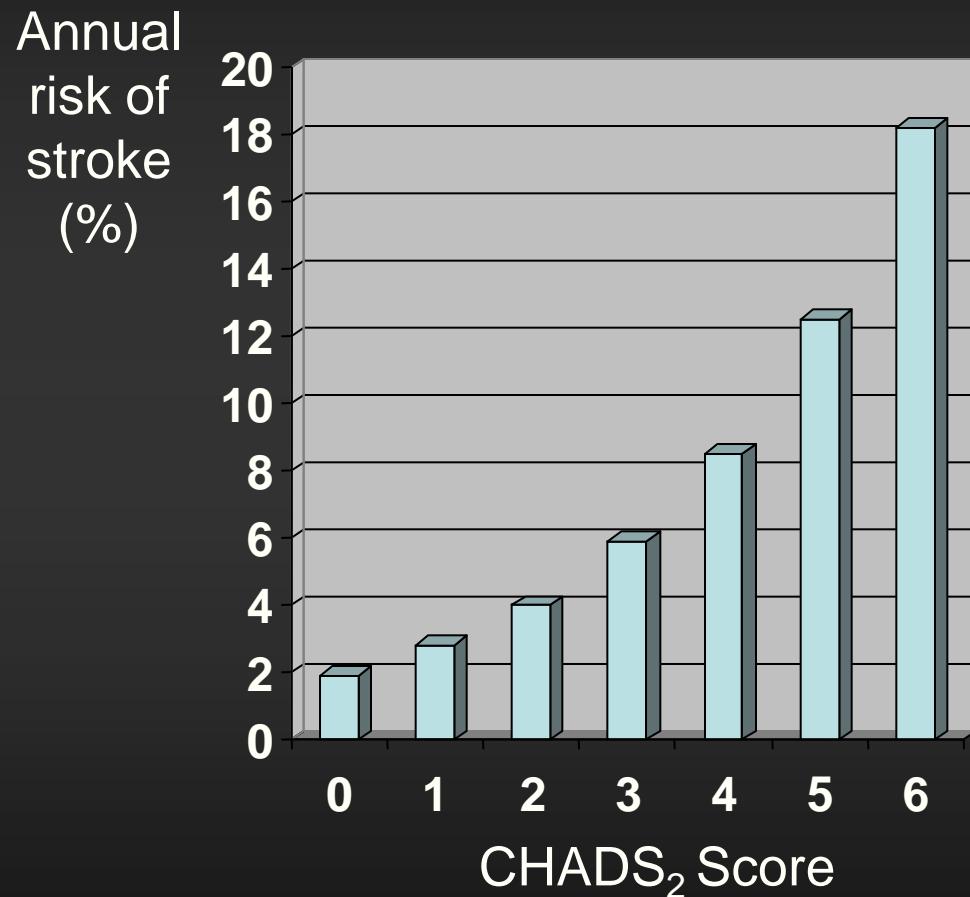
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Disclosure

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AF : CHADS₂ Score



- CHF +1
- Hypertension +1
- Age >75 +1
- Diabetes +1
- Stroke +2

Score CHADS₂ max = 6

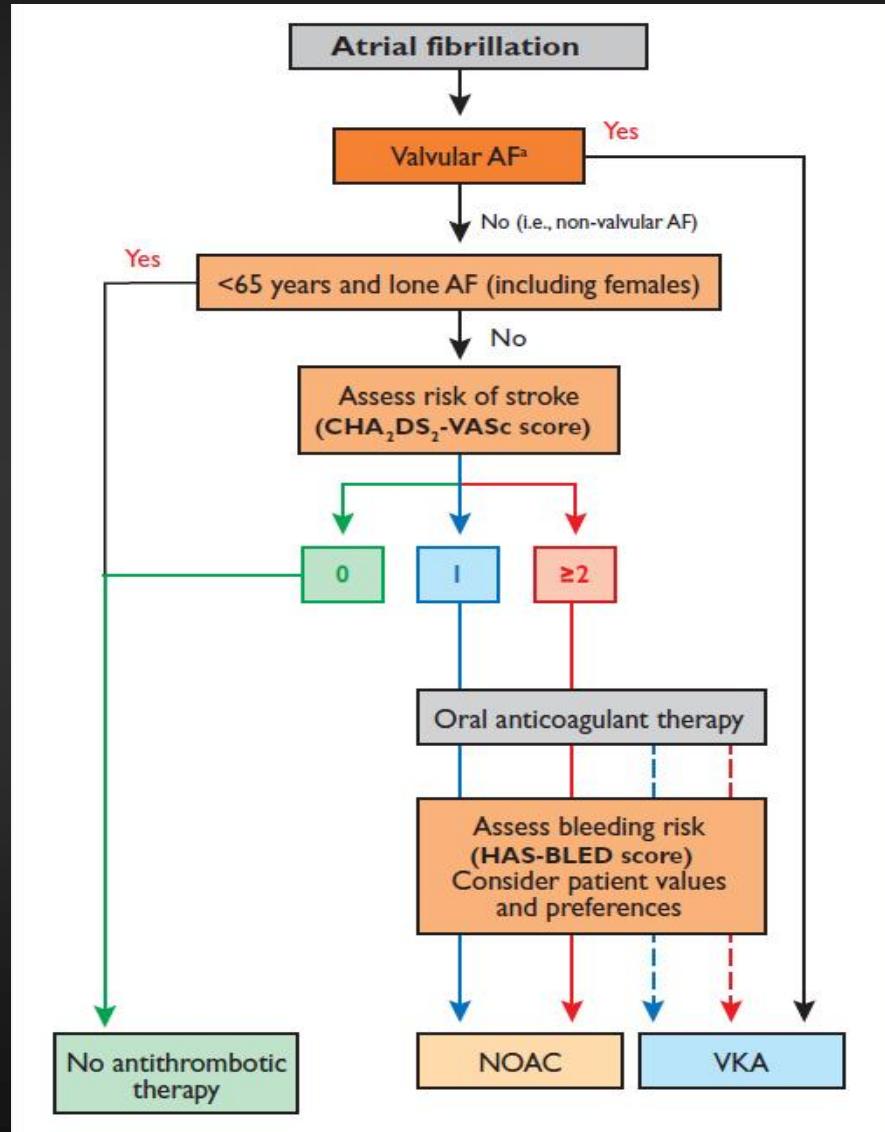
Adapted from Gage et al, JAMA 2001

The CHA₂DS₂VASc score in non-valvular AF

Stroke risk factors	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Aged ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease [prior MI, PAD, or aortic plaque]	1
Aged 65–74 years	1
Sex category [i.e. female gender]	1

(c) Adjusted stroke rate according to CHA ₂ DS ₂ -VASc score		
CHA ₂ DS ₂ -VASc score	Patients (n=7329)	Adjusted stroke rate (%/year) ^b
0	1	0%
1	422	1.3%
2	1230	2.2%
3	1730	3.2%
4	1718	4.0%
5	1159	6.7%
6	679	9.8%
7	294	9.6%
8	82	6.7%
9	14	15.2%

2012 update of the ESC Guidelines for the management of AF



Camm AJ et al,
Eur Heart J 2012

Stroke Risk Stratification Schema. ACCP 9

risk factors: female sex, age 65 to 74 years, and vascular disease (defined as a history of MI, peripheral arterial disease, or complex aortic plaque). The CHA₂DS₂-VASc score has been evaluated in at least five separate cohorts since its original description. With the exception of a recent study by Olesen et al,²⁴ all other studies have found that the predictive ability of CHA₂DS₂-VASc is similar to that of the CHADS₂ score (C statistics of each risk score is ~0.6 across the various studies) and not statistically significantly greater than that of CHADS₂.^{36,40-43} Because the CHADS₂ score has been extensively validated and is easy for clinicians to remember and use, we use the CHADS₂ score as the principal approach for our risk-based treatment recommendations.

Stroke prevention in AF

ACCP 9, 2012

1st line therapy in AF

- CHADS2 = 0 : no antithrombotic therapy
- CHADS2 ≥1 : oral anticoagulation

Antithrombotic Therapy and Prevention of Thrombosis,
9th ed: American College of Chest Physicians
Evidence-Based Clinical Practice Guidelines. *Chest* 2012

CHA₂DS₂-VASc score for refining stroke risk stratification in AF patients with a CHADS₂ score 0: a nationwide cohort study.

Olesen JB, Torp-Pedersen C, Hansen ML, Lip GY.
Thromb Haemost. 2012

CHADS ₂ score = 0 n=19,444	
Age, mean (SD)	58.8 (11.9)
Congestive heart failure	0
Hypertension	0
Age ≥75 years	0
Diabetes mellitus	0
Stroke (previous)	0
Vascular disease	1,592 (8.2)
Age 65–74 years	7,526 (38.7)
Sex category (female)	7,258 (37.3)
Antiplatelet treatment	
Aspirin	3,322 (17.1)
Clopidogrel or persantine	332 (1.7)
CHA ₂ DS ₂ -VASc score	
0	7,536 (38.8)
1	7,739 (39.8)
2	3,870 (19.9)
3	299 (1.5)
4	0

Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with AF

Olesen, Lip et al BMJ 2011

Scale†	Event rates per 100 person-y			At 1 y C-statistic (95% CI)‡
	Low risk (score 0)	Intermediate risk (score 1)	High risk (score > 1)	
CHADS ₂	1.7	4.8	12	0.72 (0.69 to 0.75)
CHA ₂ DS ₂ -VASc	0.78	2.0	8.8	0.85 (0.83 to 0.87)
At 5 y				
CHADS ₂	1.3	3.7	8.3	0.80 (0.78 to 0.81)
CHA ₂ DS ₂ -VASc	0.69	1.5	6.0	0.88 (0.87 to 0.89)
At 10 y				
CHADS ₂	1.2	3.6	8.0	0.81 (0.80 to 0.83)
CHA ₂ DS ₂ -VASc	0.66	1.5	5.7	0.89 (0.88 to 0.90)

†CHADS₂ = Congestive heart failure, Hypertension, Age ≥ 75 y, Diabetes mellitus, and previous thromboembolism (double points); CHA₂DS₂-VASc = Congestive heart failure, Hypertension, Age ≥ 75 y (double points), Diabetes mellitus, previous thromboembolism (double points), Vascular disease, Age 65 to 74 y, and female Sex.

‡Based on Cox regression models using 3 risk groups and with covariates analyzed as categorical variables.

CHA₂DS₂VASc

Validation in a nationwide cohort study

- All patients with AF in Denmark, no VKA, period 1997-2006.
- n=73,538

Table 2 | Event rate (95% CI) of hospital admission and death due to thromboembolism* per 100 person years

Score/risk category	1 year's follow-up	5 years' follow-up	10 years' follow-up
CHA₂DS₂-VASc: prevalence,%			
Low risk (0) 8%	0.78 (0.58 to 1.04)	0.69 (0.59 to 0.81)	0.66 (0.57 to 0.76)
Intermediate risk (1) 12%	2.01 (1.70 to 2.36)	1.51 (1.37 to 1.67)	1.45 (1.32 to 1.58)
High risk (2-9) 80%	8.82 (8.55 to 9.09)	6.01 (5.88 to 6.14)	5.72 (5.60 to 5.84)

*Includes peripheral artery embolism, ischaemic stroke, and pulmonary embolism.

- C statistics at 10 years' follow-up :

$$\text{CHADS}_2 = 0.81$$

$$\text{CHA}_2\text{DS}_2\text{-VASc} = 0.89$$

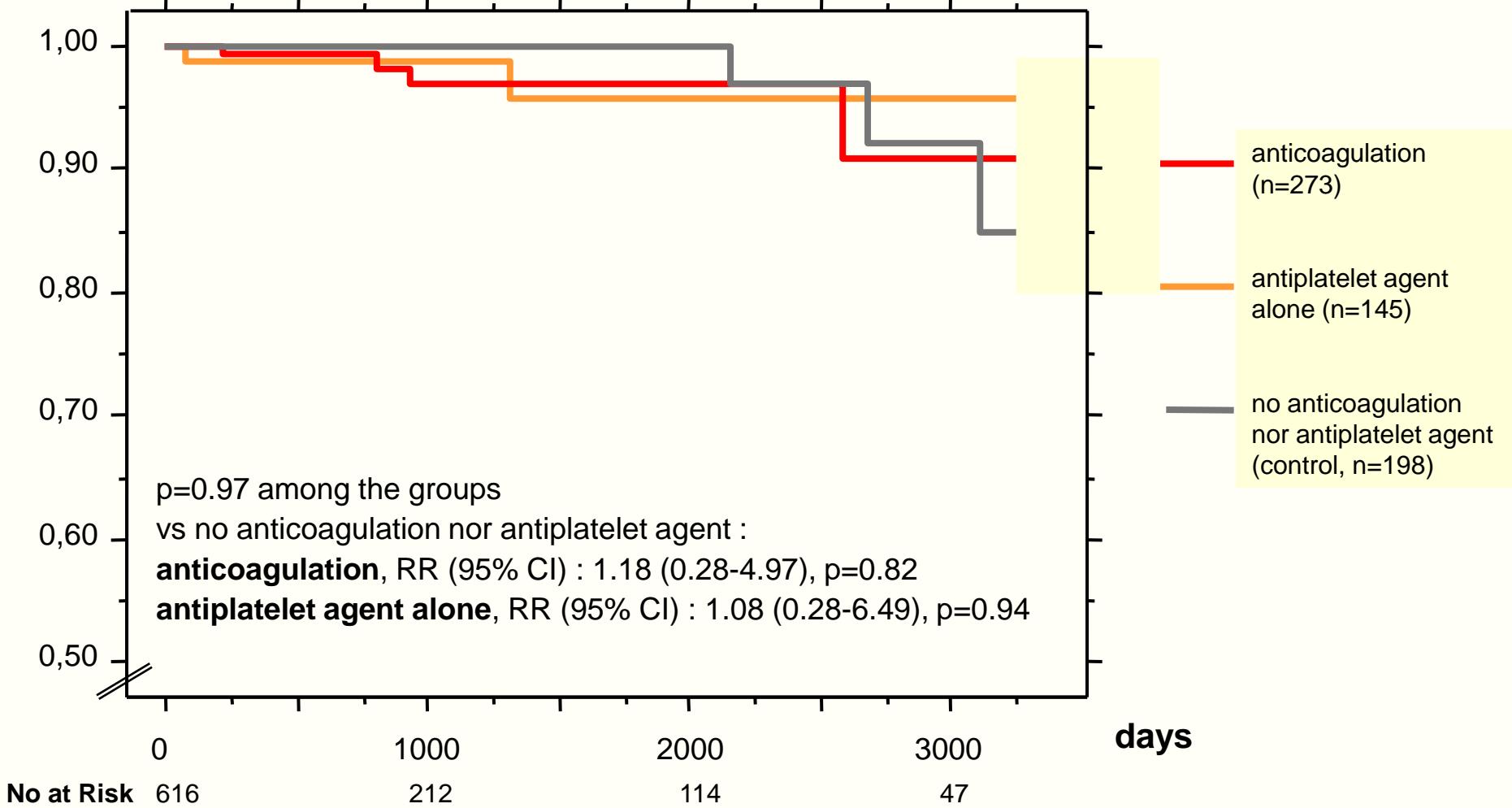
Olesen, Lip, Hansen et al, *BMJ* 2011

Stroke/TE event in AF with CHA₂DS₂VASc score =0

616 patients, 862 ± 1122 days FU, 10 events

Annual risk of stroke =0.64%

Event free



Stroke prevention in AF – ESC 2010

Recommendations for antithrombotic therapy

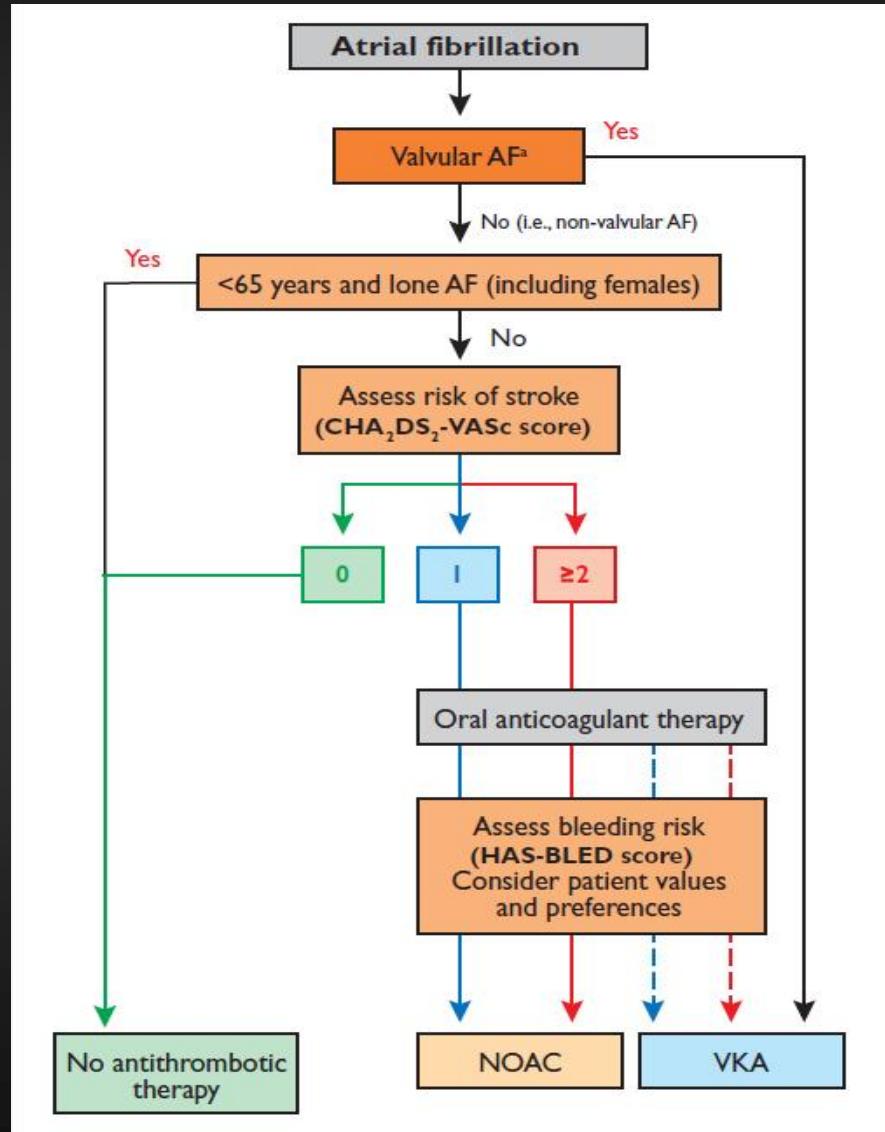
Female gender

« Female sex results in an adjusted RR of 1.6 [95% CI 1.3–1.9] for thrombo-embolism. Gender analyses from population studies, cohort studies, trial cohorts, and surveys also suggest higher thrombo-embolism rates in female subjects ».

...

« In some patients, for example, women aged <65 with no other risk factors (i.e. a CHA2DS2-VASc score of 1) may consider aspirin rather than OAC therapy ».

2012 update of the ESC Guidelines for the management of AF



Camm AJ et al,
Eur Heart J 2012

Pattern of AF and risk of outcomes: The Loire Valley Atrial Fibrillation Project Banerjee et al, *Int J Cardiol* 2013

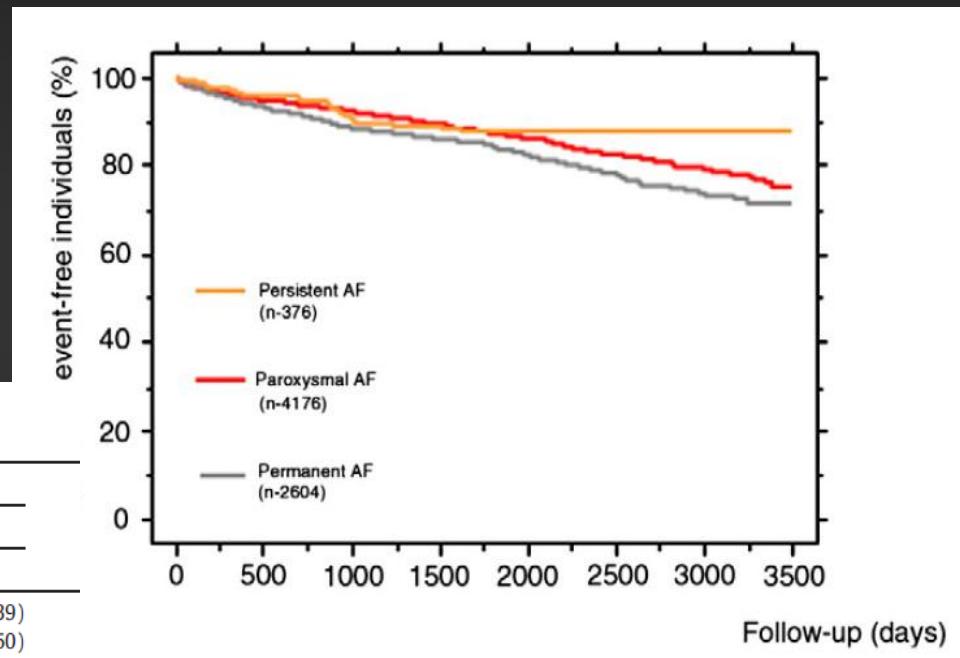
- Stroke and thromboembolism by pattern of non valvular AF

Table 3

Risk [hazard ratio (95% confidence interval)] of stroke and thromboembolism in all patients.

	Stroke and thromboembolism	
	Univariate	Multivariate
	HR (95% CI)	HR (95% CI)
Hypertension	1.51 (1.28–1.79)	1.16 (0.97–1.39)
Age ≥ 75	2.39 (2.01–2.84)	2.75 (2.16–3.50)
Diabetes	1.24 (1.00–1.54)	1.06 (0.85–1.33)
Previous stroke	2.90 (2.33–3.61)	2.58 (2.08–3.21)
Vascular disease	1.52 (1.28–1.80)	1.34 (1.12–1.61)
Heart failure	1.42 (1.19–1.68)	1.20 (1.00–1.44)
Age 65–74	1.80 (1.38–2.35)	1.60 (1.22–2.09)
Female gender	1.29 (1.09–1.53)	1.12 (0.93–1.34)
Persistent AF ^a	1.38 (0.93–2.07)	1.13 (0.76–1.70)
Permanent AF ^a	1.30 (1.10–1.55)	1.44 (0.96–2.16)
CHADS ₂	1.47 (1.38–1.56)	1.32 (1.23–1.42)
CHADS ₂ VASc	1.37 (1.30–1.43)	1.37 (1.30–1.43)

^a Calculated with paroxysmal AF as baseline risk.



TIARA pilot study

TEE-guided Randomized Comparison of Aspirin and VKA in Patients with Atrial Fibrillation and an Increased Risk of Stroke

Trang Dinh, MD

No conflict of interest

Maastricht University Medical Centre, the Netherlands

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Joep L.R.M. Smeets, Emile C. Cheriex, Jan-Eize Lindeboom, Wilfred F.
Heesen, Robert G. Tielemans, Martin H. Prins, Harry J.G.M. Crijns,
on behalf of the TIARA-investigators



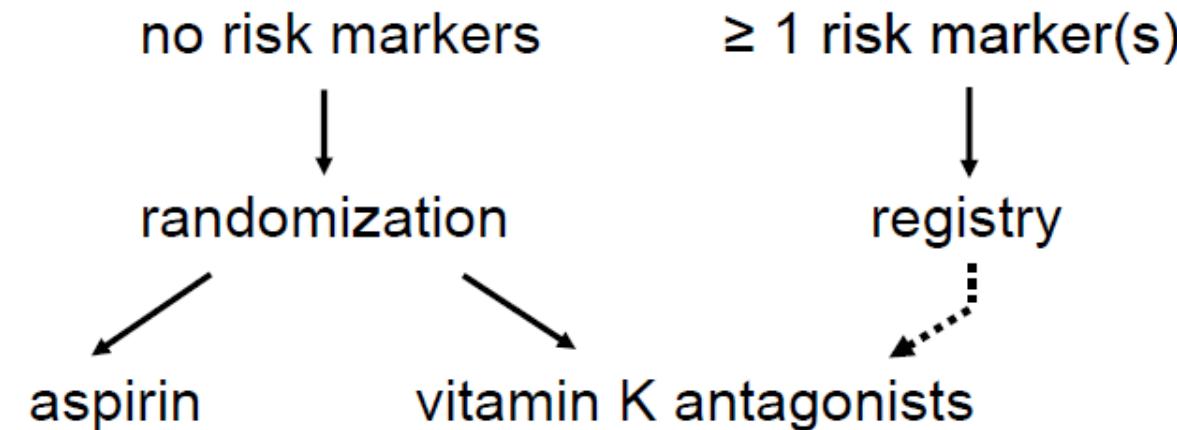
Academisch ziekenhuis
Maastricht

Study design

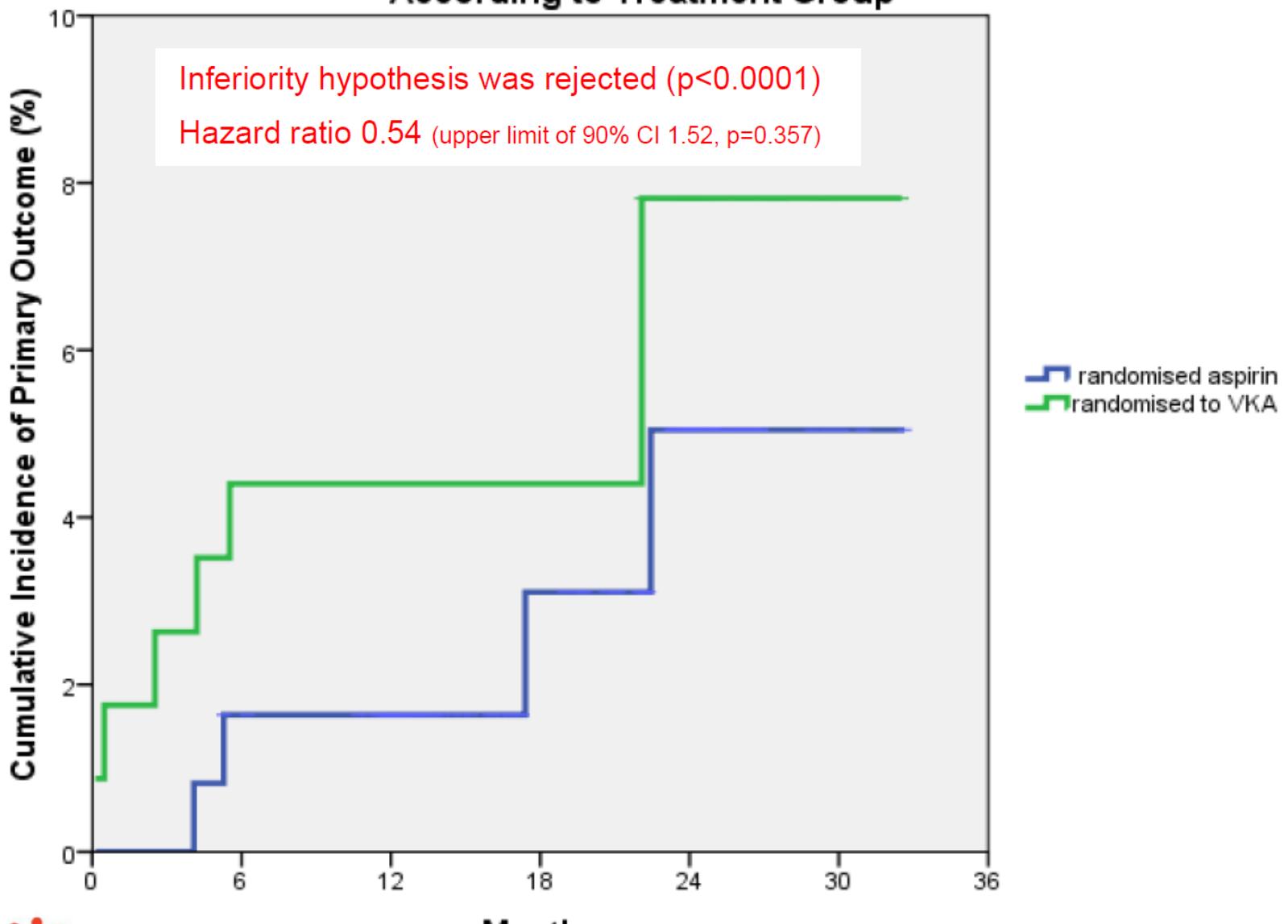
TEE risk markers
Low LAA flow velocity (<25 cm/s)
Spontaneous echo contrast
Thrombus
Complex aortic plaque

Inclusion

TEE



Kaplan-Meier Estimates of the Cumulative Incidence of the Primary Outcome, According to Treatment Group



AF: HAS BLED bleeding risk 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

- a HASBLED score of ≥ 3 indicates ‘high risk’
- some caution and regular review of the patient is needed following the initiation of antithrombotic therapy

FA: Risque de saignement

- Un score HASBLED ≥ 3 témoigne d'un risque hémorragique plus élevé...
- ... mais ne constitue pas une contrindication au traitement anticoagulant
- Attire l'attention sur quelques FdR modifiables
- Des précautions et un suivi régulier du patient sont nécessaires après l'initiation du traitement antithrombotique

Validation of the HAS BLED score in anticoagulated patients with AF

- 7,329 patients with AF in the SPORTIF III and V trials

Contemporary Bleeding Risk Stratification Schemas				
	Low	Moderate	High	Calculation of Bleeding Risk Score
Kuljer et al., 1999 (9)	0	1-3	>3	(1.6 × age) + (1.3 × sex) + (2.2 × cancer) with 1 point for age ≥60 yrs, female or malignancy, and 0 if none
Beyth et al., 1998 (8)	0	1-2	≥3	Age ≥65 yrs, GI bleed in past 2 weeks, previous stroke, comorbidities (recent MI, Hct <30%, diabetes, creatinine >1.5 ml/l) with 1 point for presence of each condition and 0 if absent
Gage et al., 2006 (7)	0-1	2-3	≥4	HEMORR ₂ HAGES score: liver/renal disease, ETOH abuse, malignancy, age >75 yrs, low platelet count or function, rebleeding risk, uncontrolled hypertension, anemia, genetic factors (CYP2C9), risk of fall or stroke, with 1 point for each risk factor present with 2 points for previous bleed
Shireman et al., 2006 (6)	≤1.07	>1.07-<2.19	>2.19	(0.49 × age >70 yrs) + (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) with 1 point for presence of each, and 0 if absent
Pisters et al., 2010 (16)	0	1-2	≥3	HAS-BLED score: Hypertension, Abnormal Renal/Liver Function (1 point each), Stroke, Bleeding History or Predisposition, Labile INR, Elderly Drugs/Alcohol concomitantly (1 point each); maximum 9 points

- Of the tested schemas, the HAS-BLED score performed best, with a stepwise increase in rates of major bleeding with increasing HAS-BLED score ($p<0.0001$)

A New Risk Scheme to Predict Warfarin-Associated Hemorrhage

The ATRIA Study. Fang MC et al, JACC 2011

- Anemia (3 points)
- Severe renal disease (GFR<30 ml/^{min}) or dialysis-dependent, 3 points)
- Age >75 years (2 points)
- Prior bleeding (1 point)
- Hypertension (1 point)

Table 3

Final ATRIA Risk Score: Model Regression Coefficients and Hazard Ratios From Derivation, Validation, and Combined Cohorts

Variable	Points	Derivation Cohort		Validation Cohort		Combined Cohort	
		Regression Coefficient	Hazard Ratio	Regression Coefficient	Hazard Ratio	Regression Coefficient	Hazard Ratio
Anemia	3	1.19	3.28	1.17	3.22	1.18	3.27
Severe renal disease*	3	0.97	2.63	0.88	2.40	0.93	2.53
Age ≥75 yrs	2	0.71	2.03	0.65	1.92	0.69	1.99
Any prior hemorrhage diagnosis	1	0.52	1.68	0.28	1.32	0.44	1.56
Diagnosed hypertension	1	0.27	1.31	0.43	1.54	0.32	1.38

*Defined as estimated glomerular filtration rate <30 ml/min or dialysis-dependent.

ATRIA = Anticoagulation and Risk Factors in Atrial Fibrillation.

Assessing the Risk of Bleeding in AF

The Loire Valley Atrial Fibrillation Project

- 7156 patients with nonvalvular AF in a 4-hospital institution, seen between 2000 and 2010

Table 6. Comparison of c-Statistics (95% CIs) for Different Bleeding Risk Scoring Systems in Patients With Atrial Fibrillation

	All Patients	C-statistic (95% CI)†	
		Patients on VKA	Patients Not on VKA
HAS-BLED‡	0.61 (0.59–0.63)	0.61 (0.58–0.65)	0.60 (0.56–0.64)
HAS-BLED§	0.59 (0.57–0.61)	0.58 (0.55–0.61)	0.60 (0.54–0.64)
HEMORR2HAGES‡	0.58 (0.56–0.61)	0.59 (0.56–0.62)	0.59 (0.54–0.63)
HEMORR2HAGES§	0.54 (0.51–0.56)	0.53 (0.50–0.57)	0.55 (0.50–0.59)
Beyth‡	0.60 (0.57–0.62)	0.60 (0.56–0.63)	0.60 (0.56–0.64)
Beyth§	0.57 (0.54–0.59)	0.56 (0.53–0.59)	0.58 (0.54–0.62)
Kuijjer‡	0.52 (0.50–0.55)*	0.52 (0.49–0.55)*	0.54 (0.50–0.58)
Kuijjer§	0.53 (0.50–0.55)*	0.53 (0.50–0.56)	0.53 (0.49–0.57)
Shireman‡	0.56 (0.54–0.58)	0.56 (0.53–0.60)	0.57 (0.53–0.61)
Shireman§	0.52 (0.50–0.55)*	0.53 (0.50–0.56)	0.53 (0.48–0.57)
ATRIA‡	0.59 (0.57–0.62)	0.60 (0.56–0.63)	0.59 (0.55–0.64)
ATRIA§	0.54 (0.52–0.57)	0.55 (0.52–0.59)	0.47 (0.42–0.51)

HAS-BLED indicates hypertension, abnormal renal and liver function, stroke, bleeding history or predisposition, labile international normalized ratio (INR), elderly (>65 y).

Assessing the Risk of Bleeding in AF

The Loire Valley Atrial Fibrillation Project

- 7156 patients with nonvalvular AF in a 4-hospital institution, seen between 2000 and 2010

Table 7. Comparison of the NRI Between HAS-BLED and Other Contemporary Bleeding Risk Schemas

HAS-BLED vs	Difference in Predicted Probability of an Event					
	Patients With Event	Patients Without event	NRI	SE	z Score	P Value
HEMORR ₂ HAGES	0.271	-0.159	0.112	0.023	4.87	<0.0001
Beyth	0.233	-0.142	0.091	0.021	4.26	<0.0001
Kuijjer	0.265	-0.151	0.115	0.024	4.81	<0.0001
Shireman	0.282	-0.165	0.117	0.023	5.01	<0.0001
ATRIA	0.184	-0.117	0.066	0.021	3.18	0.0007

HAS-BLED score indicates hypertension, abnormal renal and liver function, stroke, bleeding history or predisposition, labile international normalized ratio (INR), elderly, drugs/alcohol concomitantly score; NRI: net reclassification improvement.

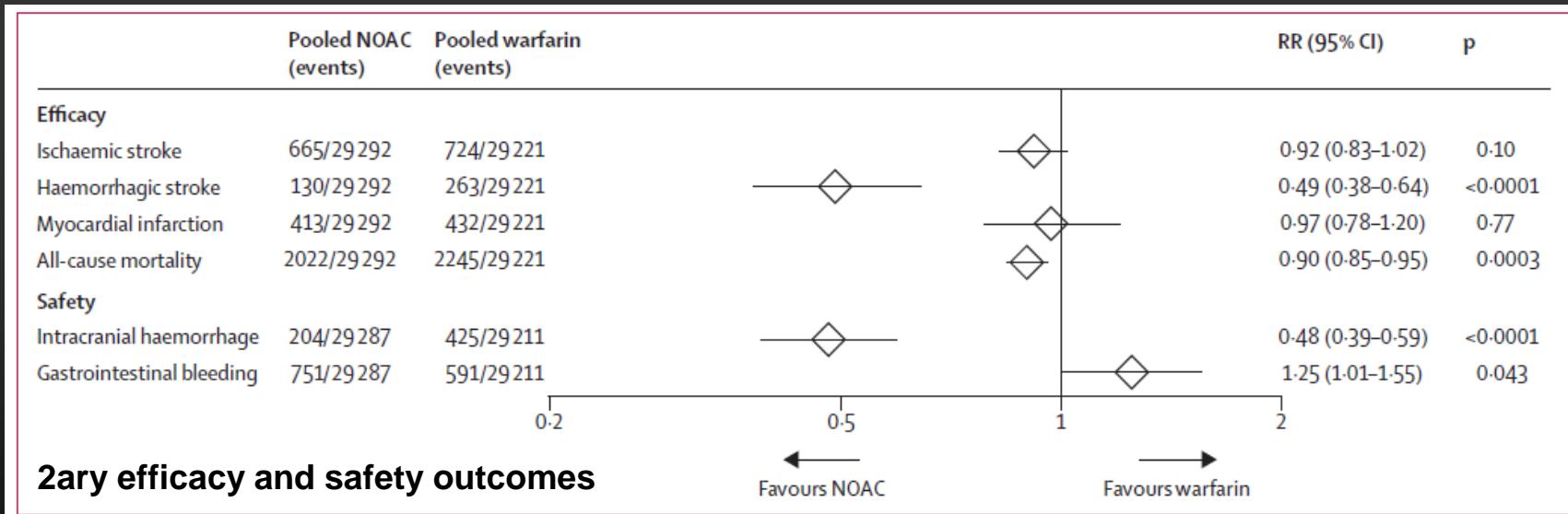
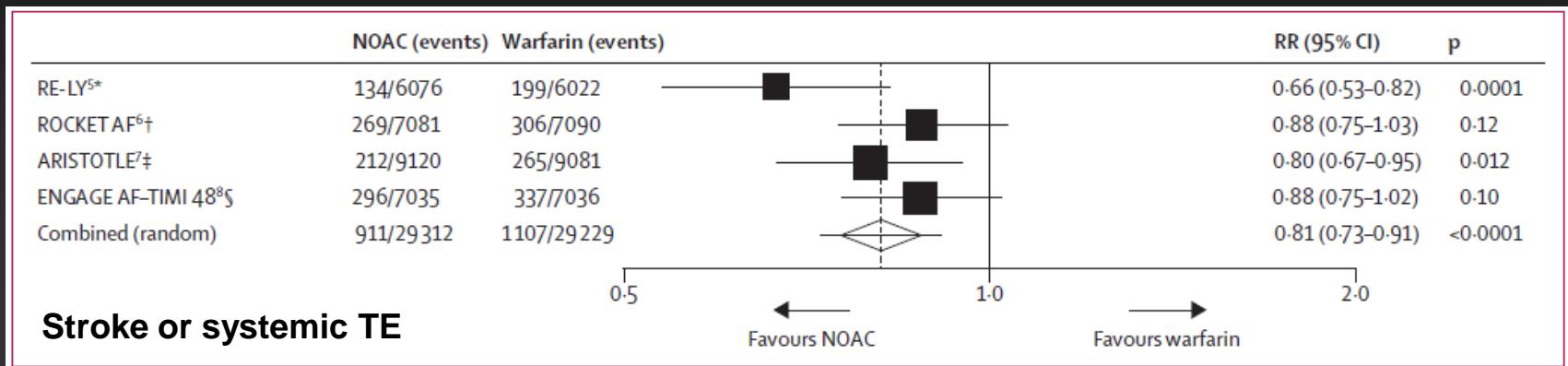
Quality of anticoagulation control amongst AF patients on warfarin: The SAMe-TT2R2 score

Acronym	Definitions	Points
S	Sex (female)	1
A	Age (less than 60 years)	1
M	Medical history*	1
e		
T	Treatment (interacting Rx eg. amiodarone for rhythm control)	1
T	Tobacco use (within 2 years)	2
R	Race (non Caucasian)	2
	Maximum points	8

*2 of the following: hypertension, diabetes, myocardial infarction, peripheral artery disease, congestive heart failure, previous stroke, pulmonary disease, hepatic or renal disease.

- SAMe-TT2R2 can predict poor INR control
- Aid decision by identifying AF patients doing well on VKA (SAMe-TT2R2 score=0-1), or those (≥ 2) who require interventions to achieve acceptable anticoagulation control.

New oral anticoagulants and warfarin in patients with atrial fibrillation



Conclusion

- Sur les 10 patients avec FA qui font un AVC ce matin entre 9h et 12h en France :
 - 8 ont un risque élevé qui aurait du être identifié
 - 6 auraient du recevoir un ACO
 - 3 pourront retourner à leur domicile
 - 5 iront “en institution” au décours
 - 2 vont en décéder
- Une stratification de risque efficace est nécessaire pour identifier et traiter ces patients.

Adapted from The Stroke Association: www.stroke.org.uk.

Office of National Statistics Health Statistics Quarterly (12) Winter 2001 "Stroke incidence and risk factors in a population based cohort study". Scottish Stroke Care Audit 2005/2006.

Novel composite stroke and bleeding risk score in AF

The AMADEUS study.

Lip GY, et al Chest. 2013 [Epub ahead of print]

- Based on the regression models, two novel composite risk prediction scores for stroke (\pm CV events) or bleeding were developed and compared to existing individual stroke and bleeding risk scores and externally validated in a ‘real world’ cohort of 441 anticoagulated outpatients with AF.

Composite score 1	$(0.05 \times \text{Age}) + (0.6 \times \text{Previous stroke or TIA}) + (0.9 \times \text{concomitant aspirin}) - (1.8 \times \text{TTR})$
Composite score 2	$(0.05 \times \text{Age}) + (0.6 \times \text{Previous stroke or TIA}) + (0.7 \times \text{concomitant aspirin}) + (0.6 \times \text{LV dysfunction}) - (1.4 \times \text{TTR})$

Renal Impairment and Ischemic Stroke Risk Assessment in AF

The Loire Valley Atrial Fibrillation Project

Banerjee et al. JACC 2013

Table 2

Rate of Stroke/TE per 100 Person-Years in All Patients and in Patients With CHADS₂ Score = 0 With and Without Renal Impairment

	1-Yr Follow-Up		
	Person-Yrs	Stroke/TE Events	Stroke/TE Rate (CI)
Overall (whole cohort)			
Total	3,669	171	4.7 (3.5–6.2)
eGFR ≥60	1,863	64	3.4 (2.4–4.8)
eGFR = 30–59	1,610	92	5.7 (4.2–7.8)
eGFR <30	196	15	7.7 (4.3–13.6)
Normal renal function	2,738	119	4.4 (3.2–5.9)
Renal impairment	931	52	5.6 (3.9–8.1)
eGFR = 30–59	735	37	5.0 (3.3–7.6)
eGFR <30	196	15	7.7 (4.3–13.6)
CHADS₂ = 0			
Total	688	11	1.6 (0.8–3.0)
eGFR ≥60	521	9	1.7 (0.9–3.4)
eGFR = 30–59	163	2	1.2 (0.3–5.0)
eGFR <30	4	0	—
Normal renal function	614	10	1.6 (0.8–3.2)
Renal impairment	74	1	1.4 (0.2–9.8)
eGFR = 30–59	70	1	1.4 (0.2–10.4)
eGFR <30	4	0	—

CI = confidence interval; TE = thromboembolism; other abbreviations as in Table 1.

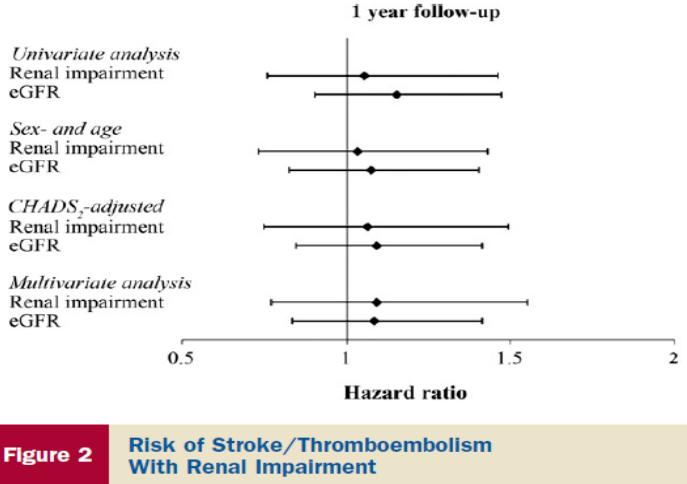


Table 4

NRI by Adding Renal Impairment to CHA2DS₂VASc Scores

	NRI			
	NRI	SE	Z	p Value
CHADS ₂ Model 1	-0.015	0.011	-0.03	0.49
CHADS ₂ Model 2	-0.051	0.010	0.27	0.61
CHADS ₂ Model 3	-0.016	0.011	-0.08	0.47
CHADS ₂ Model 4	0.002	0.011	0.54	0.71
CHA ₂ DS ₂ VASc Model 1	-0.018	0.008	-0.90	0.18
CHA ₂ DS ₂ VASc Model 2	-0.039	0.008	-0.80	0.21
CHA ₂ DS ₂ VASc Model 3	-0.018	0.008	-0.90	0.18
CHA ₂ DS ₂ VASc Model 4	-0.001	0.009	-0.05	0.48

Model 1 = 1 point for renal impairment; Model 2 = 1 point for eGFR 30–59, and 2 points for eGFR <30;

Model 3 = 1 point for renal impairment, and 2 points for renal impairment and eGFR <30; Model 4 = 1 point for eGFR <30

Ejection Fraction in AF and Heart Failure Loire Valley AF Project

- 1276 non valvular AF patients with HF and measured EF were included.
- No differences in rates of stroke ($P = 0.17$) and stroke/TE ($P = 0.11$) between patients with HFPEF and those with HF and reduced EF.

Table 3 Hazard ratio (95% confidence interval) of stroke and thrombo-embolism in patients with heart failure and measured ejection fraction

	Univariate HR (95% CI)	Multivariate HR (95% CI)
Hypertension	1.14 (0.80–1.63)	0.91 (0.62–1.43)
Age ≥ 75	1.72 (1.10–2.70)	1.37 (0.85–2.20)
Diabetes	1.05 (0.70–1.57)	0.94 (0.62–1.34)
Previous stroke	2.56 (1.59–4.14)	2.36 (1.45–3.86)
Vascular disease	1.43 (1.01–2.03)	1.57 (1.07–2.30)
Age 65–74	1.15 (0.71–1.89)	1.06 (0.64–1.74)
Female sex	1.49 (1.05–2.13)	1.43 (0.96–2.13)
Ejection fraction <35%*	0.72 (0.45–1.15)	0.75 (0.44–1.30)
Ejection fraction 35–49%*	1.14 (0.77–1.71)	1.27 (0.83–1.93)
Ejection fraction†	1.04 (0.96–1.12)	1.05 (0.97–1.13)

The CHA₂DS₂-VASc risk factors

The Loire Valley Atrial Fibrillation Project

- 6,438 patients with non-valvular AF, 2000-2010
- Risk of stroke and thromboembolism in patients aged <65 years

	Multivariate Hazard ratio (95% CI)
<u>Heart failure</u>	1.95 (1.04-3.66)
Hypertension	0.90 (0.49-1.66)
Diabetes	1.76 (0.86-3.59)
<u>Previous stroke</u>	5.66 (2.91-11.02)
<u>Vascular disease</u>	2.19 (1.22-3.92)
Female gender	0.70 (0.34-1.43)

Female gender as a risk factor does vary in different studies...

Conclusion

- “We have developed and validated 2 novel composite scores for stroke/thromboembolism/ bleeding that offer good discriminatory and predictive performance.
- These composite risk scores did not perform much better than the easier and more practical ‘traditional’ stroke and bleeding risk scores that are currently in use, which allow greater practically for everyday clinical practice and more personalised balancing of risks.
- Simplicity is best

assess stroke risk using CHA2DS2-VASc

assess bleeding risk with HAS-BLED”

- Lip GY, Lane DA, Buller H, Apostolakis S. Development of a novel composite stroke and bleeding risk score in patients with atrial fibrillation: The AMADEUS study. *Chest*. 2013 Sep 5.
- Apostolakis S, Lane DA, Buller H, Lip GY. Comparison of the CHADS2, CHA2DS2 -VASc and HAS-BLED scores for the prediction of clinically relevant bleeding in anticoagulated patients with atrial fibrillation: The AMADEUS trial. *Thromb Haemost*. 2013 Sep 19;110(5).

Conclusion

- On 10 patients with AF who suffer a stroke :
 - 8 should be known to be high risk of stroke
 - 6 should have been on warfarin
 - 3 will go home
 - 5 will end up in residential care
 - 2 will die
- Risk stratification is needed to identify and treat these patients early

The Stroke Association: www.stroke.org.uk.

Office of National Statistics Health Statistics Quarterly (12) Winter 2001 "Stroke incidence and risk factors in a population based cohort study". Scottish Stroke Care Audit 2005/2006.

Guidelines for the management of atrial fibrillation

Risk category	CHA ₂ DS ₂ -VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥ 2 'clinically relevant non-major' risk factors	≥ 2	OAC ^a
One 'clinically relevant non-major' risk factor	1	Either OAC ^a or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.