ΝΕΟΤΕΡΑ ΔΕΔΟΜΕΝΑ ΣΤΗΝ ΚΟΛΠΙΚΗ ΜΑΡΜΑΡΥΓΗ

Κατσαφάδος Γ. Μιχαήλ

Καρδιολόγος

SOS ΙΑΤΡΟΙ

- ΕΠΙΔΗΜΙΟΛΟΓΙΚΑ ΔΕΔΟΜΕΝΑ
- ΝΟΣΗΡΟΤΗΤΑ ΚΑΙ ΘΝΗΤΟΤΗΤΑ
- ΝΕΟΤΕΡΗ ΟΝΟΜΑΤΟΛΟΓΙΑ
- ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΩΝ ΑΣΘΕΝΩΝ ΜΕ AF
- ΕΛΕΓΧΟΣ ΤΟΥ ΡΥΘΜΟΥ ή ΕΛΕΓΧΟΣ ΣΥΧΝΟΤΗΤΟΣ
- ΠΡΟΛΗΨΗ ΘΡΟΜΒΟΕΜΒΟΛΗΣ
- ΝΕΟΤΕΡΑ ΑΝΤΙΘΡΟΜΒΩΤΙΚΑ
- ΠΕΡΙΕΓΧΕΙΡΗΤΙΚΗ ΔΙΑΧΕΙΡΙΣΗ ΑΣΘΕΝΩΝ ΥΠΟ ΑΝΤΙΠΗΚΤΙΚΗ ΑΓΩΓΗ

ΕΠΙΔΗΜΙΟΛΟΓΙΑ

- Ανευρίσκεται στο 1-2% του γενικού πληθυσμού.
- Στην Ευρώπη περισσότεροι από 6.000.000 άνθρωποι πάσχουν από ΚΜ αριθμός που αναμένεται να διπλασιαστεί τα επόμενα 50 χρόνια.
- Είναι συχνότερη στους άνδρες από τις γυναίκες.
- Η ιδιοπαθής AF αποτελεί περίπου το 10% των περιπτώσεων ΚΜ.

Camm AJ, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010;31:2369-2429.

ΘΝΗΤΟΤΗΤΑ ΚΑΙ ΝΟΣΗΡΟΤΗΤΑ

Table 3 Clinical events (outcomes) affected by AF

Outcome parameter	Relative change in AF patients
1. Death	Death rate doubled.
2. Stroke (includes haemorrhagic stroke and cerebral bleeds)	Stroke risk increased; AF is associated with more severe stroke.
3. Hospitalizations	Hospitalizations are frequent in AF patients and may contribute to reduced quality of life.
4. Quality of life and exercise capacity	Wide variation, from no effect to major reduction. AF can cause marked distress through palpitations and other AF-related symptoms.
5. Left ventricular function	Wide variation, from no change to tachycardiomyopathy with acute heart failure.

AF = atrial fibrillation.
Outcomes are listed in hierarchical order modified from a suggestion put forward in a recent consensus document.[3] The prevention of these outcomes is the main therapeutic goal in AF patients.

Η παροξυσμική AF και η μόνιμη AF έχουν παρόμοιο κίνδυνο για ΑΕΕ!!!!
20-25% όλων των ΑΕΕ προκαλούνται από καρδιογενή έμβολα.

Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the longterm risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. *Am J Med*. 2002;113:359-364.

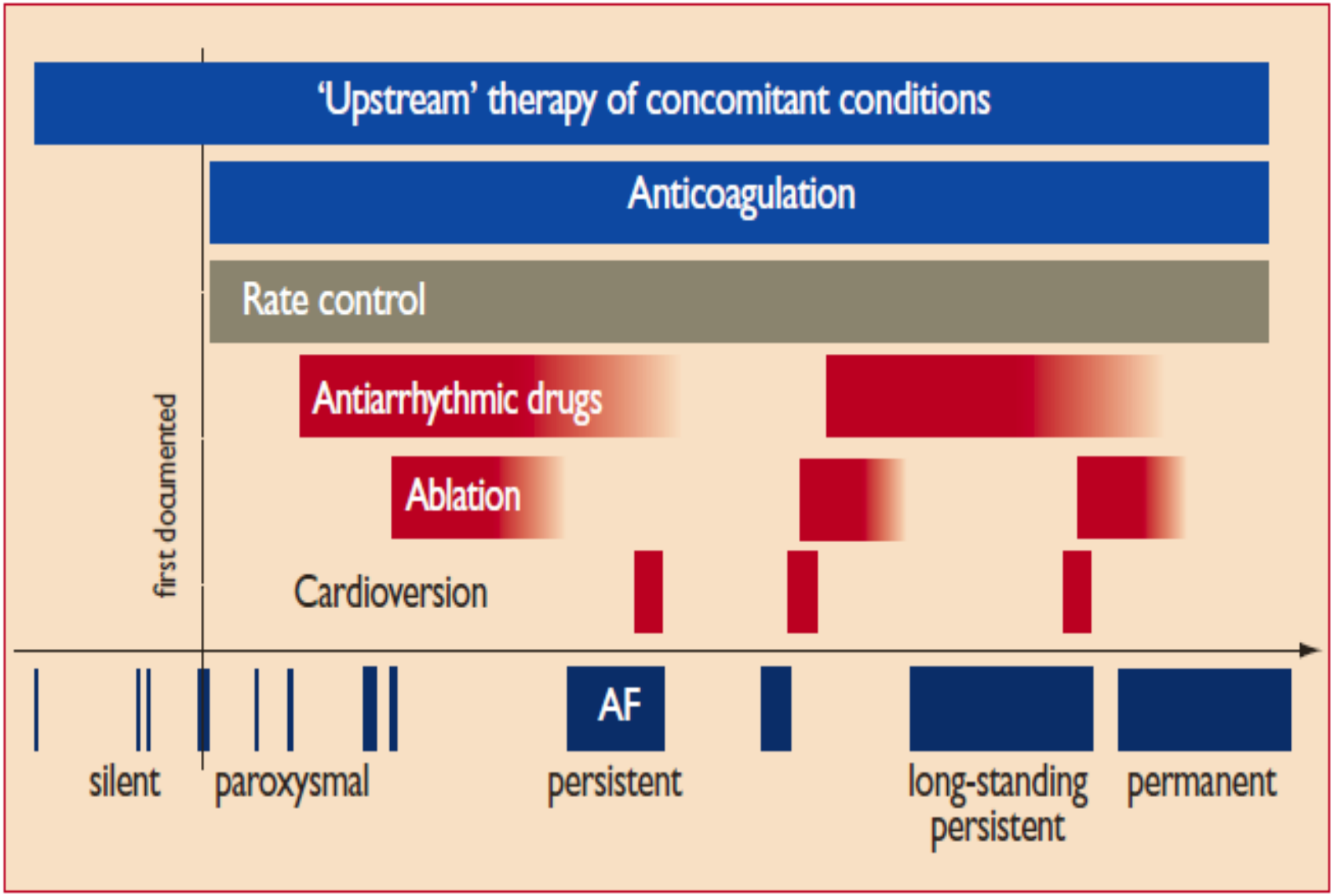
ΣΥΓΧΡΟΝΗ ΟΝΟΜΑΤΟΛΟΓΙΑ ΤΗΣ AF

- Πρωτοδιαγνωσθείσα (first diagnosed) → Αναφέρεται σε ασθενείς που εμφανίζουν για πρώτη φορά ΚΜ ανεξάρτητα από την διάρκεια της και την βαρύτητα των συμπτωμάτων της.
- Παροξυσμική (paroxysmal)→ Όταν η ΚΜ τερματίζεται αυτόματα (συνήθως μέσα σε 48 ώρες αν και μπορεί να διαρκέσει μέχρι και 7 ημέρες). Το χρονικό όριο των 48 ωρών είναι σημαντικό γιατί μετά την πάροδο του η πιθανότητα ανάταξης της ΚΜ είναι μικρή και πρέπει να γίνεται έναρξη αντιπηκτικής αγωγής.

- Εμμένουσα (persistent) → Όταν η αρρυθμία επιμένει > 7 ημέρες ή όταν απαιτείται τερματισμός της αρρυθμίας φαρμακευτικά ή με DC ηλεκτρική καρδιοανάταξη.
- Επί μακρόν εμμένουσα (long standing persistent) → Διάρκεια της ΚΜ > 1 έτος κατά την χρονική στιγμή που αποφασίζεται να ακολουθηθεί μια στρατηγική ελέγχου του ρυθμού.
- Μόνιμη ή χρόνια → Σε περιπτώσεις όπου δεν διενεργείται έλεγχος του ρυθμού αλλά μόνο έλεγχος της συχνότητος.

- Σιωπηρή (silent) → Εκδήλωση της αρρυθμίας μέσω μιας επιπλοκής αυτής (ΑΕΕ, ταχυμυοκαρδιοπάθεια) ή τυχαία διάγνωση αυτής στο ΗΚΓ.
- Ιδιοπαθής (Lone AF) Αναφέρεται σε σχετικά νέους ασθενείς (<60 ετών) δίχως κλινικά ή υπερηχογραφικά ευρήματα καρδιοπνευμονικής νόσου ή ΑΥ. Καλύτερη πρόγνωση όσον αφορά τα θρομβοεμβολικά επεισόδια και την θνητότητα.

Camm AJ, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010;31:2369-2429.


'Upstream' therapy of concomitant conditions
Anticoagulation
Rate control
Antiarrhythmic drugs
Ablation
Cardioversion
first documented
AF
silent
paroxysmal
persistent
long-standing persistent
permanent

ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΗΣ AF

Πρόληψη των επιπλοκών της ΚΜ (πρόληψη θρομβοεμβολής)

Έλεγχος των συμπτωμάτων ο οποίος μπορεί να επιτευχθεί με τις παρακάτω 2 στρατηγικές (ή με συνδυασμό αυτών):

- Έλεγχος της συχνότητος
- Έλεγχος του ρυθμού (αποκατάσταση του SR και διατήρηση του)

ΕΛΕΓΧΟΣ ΤΟΥ ΡΥΘΜΟΥ ή ΤΗΣ ΣΥΧΝΟΤΗΤΟΣ

Table 13 General characteristics of rhythm control and rate control trials in patients with AF[86–92]

Trial	Ref	Patients (*n*)	Mean age (years)	Mean follow-up (years)	Inclusion criteria	Primary outcome parameter	Patients reaching primary outcome (*n*)		
							Rate control	Rhythm control	*P*
PIAF (2000)	92	252	61.0	1.0	Persistent AF (7–360 days)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	0.32
AFFIRM (2002)	86	4060	69.7	3.5	Paroxysmal AF or persistent AF, age ≥65 years, or risk of stroke or death	All-cause mortality	310/2027 (25.9%)	356/2033 (26.7%)	0.08
RACE (2002)	87	522	68.0	2.3	Persistent AF or flutter for <1 years and 1–2 cardioversions over 2 years and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, pacemaker implantation, thrombo-embolic events, severe adverse effects of antiarrhythmic drugs	44/256 (17.2%)	60/266 (22.6%)	0.11
STAF (2003)	88	200	66.0	1.6	Persistent AF (>4 weeks and <2 years), LA size >45 mm, CHF NYHA II–IV, LVEF <45%	Composite: overall mortality, cerebrovascular complications, CPR, embolic events	10/100 (10.0%)	9/100 (9.0%)	0.99
HOT CAFÉ (2004)	89	205	60.8	1.7	First clinically overt persistent AF (≥7 days and <2 years), age 50–75 years	Composite: death, thrombo-embolic events; intracranial/major haemorrhage	1/101 (1.0%)	4/104 (3.9%)	>0.71
AF-CHF (2008)	90	1376	66	3.1	LVEF ≤35%, symptoms of CHF, history of AF (≥6 h or DCC <last 6 months)	Cardiovascular death	175/1376 (25%)	182/1376 (27%)	0.59
J-RHYTHM (2009)	91	823	64.7	1.6	Paroxysmal AF	Composite of total mortality, symptomatic cerebral infarction, systemic embolism, major bleeding, hospitalization for heart failure, or physical/ psychological disability	89/405 (22.0%)	64/418 (15.3%)	0.012

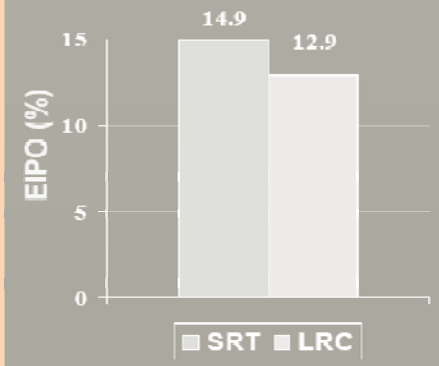
AF = atrial fibrillation; AFFIRM = Atrial Fibrillation Follow-up Investigation of Rhythm Management; CHF = congestive heart failure; CPR = cardiopulmonary resuscitation; DCC = direct current cardioversion; HOT CAFÉ = How to Treat Chronic Atrial Fibrillation; J-RHYTHM = Japanese Rhythm Management Trial for Atrial Fibrillation; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PIAF = Pharmacological Intervention in Atrial Fibrillation; RACE = RAte Control versus Electrical cardioversion for persistent atrial fibrillation; STAF = Strategies of Treatment of Atrial Fibrillation.

ΑΥΣΤΗΡΟΣ Η ΕΠΙΕΙΚΗΣ ΕΛΕΓΧΟΣ ΣΥΧΝΟΤΗΤΟΣ (strict vs lenient):

American Heart Association. | American Stroke Association.
Learn and Live.

Rate Control Efficacy in Permanent Atrial Fibrillation (PAF): a Comparison Between Lenient Versus Strict Rate Control in Patients With Heart Failure. The RACE II Study

BACKGROUND: Control of sinus rhythm vs. rate control are competing strategies with respect to improved outcomes in PAF pts with CHF. The lenient (<110 BPM) versus strict (<80 BPM) rate control in pts with PAF has not been studied. **PURPOSE:** Determine if lenient (LRC) or strict (SRT) rate control in pts with PAF is inferior. **METHODS:** Pts were randomized to receive rate control drug which was adjusted to achieve LRC (*n* = 311) or SRT (*n* = 303) resting heart rate during follow up visits at 1, 2, and 3 months and annually thereafter. Mean follow up was 37 months.



Primary Endpoints: Time to CVD event including death, stroke, blood clot, bleeding, hospitalization or arrhythmia.

Secondary Endpoints: Any cause death, symptoms and NY Heart Association (NYHA) functional status

Results:

Primary Endpoint: The Estimated Incidence of Primary Outcome (EIPO) for SRT and LRC was 14.9 and 12.9 respectively. **Secondary Endpoints (SRT vs. LRT):** Any cause death (18 vs. 17), symptoms (46% vs. 45.6%) and NYHA functional status class I (23.4% vs. 23.3%) were statistically identical for each arm

Conclusion: LRC is not inferior to SRT in pts with PAF

Van Gelder IC, ACC Atlanta , GA

Van Gelder IC et al. Lenient versus strict rate control in patients with atrial fibrillation. N Engl J Med 2010;362:1363–1373.

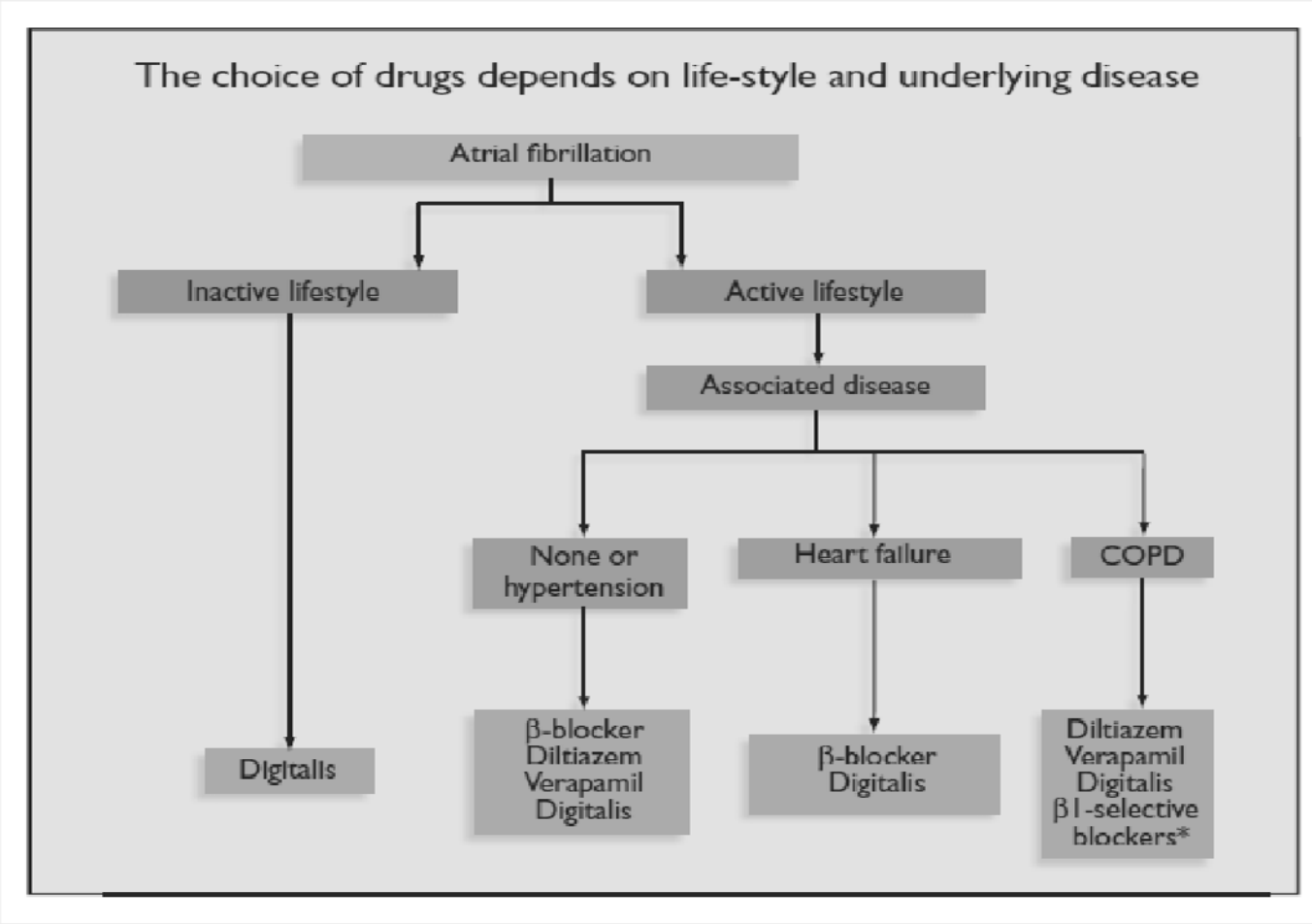


Figure 9 Rate control. COPD = chronic obstructive pulmonary disease. *Small doses of β1-selective blockers may be used in COPD if rate control is not adequate with non-dihydropyridine calcium channel antagonists and digoxin. Amiodarone is also used for rate control in patients who do not respond to glycosides, β-blockers or non-dihydropyridine calcium antagonists. Dronedarone may also be used for rate control in patient with recurrent episodes of atrial fibrillation.

ΕΛΕΓΧΟΣ ΤΟΥ ΡΥΘΜΟΥ

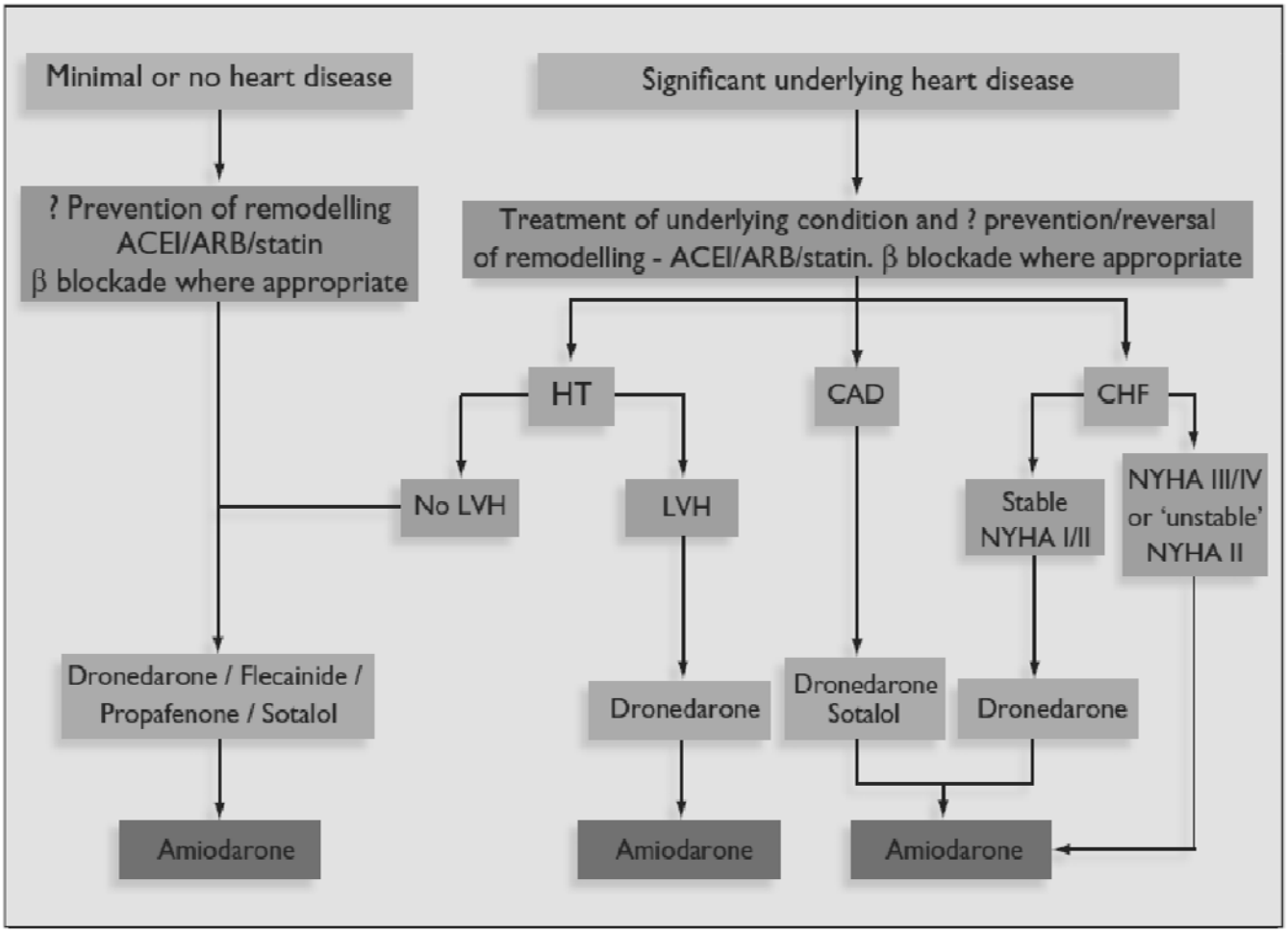


Figure 11 Choice of antiarrhythmic drug according to underlying pathology. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CAD = coronary artery disease; CHF = congestive heart failure; HT = hypertension; LVH = left ventricular hypertrophy; NYHA = New York Heart Association; unstable = cardiac decompensation within the prior 4 weeks. Antiarrhythmic agents are listed in alphabetical order within each treatment box. ? = evidence for 'upstream' therapy for prevention of atrial remodelling still remains controversial.

ΠΡΟΛΗΨΗ ΘΡΟΜΒΟΕΜΒΟΛΗΣ

Stroke Prevention

$CHADS_2$ Risk Criteria	Risk Value(s)
Prior stroke or TIA	2
Age > 75y	1
Hypertension	1
Diabetes mellitus	1
Heart failure	1

Sum of risk value(s) equals $CHADS_2$ score *

*$CHADS_2$ Score	Adjusted Stroke Rate (%/yr) (95% CI)	Recommended Therapy
0	1.9 (1.2 to 3.0)	Aspirin, 81 to 325 mg daily
1	2.8 (2.0 to 3.8)	Aspirin, 81 to 325 mg daily, or Warfarin (INR 2.0 to 3.0, target 2.5)
2	4.0 (3.1 to 5.1)	Warfarin (INR 2.0 to 3.0, target 2.5)
3	5.9 (4.6 to 7.3)	Warfarin (INR 2.0 to 3.0, target 2.5)
4	8.5 (6.3 to 11.1)	Warfarin (INR 2.0 to 3.0, target 2.5)
5	12.5 (8.2 to 17.5)	Warfarin (INR 2.0 to 3.0, target 2.5)
6	18.2 (10.5 to 27.4)	Warfarin (INR 2.0 to 3.0, target 2.5)

Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA 2001;285:2864–2870.

CHA_2DS_2VASc score

Risk Factor	Score
Congestive heart failure/left ventricular dysfunction	1
Hypertension	1
Age ≥ 75	2
Diabetes mellitus	1
Stroke/TIA/systemic embolism	2
Vascular disease	1
Age 65 – 74	1
Sex category (ie, female sex)	1
Maximum score	9

Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. Chest 2010;137:263–272.

Table 3. 2010 ESC Antithrombotic AF Guidelines: Risk Categories, CHA_2DS_2-VASc Score, and Recommended Antithrombotic Therapy

Risk Category	CHA_2DS_2-VASc Score	Recommended Antithrombotic Therapy
1 major risk factor or ≥2 clinically relevant nonmajor risk factors	≥ 2	OAC*
1 clinically relevant nonmajor risk factor	1	Either OAC* or aspirin 75-325 mg daily Preferred: OAC rather than aspirin
No risk factor	0	Either aspirin 75-325 mg daily or no antithrombotic therapy Preferred: no antithrombotic therapy rather than aspirin

*OACs such as a VKA, adjusted to an intensity range of INR 2.0-3.0 (target 2.5). New OAC drugs, which may be viable alternatives to a VKA, may ultimately be considered.

From Camm AJ, et al. *Eur Heart J.* 2010;31:2369-2429.[2]

ΥΠΟΛΟΓΙΣΜΟΣ ΑΙΜΟΡΡΑΓΙΚΟΥ ΚΙΝΔΥΝΟΥ

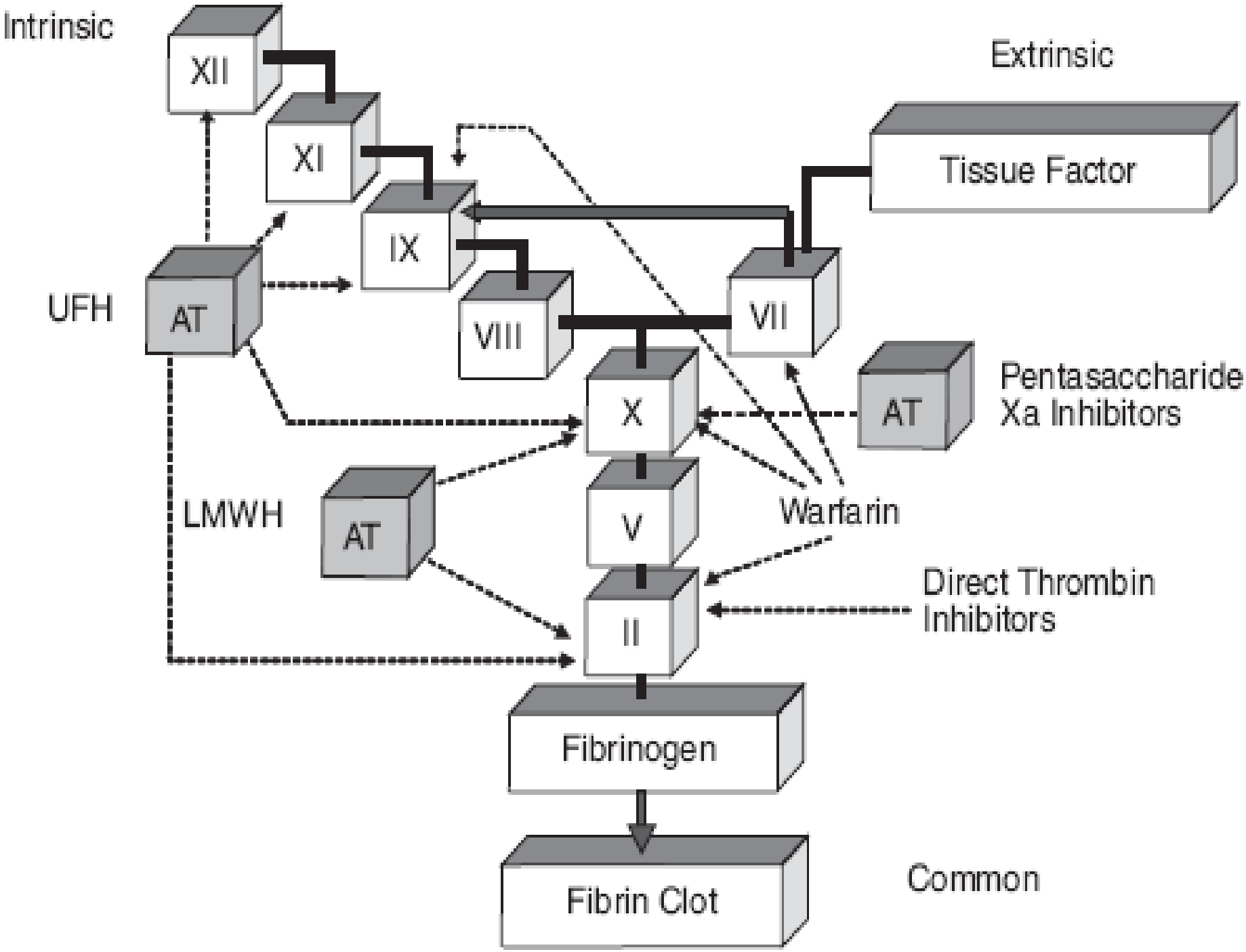
Table 10 Clinical characteristics comprising the HAS-BLED bleeding risk score

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]Hypertension' is defined as systolic blood pressure >160 mmHg. 'Abnormal kidney function' is defined as the presence of chronic dialysis or renal transplantation or serum creatinine ≥200 μmol/L. 'Abnormal liver function' is defined as chronic hepatic disease (e.g. cirrhosis) or biochemical evidence of significant hepatic derangement (e.g. bilirubin >2 x upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase >3 x upper limit normal, etc.). 'Bleeding' refers to previous bleeding history and/or predisposition to bleeding, e.g. bleeding diathesis, anaemia, etc. 'Labile INRs' refers to unstable/high INRs or poor time in therapeutic range (e.g. <60%). Drugs/alcohol use refers to concomitant use of drugs, such as antiplatelet agents, non-steroidal anti-inflammatory drugs, or alcohol abuse, etc.
INR = international normalized ratio. Adapted from Pisters *et al.*[60]

HAS – BLED > 3 σημαίνει υψηλό αιμορραγικό κίνδυνο όποτε η OAC πρέπει νε συνοδεύεται από στενή παρακολούθηση ή να χορηγούνται νεότερα αντιθρομβωτικά

Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel userfriendly score (HAS-BLED) to assess one-year risk of major bleeding in atrial fibrillation patients: The Euro Heart Survey. Chest 2010; March 18


Intrinsic
XII
XI
IX
VIII
Extrinsic
Tissue Factor
VII
UFH
AT
X
AT
Pentasaccharide
Xa Inhibitors
LMWH
AT
V
Warfarin
Direct Thrombin
Inhibitors
II
Fibrinogen
Fibrin Clot
Common

ΠΕΡΙΟΡΙΣΜΟΙ ΤΩΝ ΚΟΥΜΑΡΙΝΙΚΩΝ

- Σημαντικός κίνδυνος αιμορραγικών επιπλοκών και κυρίως ενδοκρανιακής αιμορραγίας.
- Περιορίζουν την ενεργοποίηση διαφόρων πρωτεασών της πήξης - Ανάγκη συχνής μέτρησης του INR
- Σημαντικές διακυμάνσεις του θεραπευτικού αποτελέσματος λόγω σημαντικών αλληλεπιδράσεων με διάφορες τροφές και φαρμακευτικές ουσίες.

<u>Πλεονέκτημα των κουμαρινικών – Υπάρχει αντίδοτο (κονάκιο)</u>

ΑΝΑΣΤΟΛΕΙΣ ΘΡΟΜΒΙΝΗΣ (Dabigatran – Pradaxa 110, 150)

- Ανταγωνιστικός αναστολέας της θρομβίνης
- Το προφάρμακο dabigatran etexilate μετατρέπεται πλήρως σε ενεργό Dabigatran.
- T1/2 = 14-17 ώρες.
- Απεκκρίνεται από τους νεφρούς σε ποσοστό 80%.
- Δοσολογία: 110 ή 150 mg bid (CrCl> 30 ml/min) – 75 mg bid (CrCl< 15 ml/min)

Stangier J, et al. *J Clin Pharmacol*. 2005;45:555-563.
Liesenfeld KH, et al. *Br J Clin Pharmacol*. 2006;62:527-537.
Stangier J, et al. *Br J Clin Pharmacol*. 2007;64:292-303.

RELY®

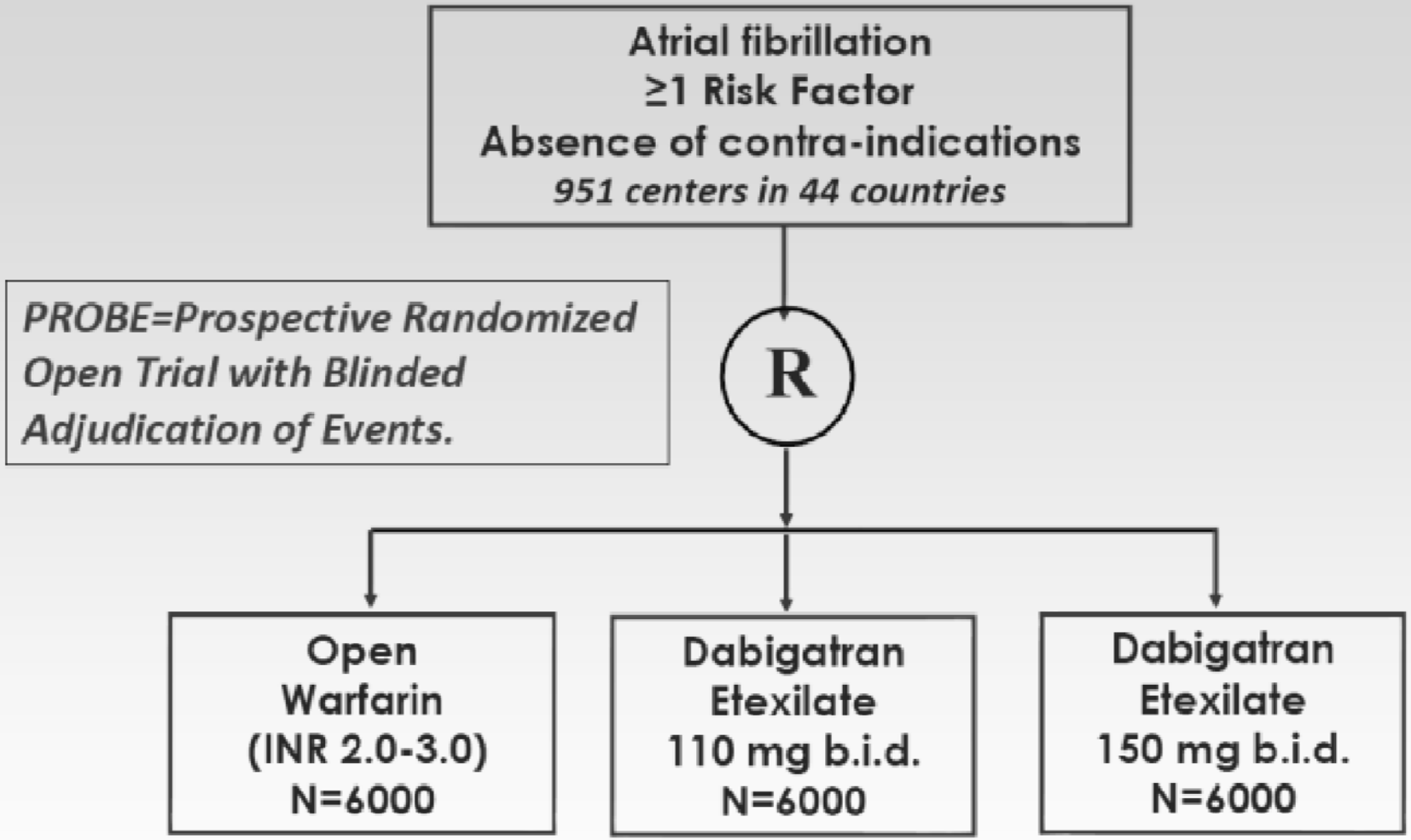
Study of stroke prevention
in atrial fibrillation

The RE-LY Study: Randomized Evaluation of Long-term anticoagulant therapY

Dabigatran Compared to Warfarin in 18,113 Patients with Atrial Fibrillation at Risk of Stroke

Design of RE-LY

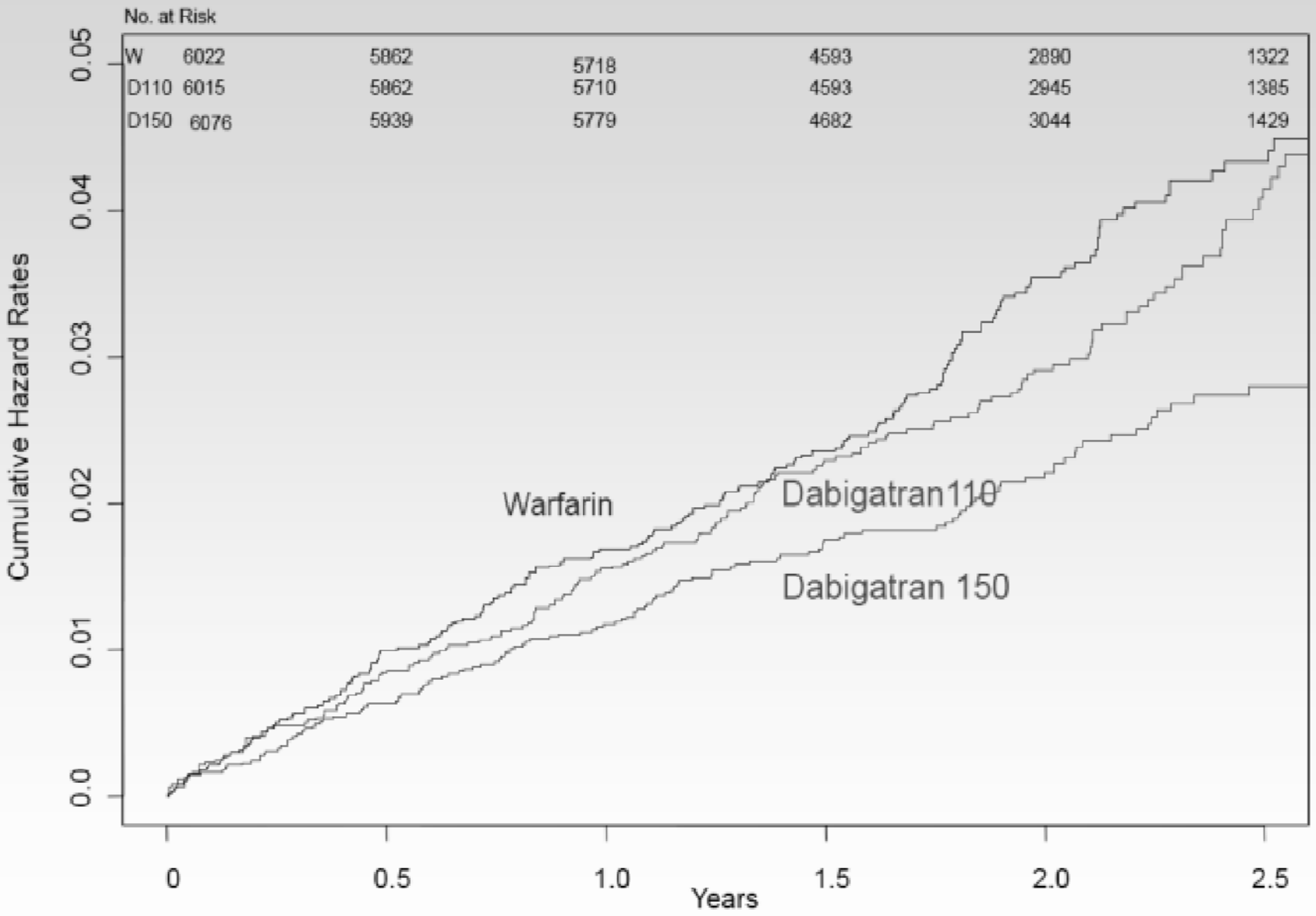
RELY®
Study of stroke prevention in atrial fibrillation



1^0 efficacy outcome = stroke or systemic embolism
1^0 safety outcome = major bleeding
Non-inferiority margin 1.46

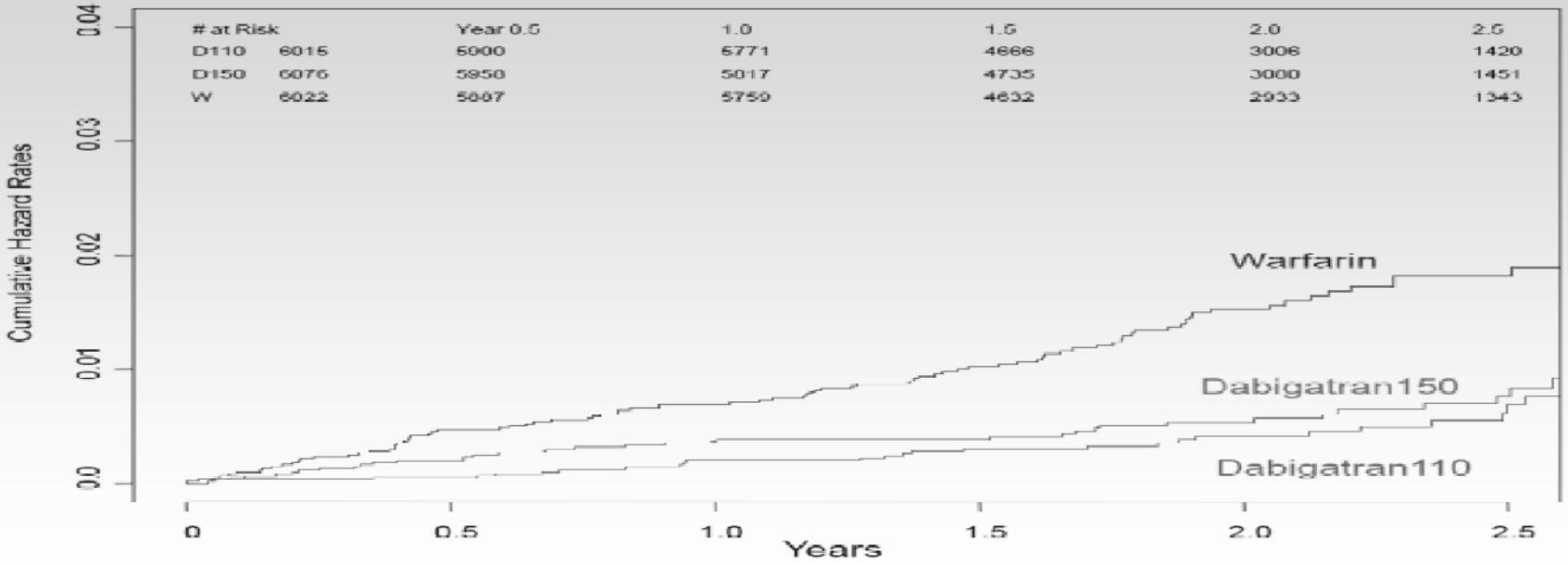
Stroke or Systemic Embolism

RELY®
Study of stroke prevention in atrial fibrillation



All Intracranial Bleeding

RELY®
Study of stroke prevention in atrial fibrillation



Major Bleeding

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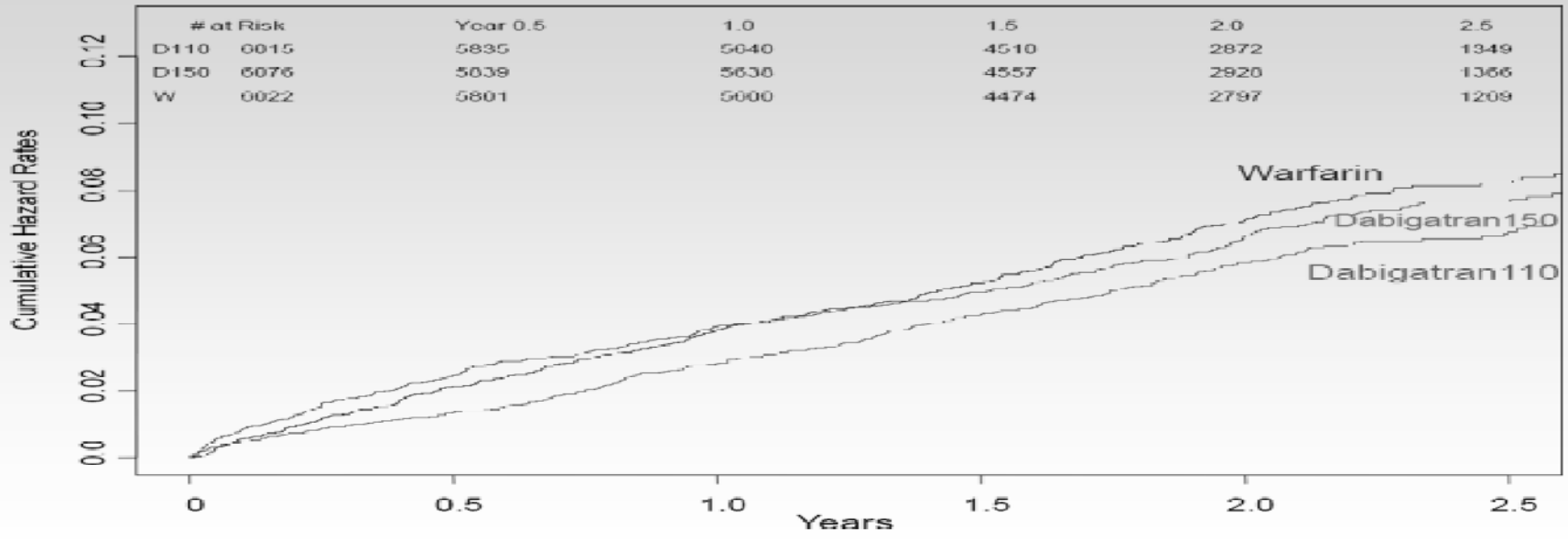
Study of stroke prevention in atrial fibrillation

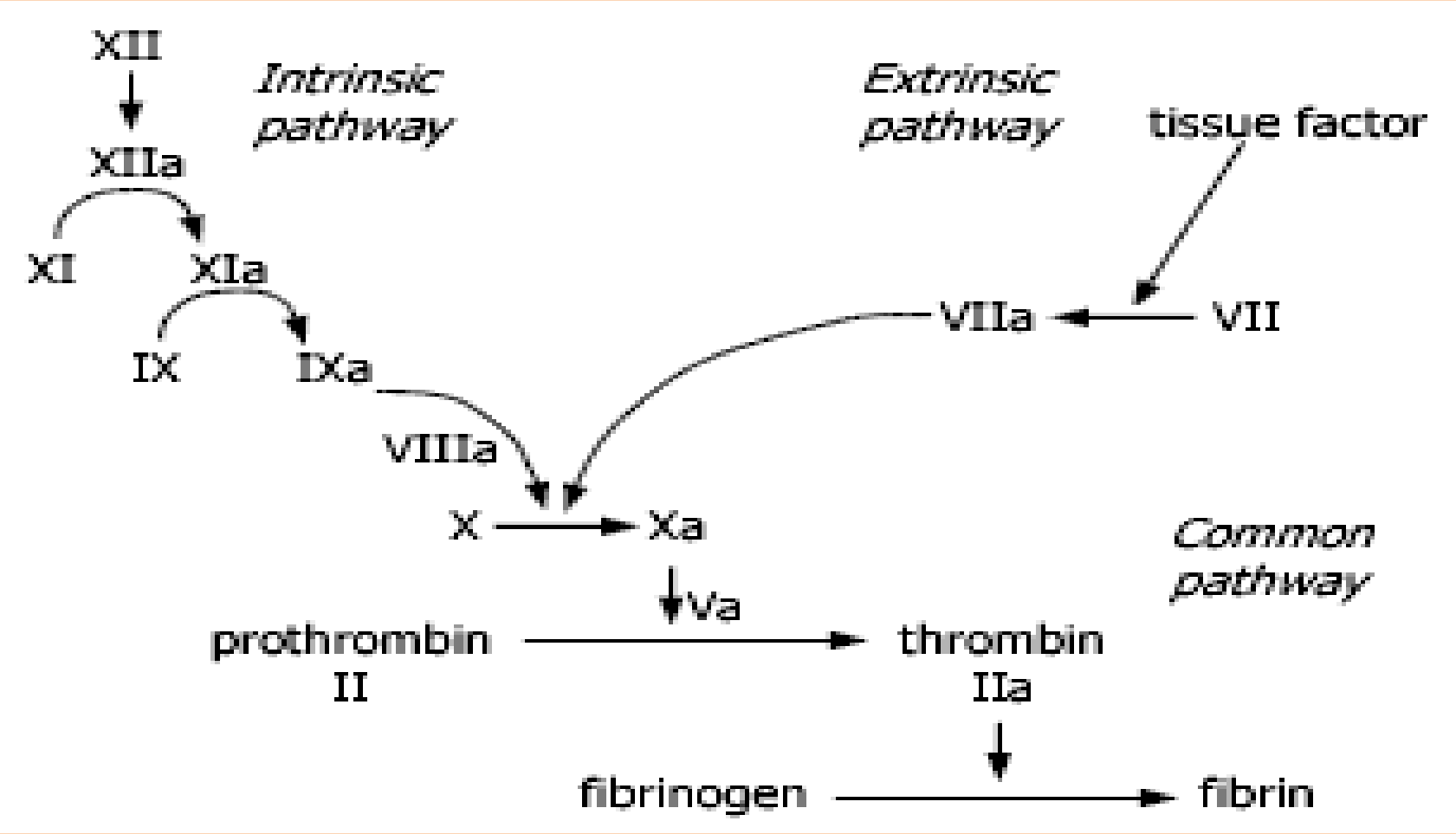


Conclusions

RELY®
Study of stroke prevention in atrial fibrillation

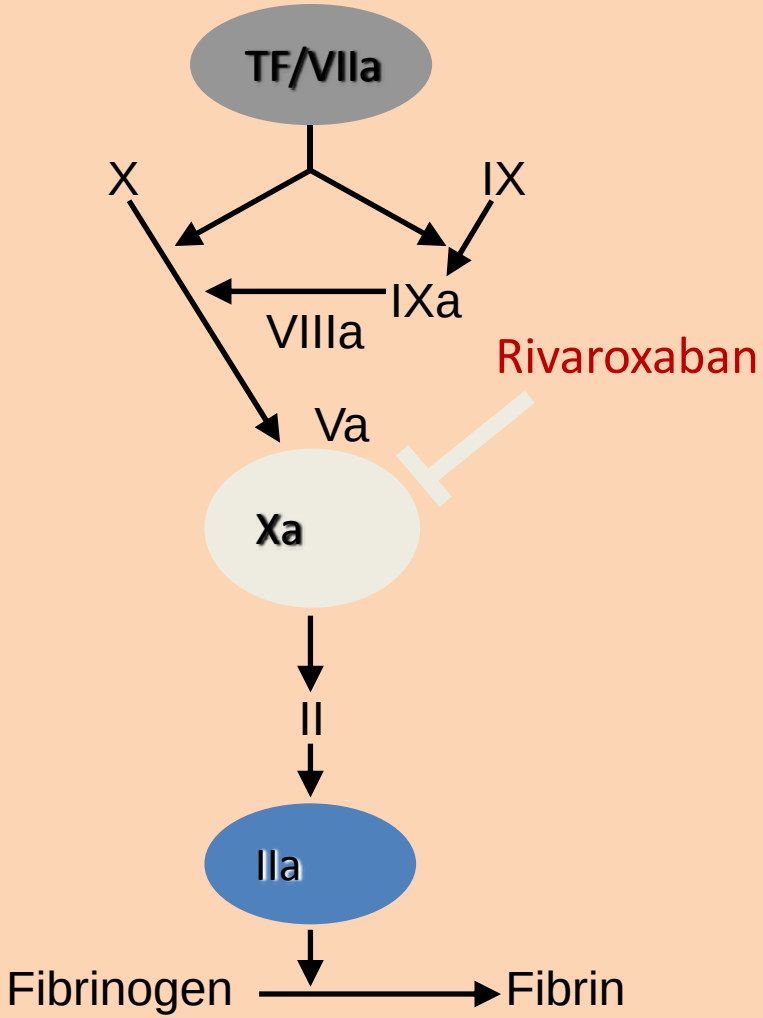
- Dabigatran 110 mg had a similar rate of stroke as warfarin with significantly reduced major bleeding
- Dabigatran 150 mg significantly reduced stoke compared to warfarin with similar risk of major bleeding
- Both doses markedly reduced intra-cranial hemorrhage
- Both doses are free of liver and other major toxicity, although they increase dyspepsia and GI bleeding

ΑΝΑΣΤΟΛΕΙΣ ΠΑΡΑΓΟΝΤΑ Χα



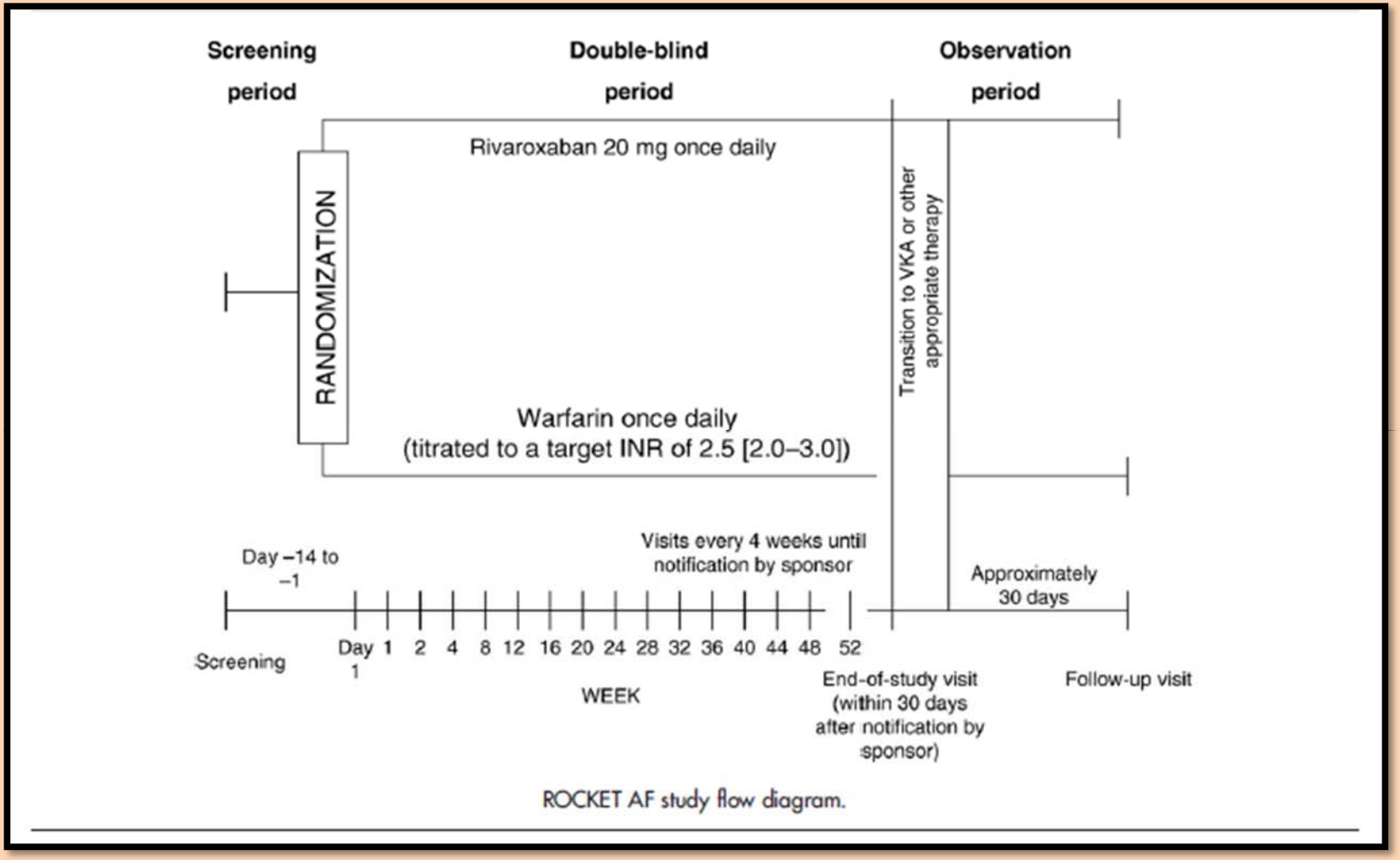
RIVAROXABAN

- Direct, specific, competitive factor Xa inhibitor
- Half-life 5-13 hours
- Clearance :
  - 1/3 direct renal excretion
  - 2/3 metabolism via CYP 450 enzymes
- Oral, once daily dosing without need for coagulation monitoring



Adapted from Weitz *et al*, 2005; 2008

ROCKET



ROCKET AF study flow diagram.

ROCKET-AF

ROCKET-AF: Primary efficacy outcome

Outcome	Rivaroxaban (n=7081)	Warfarin (n=7090)	Hazard ratio (95% CI)	p
Primary end point, noninferiority	1.71	2.16	0.79 (0.66–0.96)	<0.001
Primary end point, on-treatment superiority	1.70	2.15	0.79 (0.65–0.95)	0.015
Primary end point, intention-to-treat superiority	2.12	2.42	0.88 (0.74–1.03)	0.117
Vascular death, stroke, embolism	3.11	3.63	0.86 90.74–0.99)	0.034
Hemorrhagic stroke	0.26	0.44	0.59 (0.37–0.93)	0.024
Ischemic stroke	1.34	1.42	0.94 (0.75–1.17)	0.581
Unknown stroke	0.06	0.10	0.65 (0.25–1.67)	0.366

ROCKET-AF

ROCKET-AF: Bleeding outcomes

Outcome	Rivaroxaban (n=7081)	Warfarin (n=7090)	Hazard ratio (95% CI)	p
Major and nonmajor bleeding	14.91	14.52	1.03 (0.96–1.11)	0.442
Major bleeding	3.60	3.45	1.04 (0.90–1.20)	0.576
•>2 g/dL hemoglobin drop	2.77	2.26	1.22 (1.03–1.44)	0.019
•Transfusion	1.65	1.32	1.25 (1.01–1.55)	0.044
•Critical organ bleeding	0.82	1.18	0.69 (0.53–0.91)	0.007
•Bleeding causing death	0.24	0.48	0.50 (0.31–0.79)	0.003
Intracranial hemorrhage	0.49	0.74	0.67 (0.47–0.94)	0.019

APIXABAN

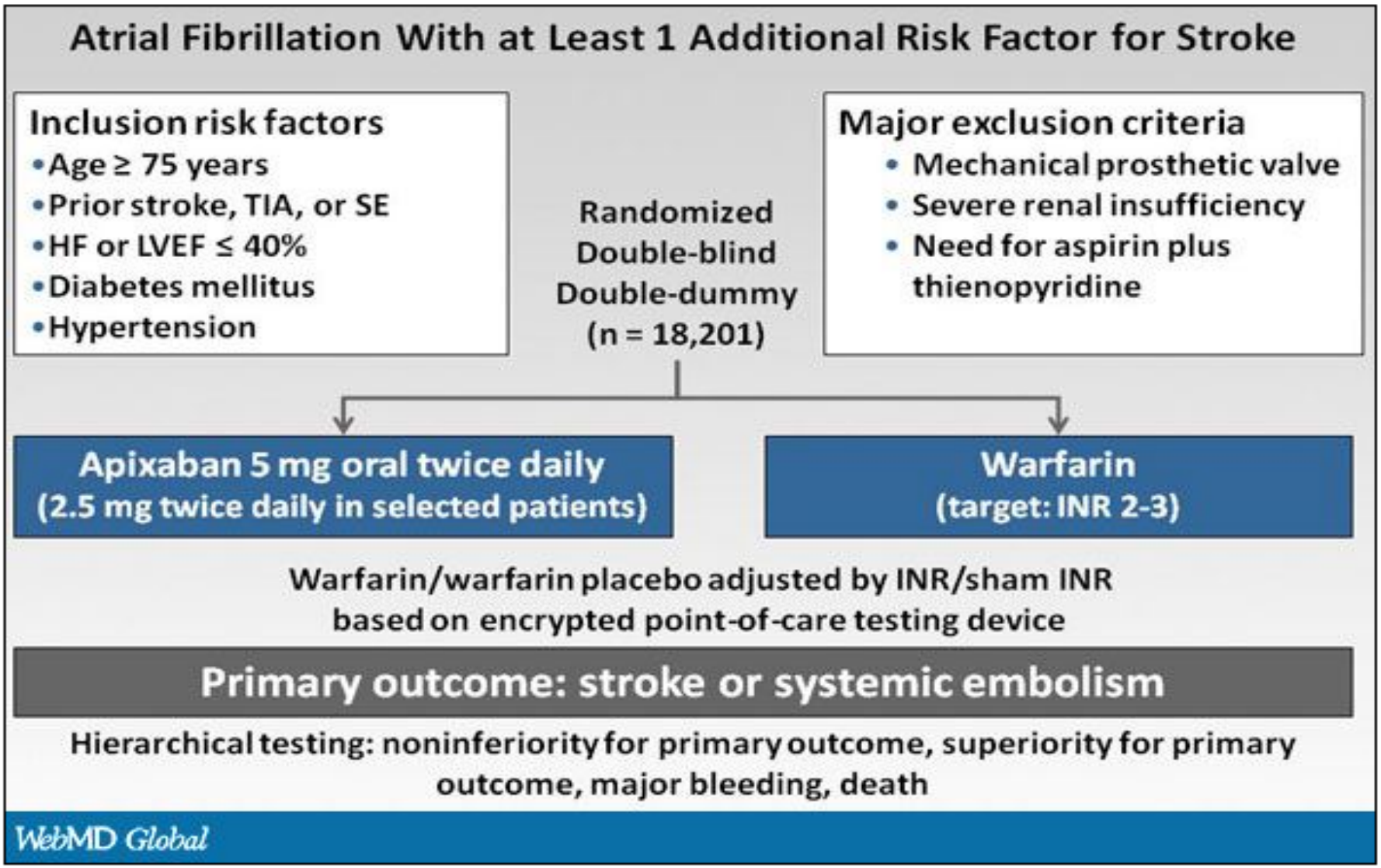


Figure 2. ARISTOTLE trial design. From Lopes RD, et al. *Am Heart J.* 2010;159:331-339.[27]

Table 5. Efficacy Results From ARISTOTLE

Outcome	Apixaban (N=9120)	Warfarin (N=9081)	Hazard Ratio (95% CI)	*P* value
	Event Rate %/y			
Primary outcome: stroke or systemic embolism	1.27	1.60	0.79 (0.66-0.95)	.01
Stroke	1.19	1.51	0.79 (0.65-0.95)	.01
Ischemic or uncertain type of stroke	0.97	1.05	0.92 (0.74-1.13)	.42
Hemorrhagic stroke	0.24	0.47	0.51 (0.35-0.75)	<.001
Systemic embolism	0.09	0.10	0.87 (0.44-1.75)	.70
Key secondary efficacy outcome: death from any cause	3.52	3.94	0.89 (0.80-0.998)	.047

From Granger CB, et al. *N Engl J Med.* 2011;365:981-992.[25]

Table 6. Safety Results From ARISTOTLE

Outcome	Apixaban (N=9088)	Warfarin (N=9052)	Hazard Ratio (95% CI)	*P* value
	Event Rate %/y			
Bleeding safety outcome: ISTH major bleeding	2.13	3.09	0.69 (0.60-0.80)	<.001
Intracranial	0.33	0.80	0.42 (0.30-0.58)	<.001
Other location	1.79	2.27	0.79 (0.68-0.93)	.004
Gastrointestinal	0.76	0.86	0.89 (0.70-1.15)	.37
Major or clinically relevant nonmajor bleeding	4.07	6.01	0.68 (0.61-0.75)	<.001
GUSTO severe bleeding	0.52	1.13	0.46 (0.35-0.60)	<.001
GUSTO moderate or severe bleeding	1.29	2.18	0.60 (0.50-0.71)	<.001
TIMI major bleeding	0.96	1.69	0.57 (0.46-0.70)	<.001
TIMI major or minor bleeding	1.55	2.46	0.63 (0.54-0.75)	<.001
Any bleeding	18.1	25.8	0.71 (0.68-0.75)	<.001

From Granger CB, et al. *N Engl J Med*. 2011;365:981-992.[25]

ΠΕΡΙΕΓΧΕΙΡΗΤΙΚΗ ΔΙΑΧΕΙΡΙΣΗ ΑΣΘΕΝΩΝ ΥΠΟ ΑΝΤΙΠΗΚΤΙΚΗ ΑΓΩΓΗ

<u>INR < 1.5 – οποιαδήποτε επέμβαση διενεργείται με ασφάλεια</u>

Υψηλού θρομβοεμβολικού κινδύνου:

- AF
- Μηχανική βαλβίδα
- Βιολογική βαλβίδα ή διόρθωση μιτροειδούς τους τελευταίους 3 μήνες.
- Πρόσφατη θρομβοεμβολή (<3 μήνες)
- Θρομβοφιλία

Αιμορραγικός κίνδυνος:

- Επεμβάσεις όπου η συμπίεση δεν είναι δυνατή
- Μείζονα χειρουργεία διάρκειας > 45 min.

Table 8 Bridging therapy of VKA with UFH or LMWH in high- and low-risk patients/procedures[125]

Low thromboembolic risk / low bleeding risk
• Continue anticoagulant therapy with INR in therapeutic range.
Low thromboembolic risk / high bleeding risk
• Discontinue anticoagulant therapy 5 days before the procedure.
• Start LMWH prophylaxis once daily or **UFH i.v.** 1 day after acenocoumarol interruption, and 2 days after warfarin interruption. Administer the last dose of LMWH at least 12 h before the procedure or give **UFH i.v.** up to 4 h prior to surgery.
• Resume LMWH or UFH at the pre-procedural dose 1–2 days (at least 12 h) after the procedure according to haemostatic status. Resume anticoagulant therapy 1 to 2 days after surgery at the pre-procedural dose + 50% boost dose for two consecutive days according to the haemostatic status.
• LMWH or UFH is continued until the INR has returned to therapeutic levels.
High thromboembolic risk
• Discontinue anticoagulant therapy 5 days before the procedure.
• Start therapeutic LMWH twice daily or **UFH i.v.** 1 day after acenocoumarol interruption, and 2 days after warfarin interruption. Administer the last dose of LMWH at least 12 h before the procedure or give **UFH i.v.** up to 4 h prior to surgery.
• Resume LMWH or UFH at the pre-procedural dose 1–2 days (at least 12 h) after the procedure according to haemostatic status. Resume anticoagulant therapy 1–2 days after surgery at the pre-procedural dose + 50% boost dose for two consecutive days according to haemostatic status.
• LMWH or UFH is continued until the INR has returned to therapeutic levels.

INR = international normalized ratio; LMWH = low molecular weight heparin; UFH = unfractionated heparin.