

심방세동의 뇌졸중 예방법



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Korean Heart Rhythm Society COI Disclosure

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The authors have no financial conflicts of interest
to disclose concerning the presentation

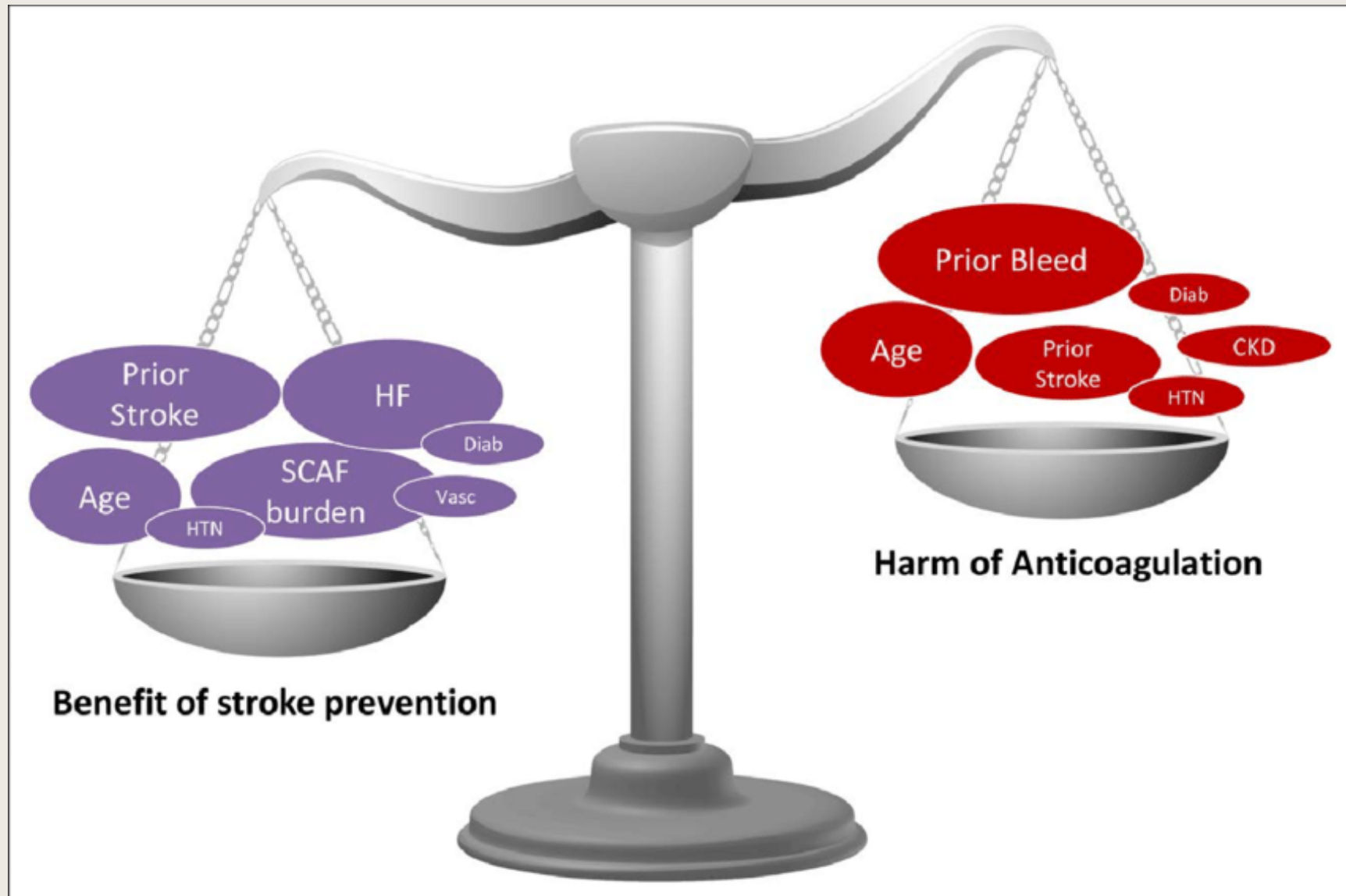


Disclosure

Relationships with commercial interests:

- None

Stroke prevention vs. Bleeding risk

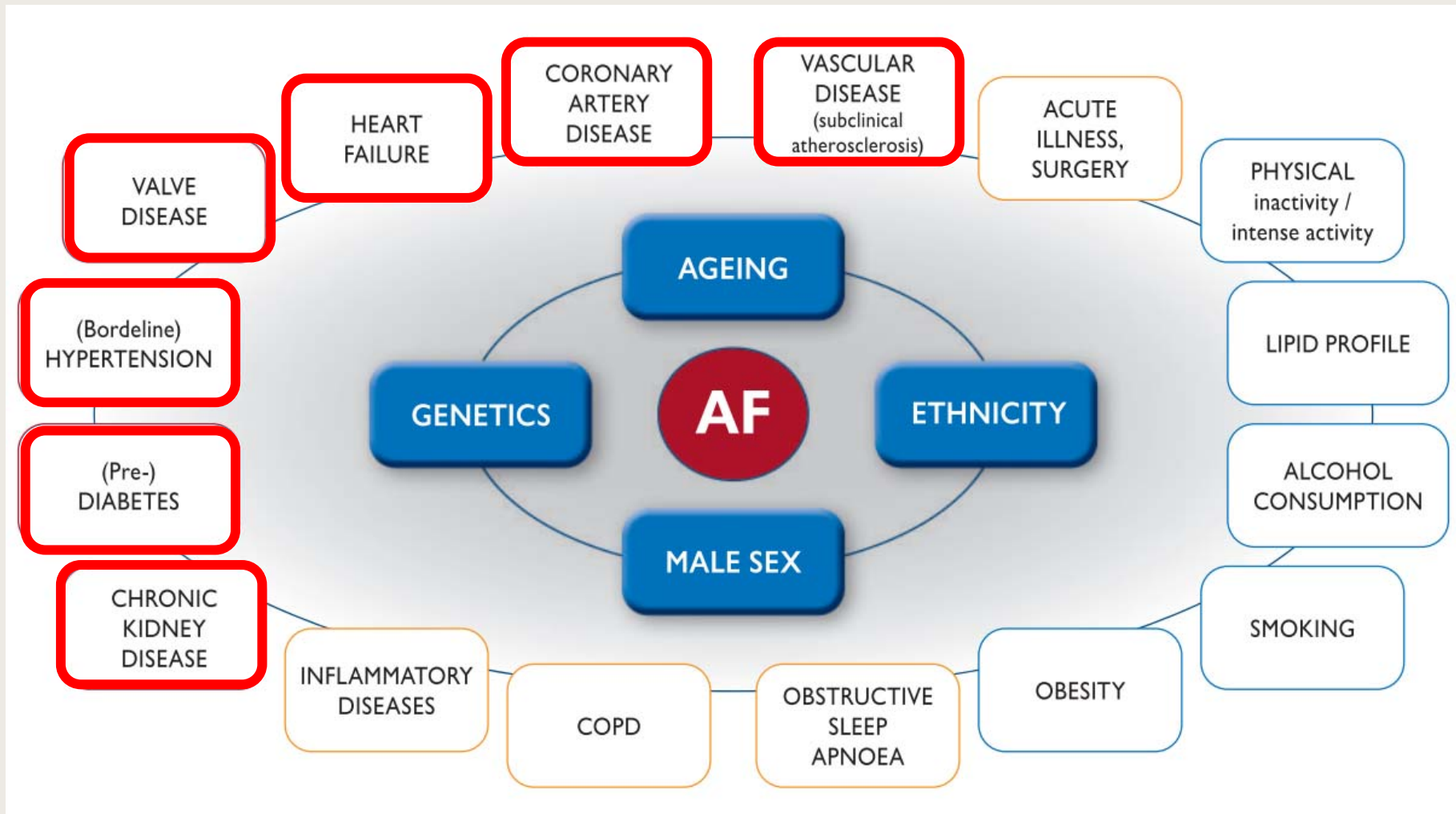


Stroke risk factors in patients with AF

Most commonly studied clinical risk factors (a systematic review) ³²⁴	Positive studies/All studies	Other clinical risk factors ³²⁵	Imaging biomarkers ^{291,326–328}	Blood/urine biomarkers ^{329–332}
Stroke/TIA/systemic embolism	15/16	Impaired renal function/ CKD	<i>Echocardiography</i>	Cardiac troponin T and I Natriuretic peptides
Hypertension	11/20	OSA	LA dilatation	Cystatin C
Ageing (per decade)	9/13	HCM	Spontaneous contrast or thrombus in LA	Proteinuria
Structural heart disease	9/13	Amyloidosis in degenerative cerebral and heart diseases	Low LAA velocities	CrCl/eGFR
Diabetes mellitus	9/14	Hyperlipidaemia	Complex aortic plaque	CRP
Vascular disease	6/17	Smoking	<i>Cerebral imaging</i>	IL-6
CHF/LV dysfunction	7/18	Metabolic syndrome ³³³	Small-vessel disease	GDF-15
Sex category (female)	8/22	Malignancy		von Willebrand factor D-dimer

CHF = congestive heart failure; CKD = chronic kidney disease; CrCl = creatinine clearance; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; GDF-15 = growth differentiation factor-15; IL-6 = interleukin 6; LA = left atrium; LAA = left atrial appendage; LV = left ventricular; OSA = obstructive sleep apnoea; TIA = transient ischaemic attack.

Risk factor for Incident AF



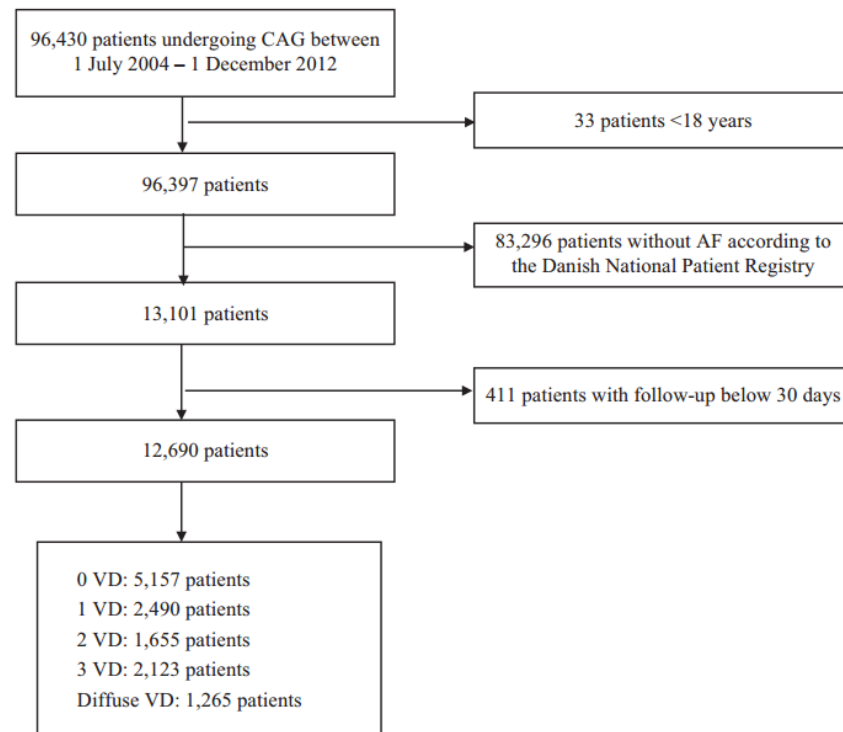
Stroke risk assessment

: CHA₂DS₂-VASc score

CHA ₂ DS ₂ -VASc score		
Risk factors and definitions	Points awarded	Comment
C Congestive heart failure Clinical HF, or objective evidence of moderate to severe LV dysfunction, or HCM	1	Recent decompensated HF irrespective of LVEF (thus incorporating HF _r EF or HF _p EF), or the presence (even if asymptomatic) of moderate-severe LV systolic impairment on cardiac imaging ³³⁵ ; HCM confers a high stroke risk ³³⁶ and OAC is beneficial for stroke reduction. ³³⁷
H Hypertension or on antihypertensive therapy	1	History of hypertension may result in vascular changes that predispose to stroke, and a well-controlled BP today may not be well-controlled over time. ³²⁴ Uncontrolled BP - the optimal BP target associated with the lowest risk of ischaemic stroke, death, and other cardiovascular outcomes is 120 - 129/<80 mmHg. ³³⁸
A Age 75 years or older	2	Age is a powerful driver of stroke risk, and most population cohorts show that the risk rises from age 65 years upwards. ³³⁹ Age-related risk is a continuum, but for reasons of simplicity and practicality, 1 point is given for age 65 - 74 years and 2 points for age ≥75 years.
D Diabetes mellitus Treatment with oral hypoglycaemic drugs and/or insulin or fasting blood glucose >125 mg/dL (7 mmol/L)	1	Diabetes mellitus is a well-established risk factor for stroke, and more recently stroke risk has been related to duration of diabetes mellitus (the longer the duration of diabetes mellitus, the higher the risk of thromboembolism ³⁴⁰) and presence of diabetic target organ damage, e.g. retinopathy. ³⁴¹ Both type 1 and type 2 diabetes mellitus confer broadly similar thromboembolic risk in AF, although the risk may be slightly higher in patients aged <65 years with type 2 diabetes mellitus compared to patients with type 1 diabetes mellitus. ³⁴²
S Stroke Previous stroke, TIA, or thromboembolism	2	Previous stroke, systemic embolism, or TIA confers a particularly high risk of ischaemic stroke, hence weighted 2 points. Although excluded from RCTs, AF patients with ICH (including haemorrhagic stroke) are at very high risk of subsequent ischaemic stroke, and recent observational studies suggest that such patients would benefit from oral anticoagulation. ³⁴³⁻³⁴⁵
V Vascular disease <u>Angiographically significant CAD</u> , previous myocardial infarction, PAD, or aortic plaque	1	Vascular disease (PAD or myocardial infarction) confers a 17 - 22% excess risk, particularly in Asian patients. ³⁴⁶⁻³⁴⁸ <u>Angiographically significant CAD</u> is also an independent risk factor for ischaemic stroke among AF patients (adjusted incidence rate ratio 1.29, 95% CI 1.08 - 1.53). ³⁴⁹ Complex aortic plaque on the descending aorta, as an indicator of significant vascular disease, is also a strong predictor of ischaemic stroke. ³⁵⁰
A Age 65 - 74 years	1	See above. Recent data from Asia suggest that the risk of stroke may rise from age 50 - 55 years upwards and that a modified CHA ₂ DS ₂ -VASc score may be used in Asian patients. ^{351,352}
Sc Sex category (female)	1	A stroke risk modifier rather than a risk factor. ³⁵³
Maximum score	9	

Should the Presence or Extent of Coronary Artery Disease be Quantified in the CHA₂DS₂-VASc Score in Atrial Fibrillation? A Report from the Western Denmark Heart Registry

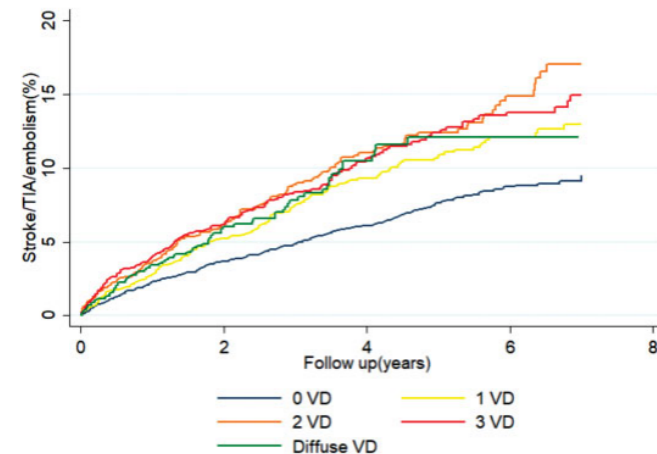
Kamilla Steensig^{1,*} Kevin K. W. Olesen^{1,2,*} Troels Thim¹ Jens C. Nielsen¹ Svend E. Jensen³
 Lisette O. Jensen⁴ Steen D. Kristensen¹ Hans Erik Bøtker¹ Gregory Y. H. Lip^{5,6,7,**} Michael Maeng^{1,**}



VD	Patients	Events	Rate per 100 person-years	IRR (95% CI)	Adjusted ^a IRR (95% CI)
0 VD	5,157	284	1.61 (1.43–1.81)	1 (reference)	1 (reference)
1 VD	2,490	185	2.30 (1.99–2.65)	1.42 (1.18–1.72)	1.15 (0.94–1.40)
2 VD	1,655	153	2.93 (2.50–3.43)	1.82 (1.49–2.22)	1.36 (1.09–1.70)
3 VD	2,123	180	2.74 (2.37–3.17)	1.70 (1.41–2.05)	1.18 (0.95–1.47)
Diffuse VD	1,265	79	2.68 (2.15–3.34)	1.66 (1.29–2.14)	1.44 (1.11–1.86)

Abbreviations: ADP, adenosine diphosphate; CI, confidence interval; IRR, incidence rate ratio; OAC, oral anticoagulant; TIA, transient ischaemic attack; VD, vessel disease.

^aAdjusted for: all variables included in the CHA₂DS₂-VASc score (congestive heart failure, hypertension, age 65–74 or ≥75 years, diabetes mellitus, previous stroke or TIA, vascular disease [peripheral artery disease, aortic plaque or previous myocardial infarction] and female sex), OAC treatment (warfarin, phenprocoumon, rivaroxaban, dabigatran etexilate and apixaban) and any anti-platelet treatment (aspirin and/or ADP-inhibitor). Both OAC treatment and anti-platelet treatment are defined as having redeemed a prescription before or within 30 days after the coronary angiography.



Risk factors for bleeding with OCA and antiplatelet therapy

Non-modifiable	Potentially modifiable	Modifiable	Biomarkers
<p><u>Age >65 years</u></p> <p>Previous major bleeding</p> <p><u>Severe renal impairment (on dialysis or renal transplant)</u></p> <p>Severe hepatic dysfunction (cirrhosis)</p> <p>Malignancy</p> <p>Genetic factors (e.g., CYP 2C9 polymorphisms)</p> <p><u>Previous stroke, small-vessel disease, etc.</u></p> <p><u>Diabetes mellitus</u></p> <p>Cognitive impairment/dementia</p>	<p>Extreme frailty ± excessive risk of falls^a</p> <p>Anaemia</p> <p>Reduced platelet count or function</p> <p>Renal impairment with CrCl <60 mL/min</p> <p>VKA management strategy^b</p>	<p><u>Hypertension/elevate SBP</u></p> <p>Concomitant antiplatelet/NSAID</p> <p>Excessive alcohol intake</p> <p>Non-adherence to OAC</p> <p>Hazardous hobbies / occupations</p> <p>Bridging therapy with heparin</p> <p>INR control (target 2.0–3.0), target TTR >70%^c</p> <p>Appropriate choice of OAC and correct dosing^d</p>	<p>GDF-15</p> <p>Cystatin C / CKD-EPI</p> <p>cTnT-hs</p> <p>Von Willebrand factor (+ other coagulation markers)</p>

Bleeding risk assessment

Risk factors and definitions		Points awarded
H	<u>Uncontrolled hypertension</u> SBP >160 mmHg	1
A	Abnormal renal and/or hepatic function Dialysis, transplant, serum creatinine >200 µmol/L, cirrhosis, bilirubin > × 2 upper limit of normal, AST/ALT/ALP >3 × upper limit of normal	1 point for each
S	Stroke <u>Previous ischaemic or haemorrhagic^a stroke</u>	1
B	Bleeding history or predisposition Previous major haemorrhage or anaemia or severe thrombocytopenia	1
L	Labile INR^b TTR <60% in patient receiving VKA	1
E	Elderly <u>Aged >65 years or extreme frailty</u>	1
D	Drugs or excessive alcohol drinking Concomitant use of antiplatelet or NSAID; and/or excessive ^c alcohol per week	1 point for each
Maximum score		9

Bleeding risk assessment

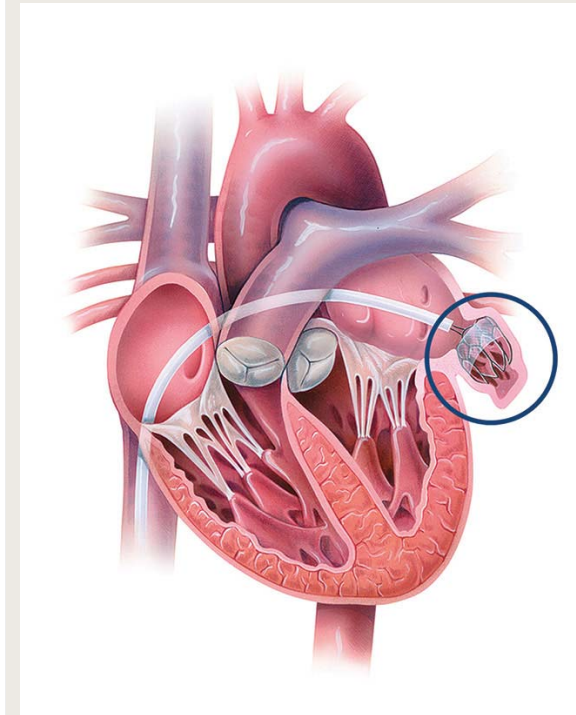
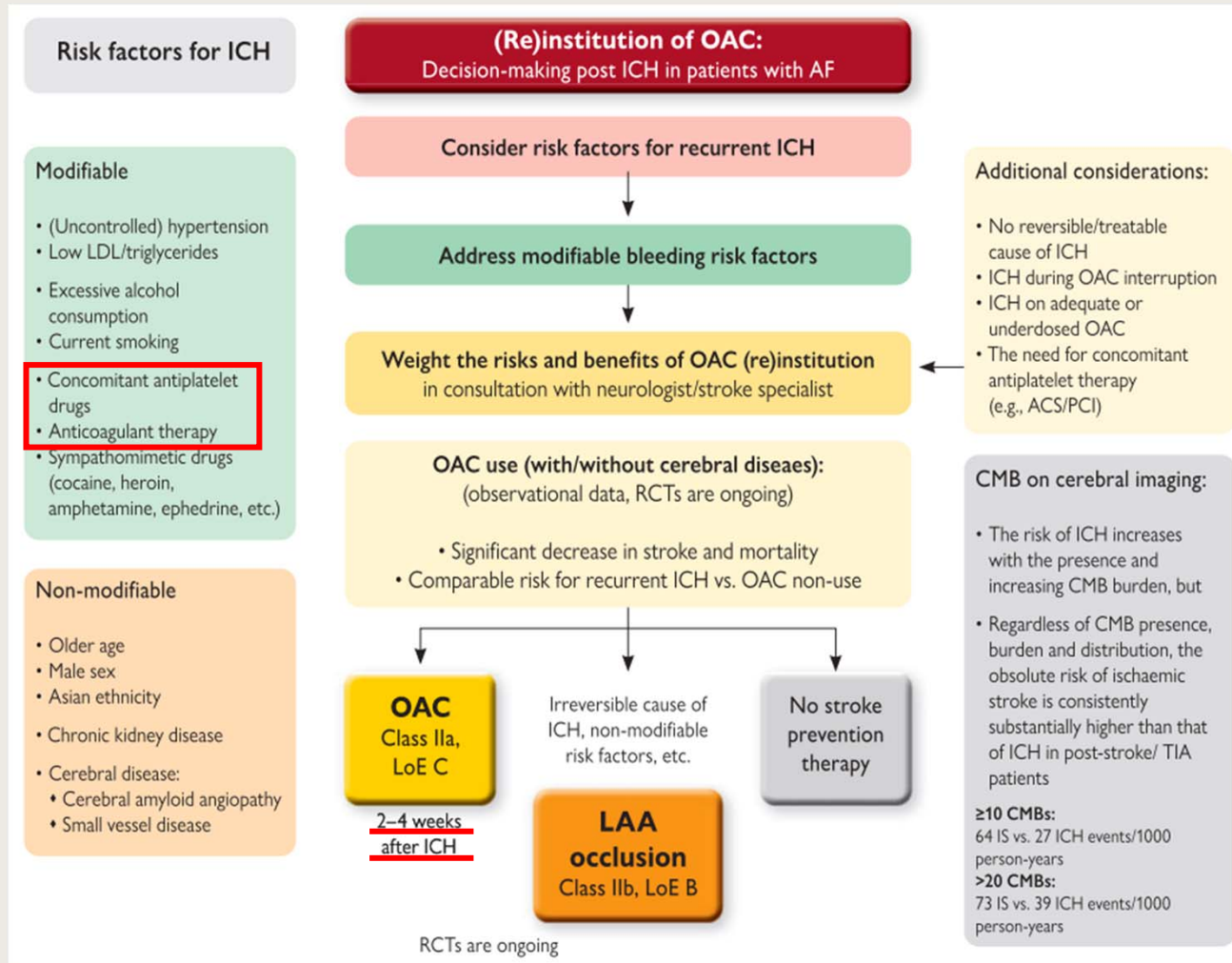
Recommendations for the prevention of thrombo-embolic events in AF

Recommendations	Class ^a	Level ^b
For bleeding risk assessment, a formal structured risk-score-based bleeding risk assessment is recommended to help identify non-modifiable and address modifiable bleeding risk factors in all AF patients, and to identify patients potentially at high risk of bleeding who should be scheduled for early and more frequent clinical review and follow-up . ^{388,395,404,406}	I	B
For a formal risk-score-based assessment of bleeding risk, the HAS-BLED score should be considered to help address modifiable bleeding risk factors, and to identify patients at high risk of bleeding (HAS-BLED score ≥ 3) for early and more frequent clinical review and follow-up. ^{388,395,404,406}	IIa	B
Stroke and bleeding risk reassessment at periodic intervals is recommended to inform treatment decisions (e.g. initiation of OAC in patients no longer at low risk of stroke) and address potentially modifiable bleeding risk factors. ^{c389,478,479}	I	B
In patients with AF initially at low risk of stroke, first reassessment of stroke risk should be made at 4 - 6 months after the index evaluation. ^{385–387}	IIa	B
Estimated bleeding risk , in the absence of absolute contraindications to OAC, should not in itself guide treatment decisions to use OAC for stroke prevention.	III	A

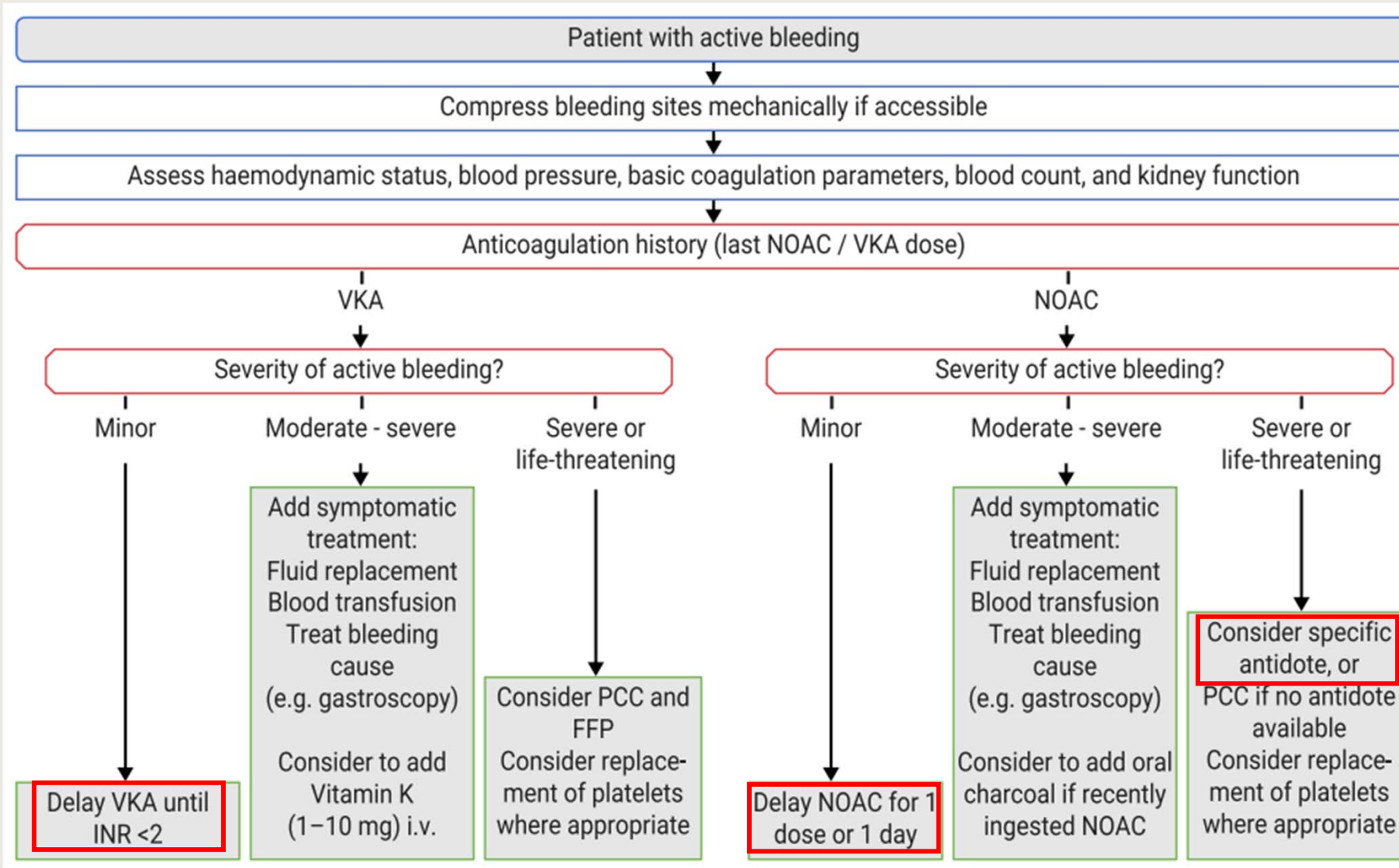
Absolute contraindications to oral anticoagulants

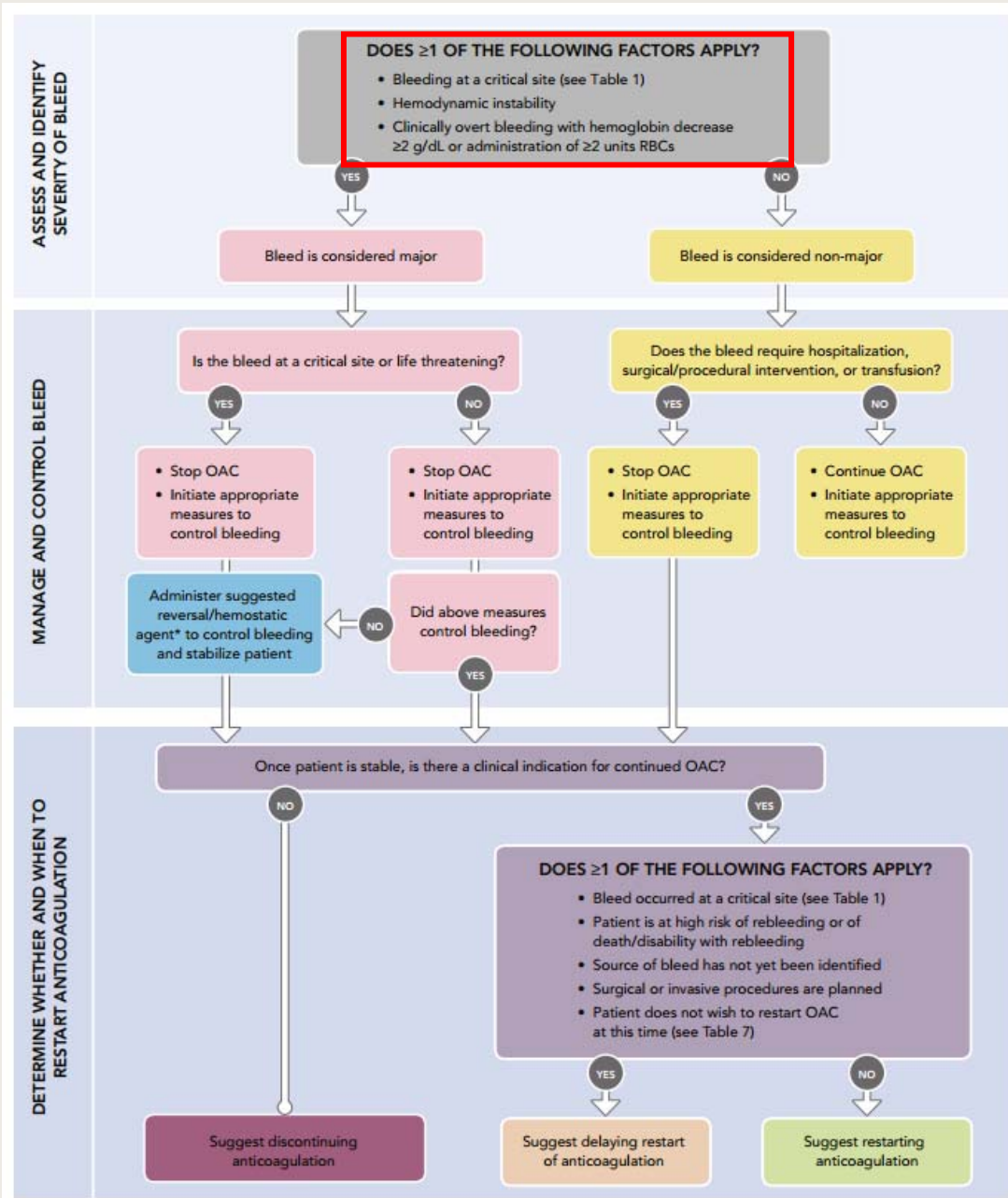
- Active serious bleeding (where the source should be identified and treated)
- Associated comorbidities
 - Severe thrombocytopenia **platelets $<50 \times 10^3/\mu\ell$**
 - Severe anemia under investigation
 - Recent high-risk bleeding event such as **intracranial haemorrhage (ICH)**
- Non-drug options may be considered in such cases

Management of patients with atrial fibrillation post-intracranial hemorrhage



Active bleeding on anticoagulant therapy : management and reversal drug

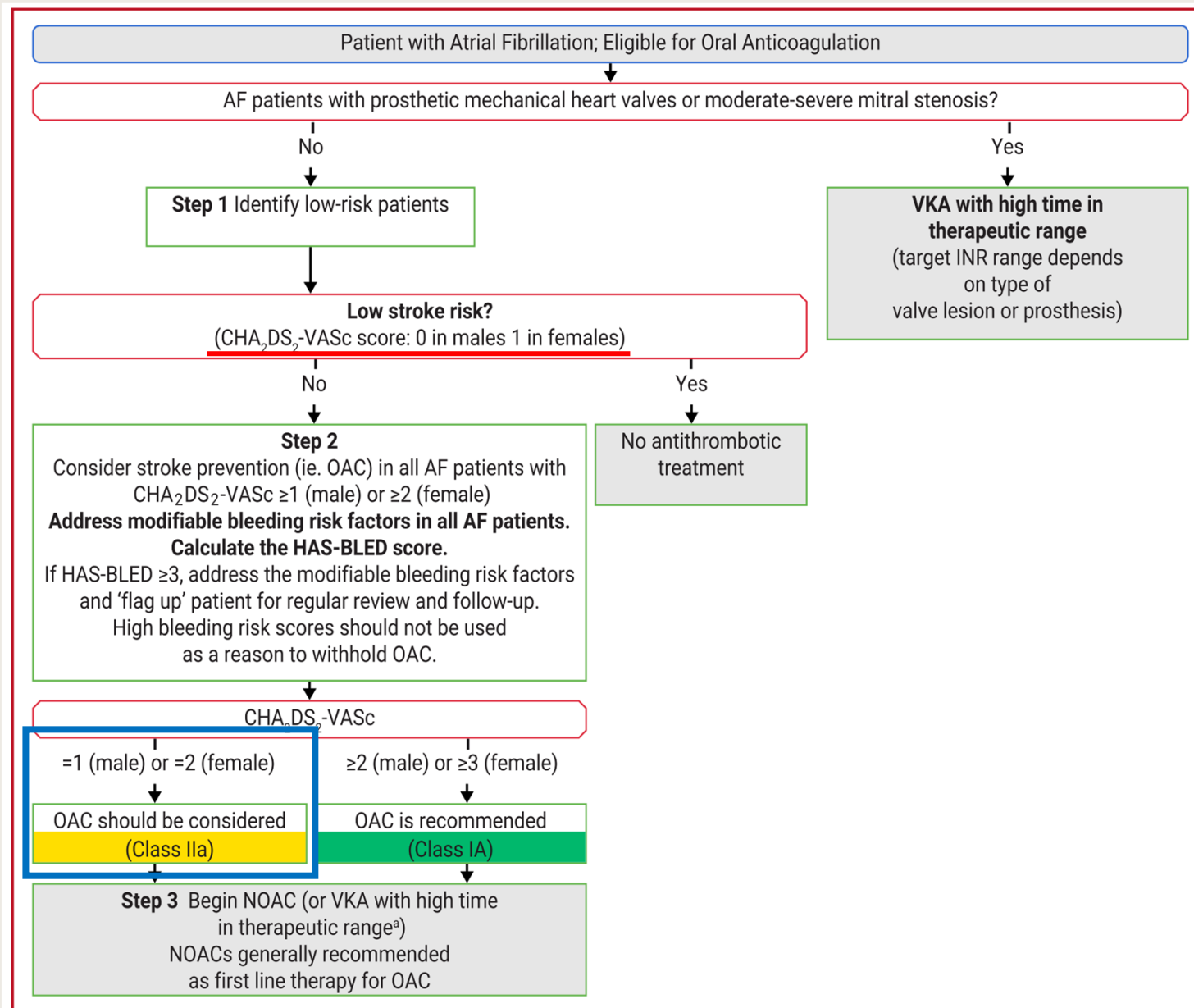




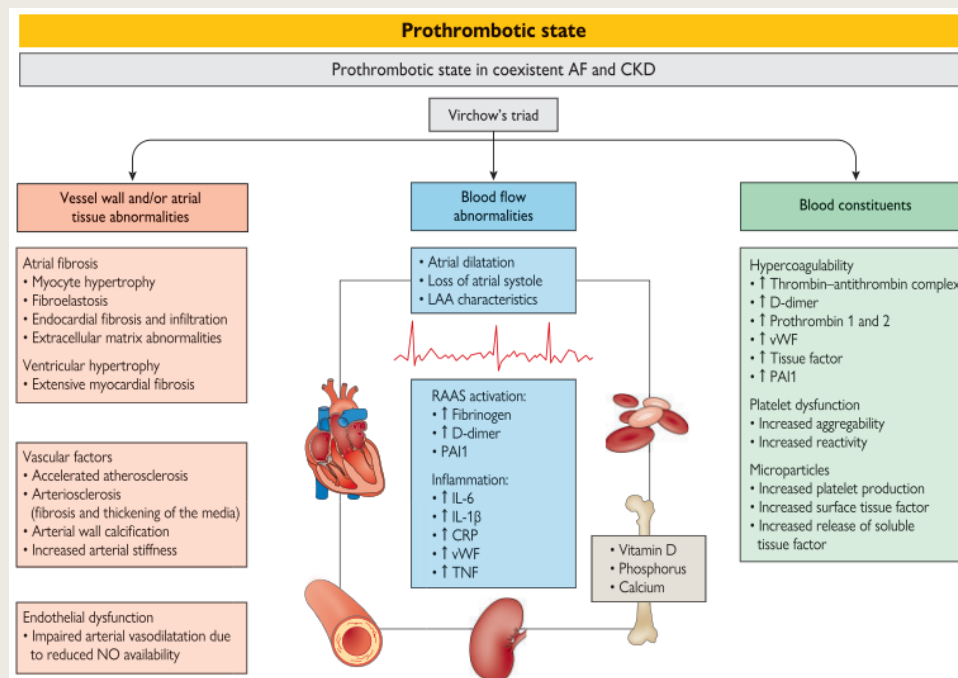
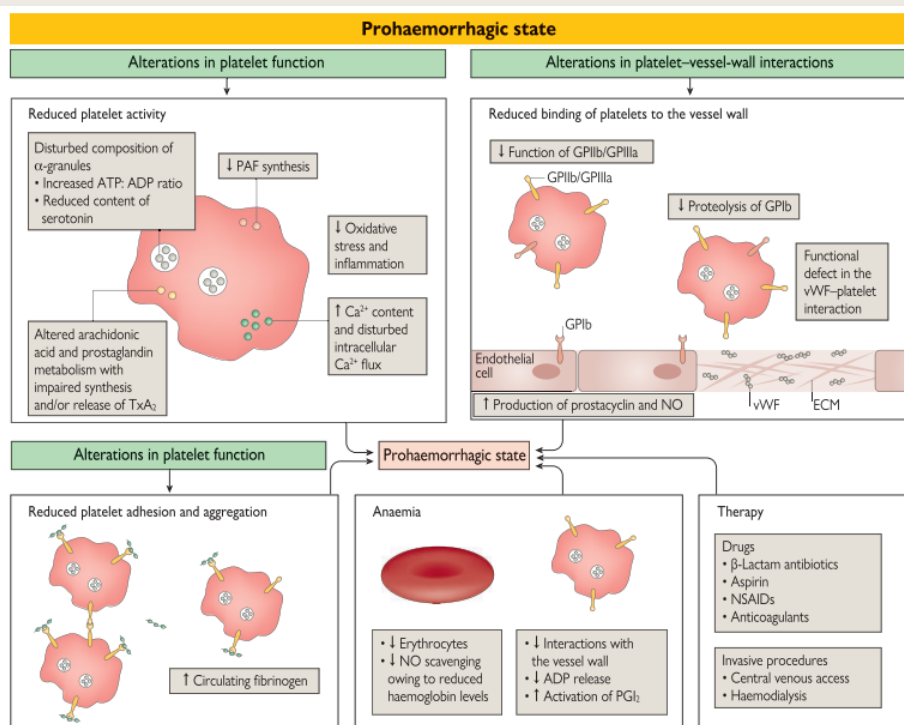
2020 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants

Type of Bleed	Initial Signs and Symptoms	Potential Consequences of Bleed
ICH: includes intraparenchymal, subdural, epidural, and subarachnoid hemorrhages	<ul style="list-style-type: none"> Unusually intense headache, emesis, reduced or loss of consciousness, vision changes, numbness, weakness, aphasia, ataxia, vertigo, seizures 	<ul style="list-style-type: none"> Stupor or coma Permanent neurological deficit Death
Other central nervous system hemorrhage: includes intraocular, intra- or extra-axial spinal hemorrhages	<ul style="list-style-type: none"> Intraocular: monocular eye pain, vision changes, blindness Spinal: back pain, bilateral extremity weakness or numbness, bowel or bladder dysfunction, respiratory failure 	<ul style="list-style-type: none"> Intraocular: permanent vision loss Spinal: permanent disability, paraplegia, quadriplegia, death
Pericardial tamponade	<ul style="list-style-type: none"> Shortness of breath, tachypnea, hypotension, paradoxical pulse, jugular venous distension, tachycardia, muffled heart sounds, rub 	<ul style="list-style-type: none"> Cardiogenic shock Death
Airway: includes posterior epistaxis	<ul style="list-style-type: none"> Airway: hemoptysis, shortness of breath, hypoxia Posterior epistaxis: profuse epistaxis, hemoptysis, hypoxia, shortness of breath 	<ul style="list-style-type: none"> Hypoxemic respiratory failure Death
Hemothorax, intra-abdominal bleeding, and retroperitoneal hemorrhage	<ul style="list-style-type: none"> Hemothorax: tachypnea, tachycardia, hypotension, decreased breath sounds Intra-abdominal (non-GI): abdominal pain, distension, hypotension, tachycardia Retroperitoneal hemorrhage: back/flank/hip pain, tachycardia, hypotension 	<ul style="list-style-type: none"> Hemothorax: respiratory failure Retroperitoneal hemorrhage: femoral neuropathy All: hypovolemic shock, death
Extremity bleeds: includes intramuscular and intra-articular bleeding	<ul style="list-style-type: none"> Intramuscular: pain, swelling, pallor, paresthesia, weakness, diminished pulse Intra-articular: joint pain, swelling, decreased range of motion 	<ul style="list-style-type: none"> Intramuscular: compartment syndrome, paralysis, limb loss Intra-articular: irreversible joint damage

How about low risk patients?



Atrial fibrillation and chronic kidney disease



Atrial fibrillation and chronic kidney disease

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Standard dose	150 mg b.i.d.	20 mg o.d.	5 mg b.i.d.	60 mg o.d.
Lower dose	110 mg b.i.d.			
Reduced dose		15 mg o.d.	2.5 mg b.i.d.	30 mg o.d.
Dose-reduction criteria	Dabigatran 110 mg b.i.d. in patients with: <ul style="list-style-type: none"> ● Age \geq80 years ● Concomitant use of verapamil, or ● Increased bleeding risk 	<u>CrCl 15 - 49 mL/min</u>	At least 2 of 3 criteria: <ul style="list-style-type: none"> ● Age \geq80 years, ● Body weight \leq60 kg, or ● <u>Serum creatinine \geq1.5 mg/dL (133 μmol/L)</u> 	If any of the following: <ul style="list-style-type: none"> ● <u>CrCl 15 - 50 mL/min,</u> ● Body weight \leq60 kg, ● Concomitant use of dronedarone, ciclosporine, erythromycin, or ketoconazole

b.i.d. = bis in die (twice a day); CrCl = creatinine clearance; o.d. = *omni die* (once daily).

NOAC dose reduction in Korean patients

	Dose reduction criteria	Dose
Dabigatran	<u>Creatinine clearance 30-50 mL/min</u> <u>P-glycoprotein inhibitors^a</u> Clopidogrel, aspirin, NSAIDs Increased bleeding risk ^b Age 75 years or more	110 mg bid
Rivaroxaban	Age 80 years or more <u>Creatinine clearance 15-50 mL/min^c</u>	15 mg qd
Apixaban	At least two: 1) age 80 years or more, 2) body weight 60 kg or less, 3) <u>creatinine \geq 1.5 mg/dL</u>	2.5 mg bid
Edoxaban	<u>P-glycoprotein inhibitors^a</u> Body weight 60 kg or less <u>Creatinine clearance 15-50 mL/min^c</u>	30 mg qd

NOAC, non-vitamin K antagonist oral anticoagulant; bid, bis in die (twice a day); qd, quaque die (once a day).

^aP-glycoprotein inhibitors: amiodarone, verapamil, dronedarone, etc.

^bIncreased bleeding risk: coagulopathy, thrombocytopenia, platelet dysfunction, recent major trauma or biopsy, infective endocarditis

^cShould be used with caution in patients with significant renal impairment (creatinine clearance 15-29 mL/min).

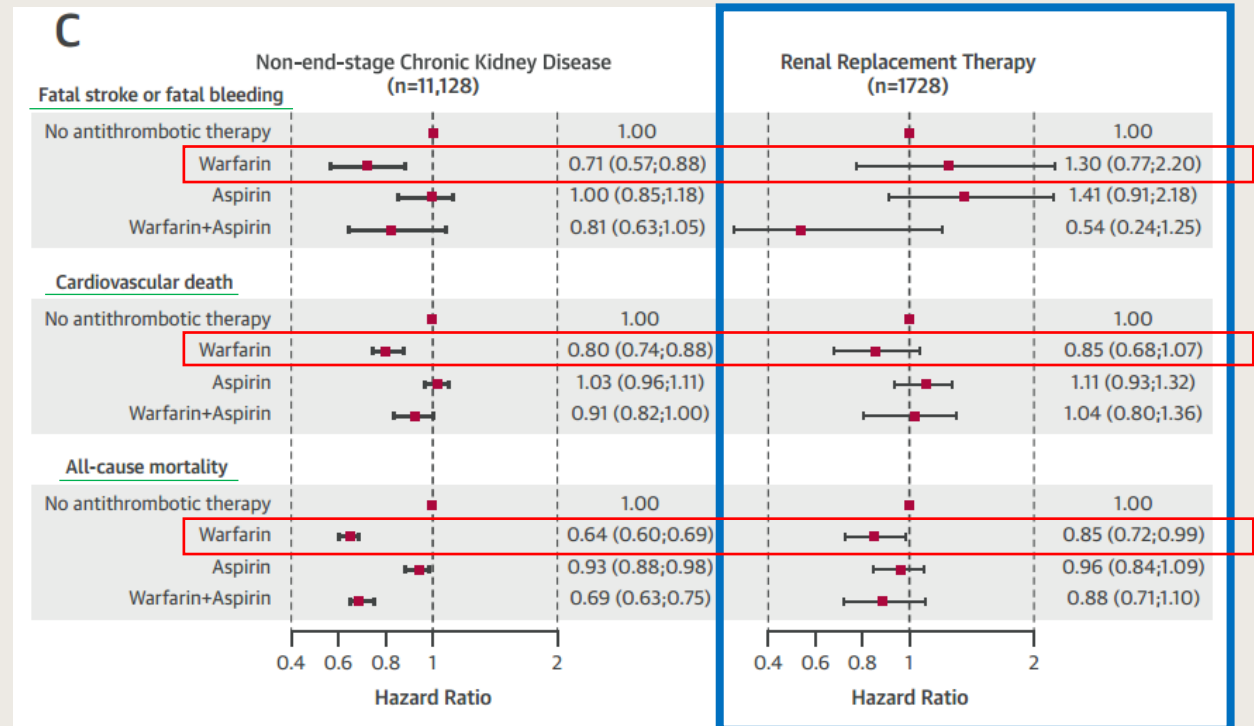
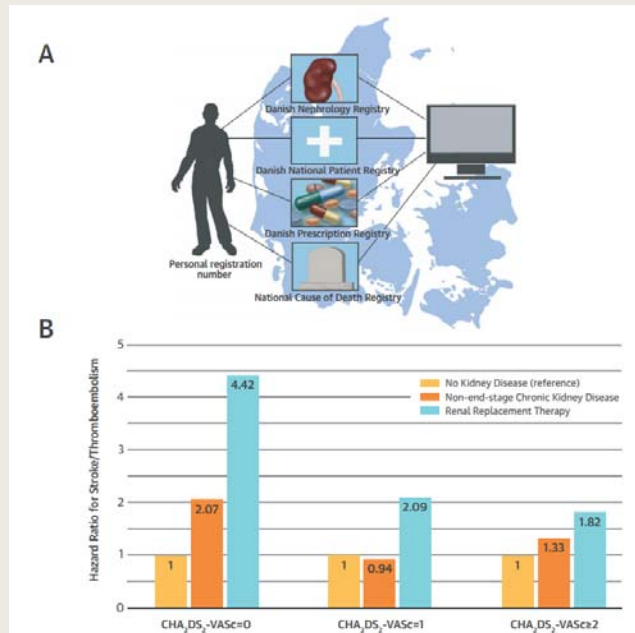
Anticoagulation in Hemodialysis Patients

	Dialysis Patients		Nondialysis Patients	
	N=1626		N=204 210	
	No. of Events	Incidence* Rate per 100 Person-Years	No. of Events	Incidence* Rate per 100 Person-Years
Stroke†	107	3.12	19 489	2.35
According to warfarin prescription (within 30 days postdischarge)				
Yes	52	3.37	9241	2.19
No	55	2.91	10 248	2.51
According to CHADS ₂ score‡				
Low risk (0)	4	1.99	2270	1.49
Moderate risk (1)	23	2.35	6078	2.06
High risk (≥ 2)	80	3.55	11 141	2.91
Bleeding§	275	8.89	34 035	4.32
According to warfarin prescription (within 30 days postdischarge)				
Yes	149	10.88	18 340	4.64
No	126	7.31	15 695	4.00
According to HAS-BLEDI score				
Low and moderate risk# (1–2)	43	8.00	26 129	4.07
High risk (≥ 3)	232	9.08	7906	5.45

Patients With AF	Outcomes	Adjusted* HR (95% CI)	Propensity Score‡ Adjusted HR (95% CI)
Dialysis (n=1626)	Stroke†	1.14 (0.78–1.67)	1.17 (0.79–1.75)
	Bleeding§	1.44 (1.13–1.85)	1.41 (1.09–1.81)
Nondialysis (n=204 210)	Stroke†	0.87 (0.85–0.90)	0.89 (0.87–0.92)
	Bleeding§	1.19 (1.16–1.22)	1.20 (1.17–1.23)

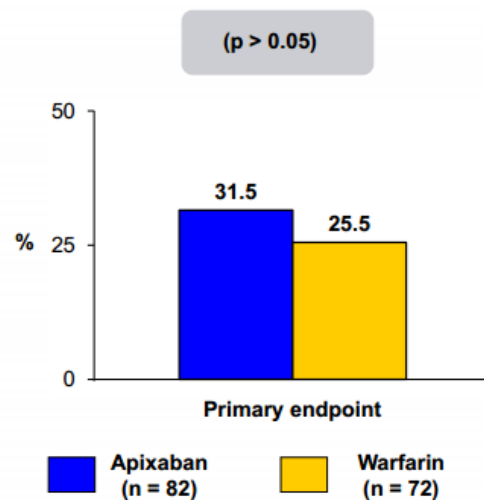
Shah M et al. Warfarin use and the risk for stroke and bleeding in patients with atrial fibrillation undergoing dialysis. *Circulation* 2014;129: 1196-1203.

Antithrombotic therapy in AF and CKD



RENAL-AF

Trial Description: Patients with AF and ESRD on hemodialysis were randomized in a 1:1 fashion to either apixaban 5 mg BID (29% on 2.5 mg BID) or warfarin with INR goal 2-3. Patients were followed for 1 year. Trial was stopped early due to loss of funding.



RESULTS

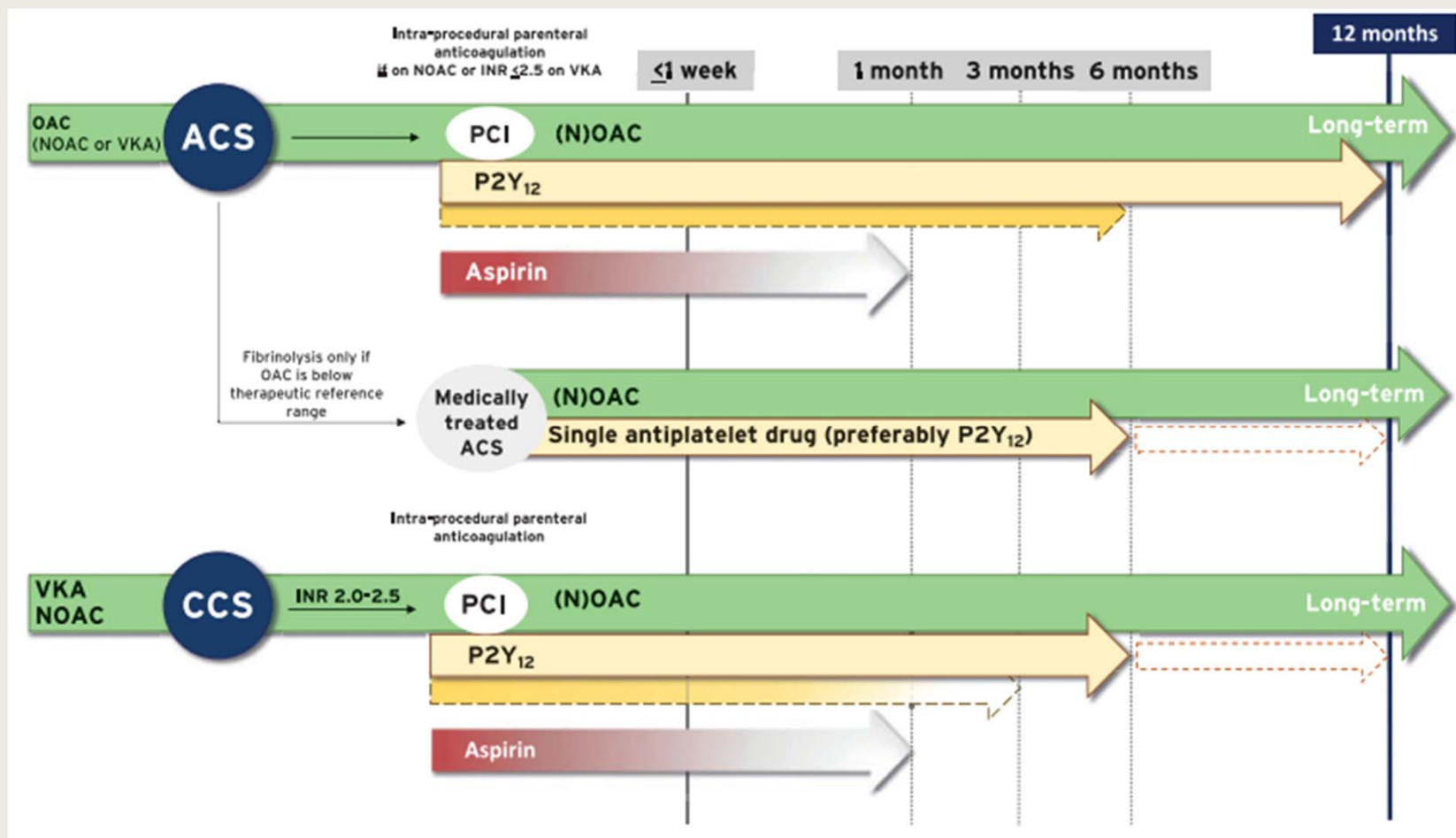
- Primary endpoint, clinically relevant nonmajor bleed: apixaban vs. warfarin: 31.5% vs. 25.5% (p > 0.05)
- Intracranial bleeding: 1.2% vs. 1.4%; GI bleeding: 2.4% vs. 8.3%
- ISTH major bleed: 8.5% vs. 9.7%; stroke: 2.4% vs. 2.8%; CV death: 11% vs. 5.6%

CONCLUSIONS

- Apixaban 5 mg BID results in similar rates of bleeding and strokes as warfarin among patients with ESRD on hemodialysis
- Time in therapeutic range with warfarin was only ~44%, with a large proportion of patients in the subtherapeutic range
- Remains unclear if lower apixaban dose (2.5 mg BID) and cessation of aspirin (used in ~40%) would have resulted in lower bleeding compared with warfarin

Presented by Dr. Sean D. Pokorney at AHA 2019

ACS, PCI and CCS in AF patients



ACS, PCI and CCS in AF patients

Recommendations for patients with AF and an ACS, PCI, or CCS¹⁰⁶⁸

General recommendations for patients with AF and an indication for concomitant antiplatelet therapy	Class ^a	Level ^b
In AF patients eligible for NOACs, <u>it is recommended to use a NOAC^c</u> in preference to a VKA in combination with antiplatelet therapy. ^{1079,1081}	I	A
In patients at high bleeding risk (HAS-BLED ≥ 3), <u>rivaroxaban 15 mg o.d.</u> should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk. ¹⁰⁸⁰	Ila	B
In patients at high bleeding risk (HAS-BLED ≥ 3), <u>dabigatran 110 mg b.i.d.</u> should be considered in preference to dabigatran 150 mg b.i.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk. ¹⁰⁷⁹	Ila	B
In AF patients with an indication for a VKA in combination with antiplatelet therapy, the VKA dosing should be carefully regulated with a target <u>INR of 2.0 - 2.5 and TTR > 70%</u> . ^{1094,1095,1104,1105}	Ila	B
Recommendations for AF patients with ACS		
In AF patients with ACS undergoing an uncomplicated PCI, <u>early cessation (≤ 1 week) of aspirin</u> and continuation of dual therapy with an OAC and a P2Y ₁₂ inhibitor (preferably clopidogrel) for up to <u>12 months</u> is recommended if the risk of stent thrombosis ^d is low or if concerns about bleeding risk ^e prevail over concerns about risk of stent thrombosis, ^d irrespective of the type of stent used. ^{1090,1092–1095}	I	A
Triple therapy with aspirin, clopidogrel, and an OAC ^f for longer than 1 week after an ACS should be considered when risk of stent thrombosis ^d outweighs the bleeding risk, ^e with the total duration (≤ 1 month) decided according to assessment of these risks, and the treatment plan should be clearly specified at hospital discharge.	Ila	C
Recommendations in AF patients with a CCS undergoing PCI		
After uncomplicated PCI, <u>early cessation (≤ 1 week) of aspirin</u> and continuation of dual therapy with OAC for up to <u>6 months</u> and clopidogrel is recommended if the risk of stent thrombosis ^d is low or if concerns about bleeding risk ^e prevail over concerns about risk of stent thrombosis, ^d irrespective of the type of stent used. ^{1076,1078–1081}	I	A
Triple therapy with aspirin, clopidogrel, and an OAC ^f for longer than 1 week should be considered when risk of stent thrombosis ^d outweighs the bleeding risk, ^e with the total duration (≤ 1 month) decided according to assessment of these risks, and the treatment plan should be clearly specified at hospital discharge.	Ila	C

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Atrial fibrillation and valvular heart disease

Recommendations for patients with valvular heart disease and AF

Recommendations	Class ^a	Level ^b
NOACs are contraindicated in patients with a prosthetic mechanical valve. ¹¹⁶⁵	III	B
Use of NOACs is not recommended in patients with AF and moderate-to-severe mitral stenosis.	III	C

Atrial fibrillation and valvular heart disease

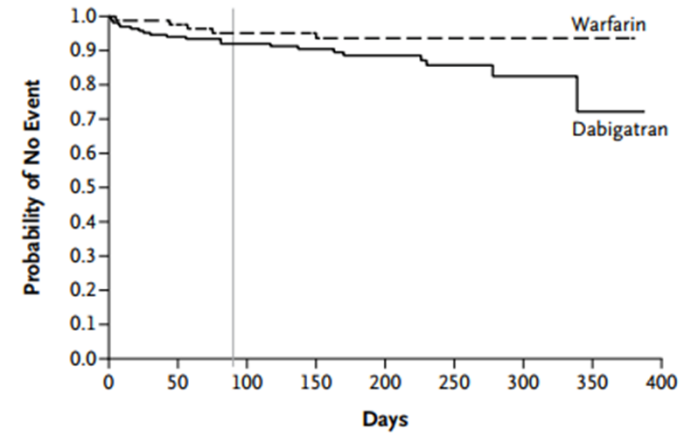
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dabigatran versus Warfarin in Patients with Mechanical Heart Valves

John W. Eikelboom, M.D., Stuart J. Connolly, M.D., Martina Brueckmann, M.D., Christopher B. Granger, M.D., Arie P. Kappetein, M.D., Ph.D., Michael J. Mack, M.D., Jon Blatchford, C.Stat., Kevin Devenny, B.Sc., Jeffrey Friedman, M.D., Kelly Guiver, M.Sc., Ruth Harper, Ph.D., Yasser Khder, M.D., Maximilian T. Lobmeyer, Ph.D., Hugo Maas, Ph.D., Jens-Uwe Voigt, M.D., Maarten L. Simoons, M.D., and Frans Van de Werf, M.D., Ph.D., for the RE-ALIGN Investigators*

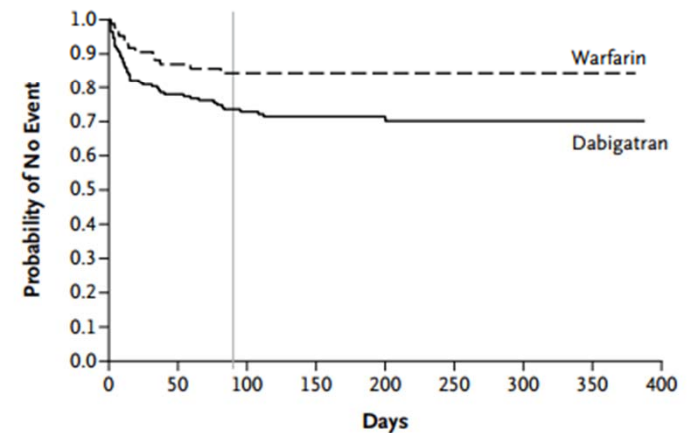
A First Thromboembolic Event



No. at Risk

Dabigatran	168	156	126	108	73	44	15	7
Warfarin	84	82	66	55	40	22	9	4

B First Bleeding Event



No. at Risk

Dabigatran	168	129	103	86	58	32	11	6
Warfarin	84	73	56	50	38	22	11	4

Figure 1. Kaplan–Meier Analysis of Event-free Survival.

Panel A shows event-free survival from the first thromboembolic event (i.e., stroke, systemic embolism, transient ischemic attack, or myocardial infarction) or death ($P=0.24$). Panel B shows event-free survival from the first bleeding event ($P=0.01$). In each panel, the vertical line indicates the start of the RE-ALIGN extension trial (RE-ALIGN-EX) and the P value was calculated with the use of the Wald chi-square test.

Atrial fibrillation and valvular heart disease

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rivaroxaban in Patients with Atrial Fibrillation and a Bioprosthetic Mitral Valve

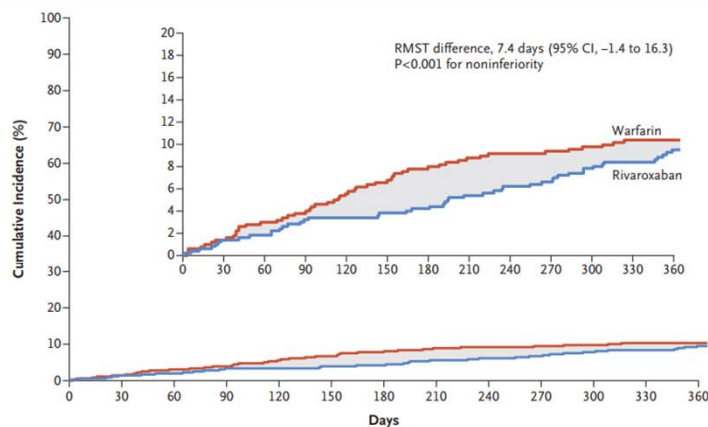


Figure 1. Kaplan–Meier Analysis of the Primary Outcome.

Shown is the primary outcome (death, major cardiovascular events, or major bleeding) in the rivaroxaban group and the warfarin group, as calculated according to the restricted mean survival time (RMST) method. The inset shows the same data on an expanded y axis.

Table 2. Secondary Efficacy Outcomes.*

Secondary Outcome	Rivaroxaban (N = 500)		Warfarin (N = 505)		Hazard Ratio (95% CI)†
	no. (%)	rate per 100 patient-yr	no. (%)	rate per 100 patient-yr	
Death from cardiovascular causes or thromboembolic events — no. (%)‡	17 (3.4)	3.53	26 (5.1)	5.44	0.65 (0.35–1.20)
Stroke					
Any	3 (0.6)	0.62	12 (2.4)	2.50	0.25 (0.07–0.88)
Nonfatal	2 (0.4)	0.41	10 (2.0)	2.09	0.20 (0.04–0.91)
Fatal	1 (0.2)	0.20	2 (0.4)	0.39	0.50 (0.05–5.50)
Hemorrhagic	0	0	5 (1.0)	1.03	NA
Ischemic	3 (0.6)	0.62	7 (1.4)	1.45	0.43 (0.11–1.66)
Transient ischemic attack	0	0	1 (0.2)	0.21	NA
Death					
Any	20 (4.0)	4.12	20 (4.0)	4.11	1.01 (0.54–1.87)
From cardiovascular causes	11 (2.2)	2.27	13 (2.6)	2.67	0.85 (0.38–1.90)
Valve thrombosis	5 (1.0)	1.04	3 (0.6)	0.62	1.68 (0.40–7.01)
Non-CNS systemic embolism	0	0	1 (0.2)	0.21	NA
Hospitalization for heart failure	22 (4.4)	4.43	19 (3.8)	3.78	1.15 (0.62–2.13)

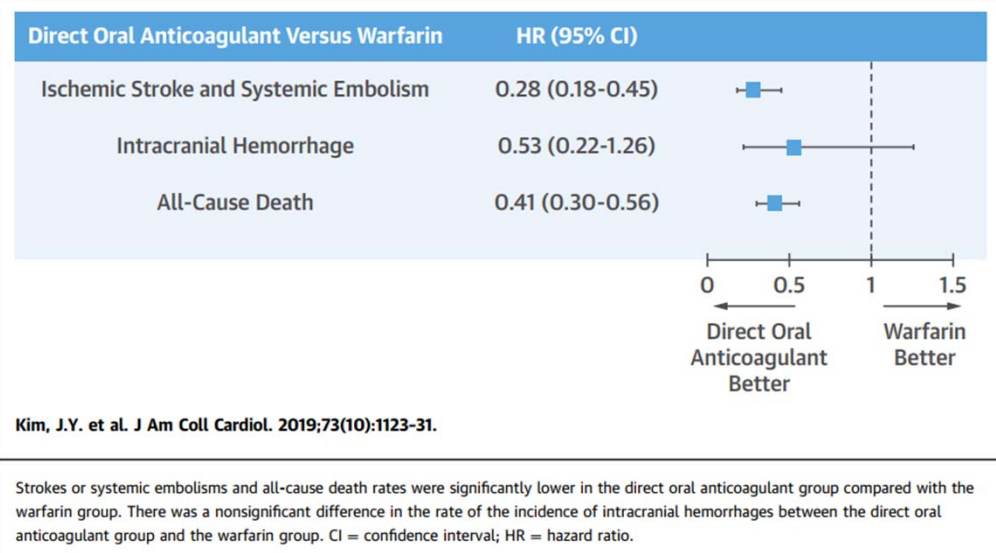
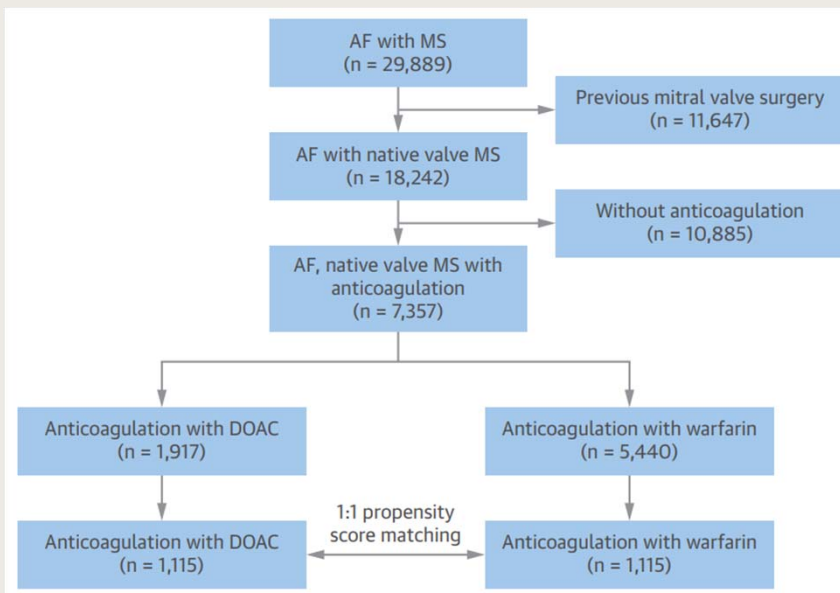
Table 3. Bleeding End Points.*

Bleeding Event	Rivaroxaban (N = 500)		Warfarin (N = 505)		Hazard Ratio (95% CI)†
	no. (%)	rate per 100 patient-yr	no. (%)	rate per 100 patient-yr	
Any bleeding	65 (13.0)	14.71	78 (15.4)	17.99	0.83 (0.59–1.15)
Major bleeding	7 (1.4)	1.46	13 (2.6)	2.72	0.54 (0.21–1.35)
Intracranial bleeding	0	0	5 (1.0)	1.03	NA
Fatal bleeding	0	0	2 (0.4)	0.41	NA
Clinically relevant nonmajor bleeding	24 (4.8)	5.12	23 (4.6)	4.87	1.05 (0.60–1.87)
Minor bleeding	37 (7.4)	8.03	49 (9.7)	10.84	0.75 (0.49–1.15)

Atrial fibrillation and valvular heart disease

Outcomes of Direct Oral Anticoagulants in Patients With Mitral Stenosis

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Summary

- Stroke risk evaluation – CHA2DS2-VASc score
- Bleeding risk assessment – HAS-BLED score
- Low risk(CV score 1 or 2 (woman) patient
- CKD / Hemodialysis patients
- ACS, PCI and CCS in AF patients – early cessation of aspirin
- Valvular AF patients

