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2012 focussed update of the ESC Guidelines for the Management of Atrial Fibrillation

An update of the 2010 ESC Guidelines for the Management of Atrial Fibrillation

Developed with the special contribution of the European Heart Rhythm Association (EHRA)

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Management of Atrial Fibrillation

Focus of 2012 Update

- Anticoagulation risk stratification
- Use of novel oral anticoagulants (NOACs)
- Left atrial appendage occlusion/excision
- Pharmacological cardioversion (vernakalant)
- Oral antiarrhythmic therapy (dronedarone, and short term therapy)
- Left atrial catheter ablation

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$CHADS_2$ score and stroke rate

$CHADS_2$ score	Patients (n = 1733)	Adjuste stroke rate (%/y)* (95% confidence interval)
0	120	1.9 (1.2 - 3.0)
1	463	2.8 (2.0 - 3.8)
2	523	4.0 (3.1 - 5.1)
3	337	5.9 (4.6 - 7.3)
4	220	8.5 (6.3 - 11.1)
5	65	12.5 (8.2 - 17.5)
6	5	18.2 (10.5 - 27.4)

*The adjusted stroke rate was derived from the multivariable analysis assuming no aspirin usage; these stroke rates are based on data from a cohort of hospitalised AF patients, published in 2001, with low numbers in those with a **$CHADS_2$ score** of 5 and 6 to allow an accurate judgement of the risk in these patients. Given that stroke rates are declining overall, actual stroke rates in contemporary non-hospitalised cohorts may also vary from these estimates. Adapted from Gage BF et al.

AF = atrial fibrillation; $CHADS_2$ = cardiac failure, hypertension, age, diabetes, stroke (doubled).

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Risk factors for stroke and thrombo-embolism in non-valvular AF

Major risk factors
Previous stroke
TIA or systemic embolism
Age ≥ 75 years

Clinically relevant non-major risk factors
CHF or moderate to severe LV systolic dysfunction [e.g. LV EF ≤ 40%]
Hypertension
Diabetes mellitus
Age 65-74 years
Female sex
Vascular disease

AF= atrial fibrillation; EF = ejection fraction (as documented by echocardiography, radionuclide ventriculography, cardiac catheterization, cardiac magnetic resonance imaging, etc.); LV = left ventricular; TIA = transient ischaemic attack.

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Risk factor-based point-based scoring system - CHA_2DS_2-VASc

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥ 75 ans	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease*	1
Age 65-74	1
Sex category [i.e. femal sex]	1
Maximum score	**9**

*Prior myocardial infarction, peripheral artery disease, aortic plaque. Actual rates of stroke in contemporary cohorts may vary from these estimates.

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Adjusted stroke rate according to CHA_2DS_2-VASc score

CHA_2DS_2-VASc score	Patients (n = 7329)	Adjusted stroke rate (%/y)
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%

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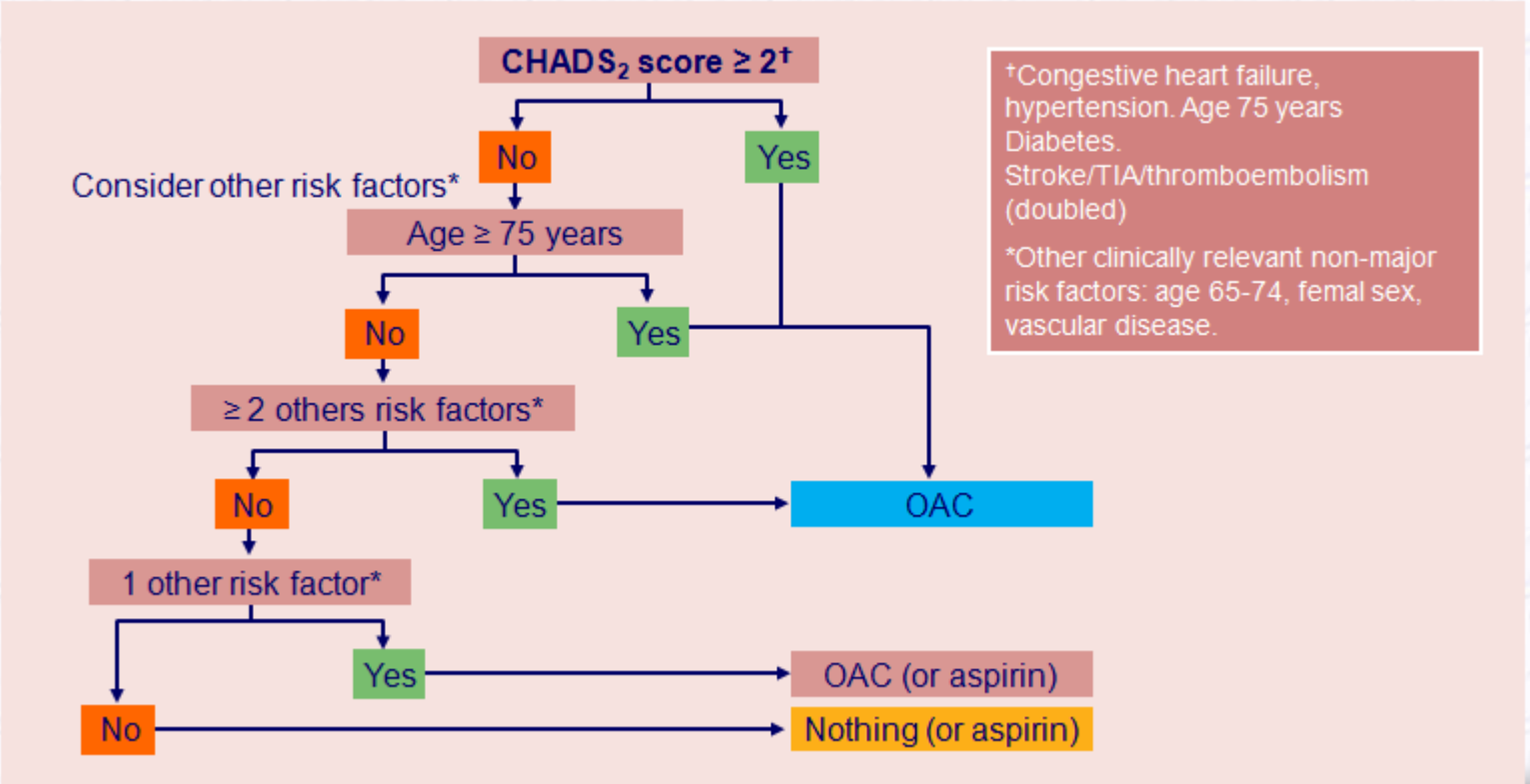
Use of oral anticoagulation for stroke prevention in AF



AF = atrial fibrillation; OAC = oral anticoagulant; TIA = transient ischaemic attack.

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Approach to thromboprophylaxis in AF

Risk category	CHA_2DS_2-VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥ 2 'clinically relevant non-major' risk factors	≥ 2	OAC
One 'clinically relevant non-major' risk factor	1	Either OAC 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.

AF = atrial fibrillation; CHA_2DS_2-VASc = cardiac failure, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled)-vascular disease, age 65–74 and sex category (female); INR = international normalized ratio; OAC = oral anticoagulation, such as a vitamin K antagonist (VKA) adjusted to an intensity range of INR 2.0–3.0 (target 2.5).

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The HAS-BLED bleeding risk score

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

*Hypertension is defined as systolic blood pressure > 160 mmHg.

INR = international normalized ratio.

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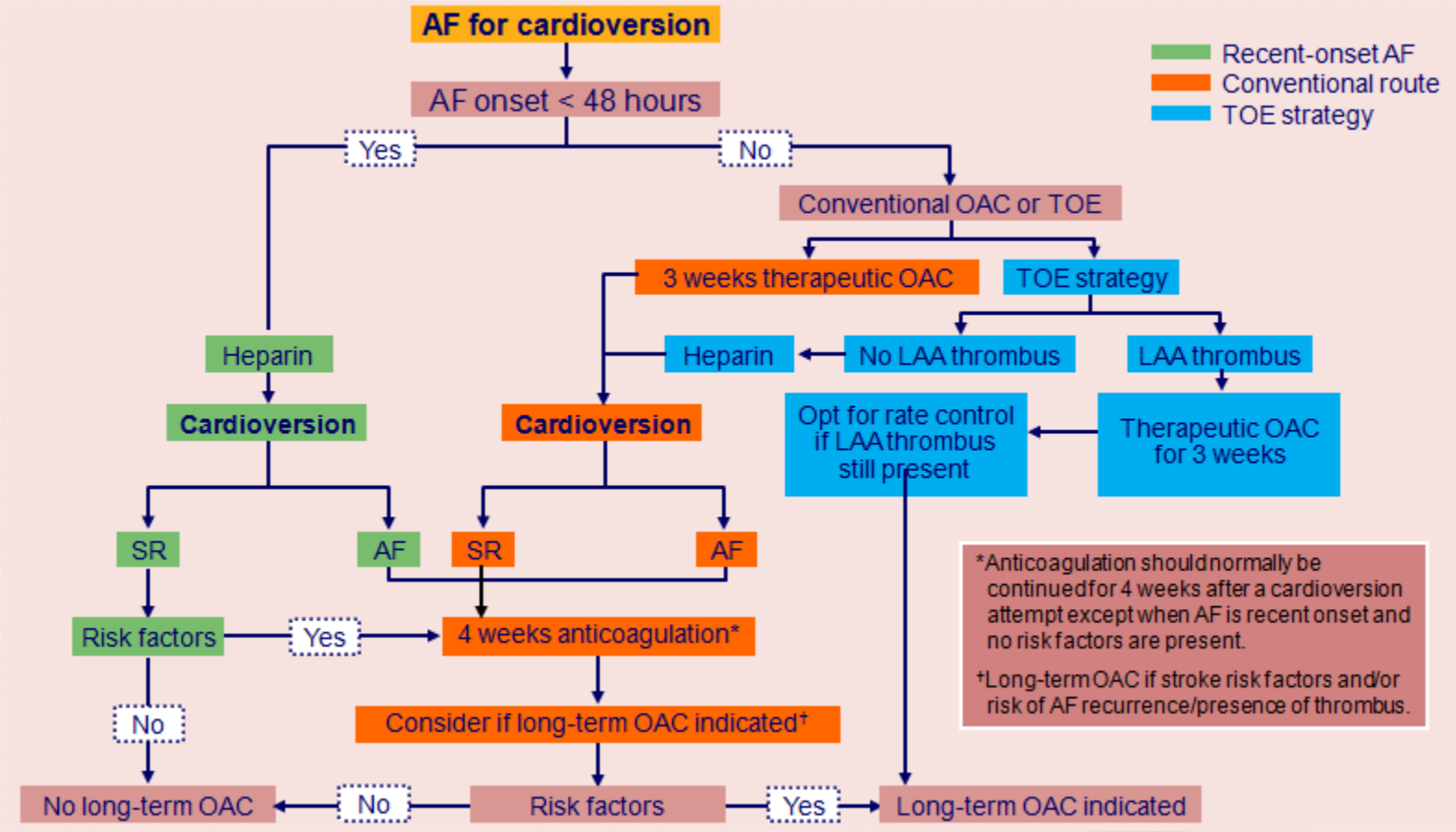
Cardioversion, TOE and anticoagulation



AF = atrial fibrillation; DCC = direct current cardioversion; LA = left atrium; LAA = left atrial appendage; OAC = oral anticoagulant; SR= sinus rhythm; TOE= transoesophageal echocardiography.

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Anticoagulation - General

Recommendations for prevention of thromboembolism in non-valvular AF - general		
Recommendations	**Class**	**Level**
Antithrombotic therapy to prevent thromboembolism is recommended for all patients with AF, except in those patients (both male and female) who are at low risk (aged <65 years and lone AF), or with contraindications.	I	A
The choice of antithrombotic therapy should be based upon the absolute risks of stroke/thromboembolism and bleeding and the net clinical benefit for a given patient.	I	A
The CHA_2DS_2-VASc score is recommended as a means of assessing stroke risk in non-valvular AF.	I	A
Female patients who are aged <65 and have lone AF (but still have a CHA_2DS_2-VASc score of 1 by virtue of their gender) are low risk and no antithrombotic therapy should be considered.	IIa	B

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Anticoagulation – General (Cont..)

Recommendations	Class	Level
In patients with a CHA_2DS_2-VASc score of 0 (i.e., aged <65 years with lone AF) who are at low risk, with none of the risk factors, no antithrombotic therapy is recommended.	I	B
In patients with a CHA_2DS_2-VASc score ≥2, OAC therapy with: • adjusted-dose VKA (INR 2–3); or • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)[d] …. is recommended, unless contraindicated.	I	A
In patients with a CHA_2DS_2-VASc score of 1, OAC therapy with: • adjusted-dose VKA (INR 2–3); or • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)[d] …. should be considered, based upon an assessment of the risk of bleeding complications and patient preferences.	IIa	A

[d] = pending EMA/FDA approval – prescribing information is awaited

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Anticoagulation - General

Recommendations for prevention of thromboembolism in non-valvular AF - general		
Recommendations	**Class**	**Level**
When patients refuse the use of any OAC (whether VKAs or NOACs), antiplatelet therapy should be considered, using combination therapy with aspirin 75–100 mg plus clopidogrel 75 mg daily (where there is a low risk of bleeding) or – less effectively – aspirin 75–325 mg daily.	**IIa**	**B**

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Anticoagulation - NOACs

Recommendations for prevention of thromboembolism in non-valvular AF - NOACs		
Recommendations	**Class**	**Level**
When adjusted-dose VKA (INR 2–3) cannot be used in a patient with AF where an OAC is recommended, due to difficulties in keeping within therapeutic anticoagulation, experiencing side effects of VKAs, or inability to attend or undertake INR monitoring, one of the NOACs, either: • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)[d] … is recommended.	I	B
Where OAC is recommended, one of the NOACs, either: • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)[d] … should be considered rather than adjusted-dose VKA (INR 2–3) for most patients with non-valvular AF, based on their net clinical benefit.	IIa	A

[d]Apixaban (pending approval EMA and FDA approval): prescribing information is awaited.

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Recommendations	Class	Level
Where dabigatran is prescribed, a dose of 150 mg b.i.d. should be considered for most patients in preference to 110 mg b.i.d., with the latter dose recommended in: • elderly patients, age ≥ 80 • concomitant use of interacting drugs (e.g. verapamil) • high bleeding risk (HAS-BLED score ≥3) • moderate renal impairment (CrCl 30–49 mL/min).	IIa	B
Where rivaroxaban is being considered, a dose of 20 mg o.d. should be considered for most patients in preference to 15 mg o.d., with the latter dose recommended in: • high bleeding risk (HAS-BLED score ≥3) • moderate renal impairment (CrCl 30–49 mL/min).	IIa	C
Baseline and subsequent regular assessment of renal function (by CrCl) is recommended in patients following initiation of any NOAC, which should be done annually but more frequently in those with moderate renal impairment where CrCl should be assessed 2–3 times per year.	IIa	B
NOACs (dabigatran, rivaroxaban, and apixaban) are not recommended in patients with severe renal impairment (CrCl <30 mL/min).	III	A

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Anticoagulation - Bleeding

Recommendations for prevention of thromboembolism in non-valvular AF - bleeding		
Recommendations	**Class**	**Level**
Assessment of the risk of bleeding is recommended when prescribing antithrombotic therapy (whether with VKA, NOAC, aspirin/clopidogrel, or aspirin).	I	A
The HAS-BLED score should be considered as a calculation to assess bleeding risk, whereby a score ≥3 indicates 'high risk' and some caution and regular review is needed, following the initiation of antithrombotic therapy, whether with OAC or antiplatelet therapy (LoE = A). Correctable risk factors for bleeding [e.g. uncontrolled blood pressure, labile INRs if the patient was on a VKA, concomitant drugs (aspirin, NSAIDs, etc.), alcohol, etc.] should be addressed (LoE = B). Use of the HAS-BLED score should be used to identify modifiable bleeding risks that need to be addressed, but should not be used on its own to exclude patients from OAC therapy (LoE = B).	IIa	A / B
The risk of major bleeding with antiplatelet therapy (with aspirin–clopidogrel combination therapy and – especially in the elderly – also with aspirin monotherapy) should be considered as being similar to OAC.	IIa	B

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Anticoagulation – Peri-cardioversion

Recommendations for prevention of thromboembolism in non-valvular AF – peri-cardioversion		
Recommendations	**Class**	**Level**
For patients with AF of ≥48 h duration, or when the duration of AF is unknown, OAC therapy (e.g. VKA with INR 2-3 or dabigatran) is recommended for ≥3 weeks prior to and for ≥4 weeks after cardioversion, regardless of the method (electrical or oral/i.v. pharmacological).	I	B
In patients with risk factors for stroke or AF recurrence, OAC therapy, whether with dose-adjusted VKA (INR 2-3) or a NOAC, should be continued lifelong irrespective of the apparent maintenance of sinus rhythm following cardioversion.	I	B

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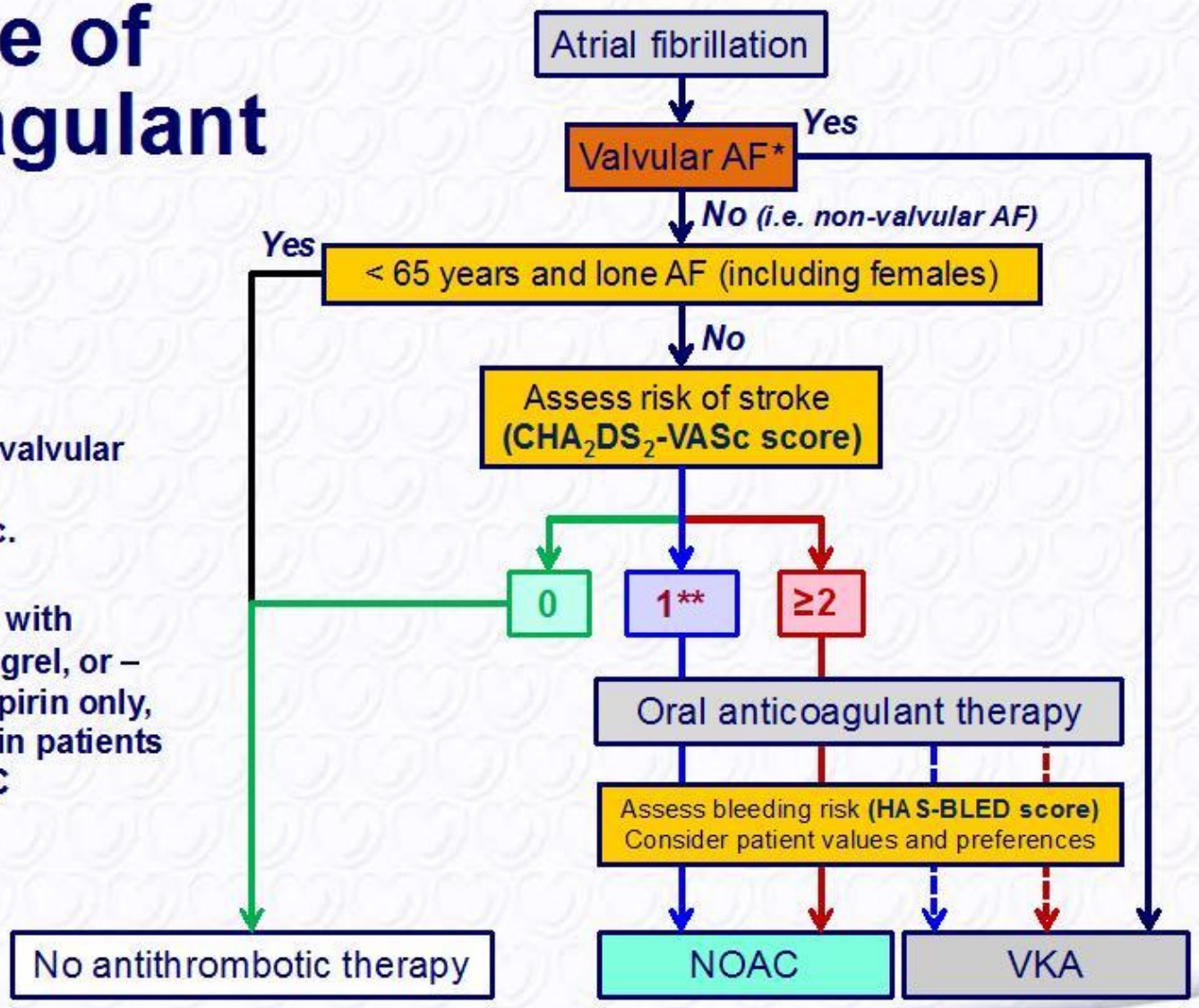
Choice of Anti-coagulant



- Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.

** Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any OAC

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LAA Closure/Occlusion/Excision

Recommendations for LAA closure/occlusion/excision		
Recommendations	**Class**	**Level**
Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.	IIb	B
Surgical excision of the LAA may be considered in patients undergoing open heart surgery.	IIb	C

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2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

Developed in Collaboration With the Society of Thoracic Surgeons

	Vitamin K Antagonists	FXa Inhibitors			Direct Thrombin Inhibitors	
	Warfarin	Rivaroxaban	Apixaban	Edoxaban	Dabigatran	Ximelagatran
Mode of action	Inhibition of hepatic synthesis of vitamin K-dependent coagulation factors	Direct inhibition of FXa	Direct inhibition of FXa	Direct inhibition of FXa	Direct inhibition of clot-bound and free thrombin (FIIa)	Direct inhibition of thrombin (FII)
Time to peak effect (hours)	72–96	0.5–3	3	1.5	2–3	1.6–1.9
Half-life hours	20–60	5–9 (9–13 in elderly)	8–13	9–11	14–17	4–5
Bioavailability %	100	80	66	50	6.5	20
Recommended therapeutic dose and frequency	Adjusted-dose based on INR; once daily	20 mg; once daily	5 mg; twice daily	30 mg or 60 mg; once daily	150 mg; twice daily	Not available in the U.S.
Monitoring	Required using INR	Not required In case of hemorrhage or renal impairment, FXa-dependent assays may be used[47]	Not required due to predictable pharmacokinetics In hemorrhage or renal impairment, FXa-dependent assays may be used[47]	Not required due to predictable pharmacokinetics	Not required except in subgroups such as patients with renal impairment [48] Ecarin clotting time can be used if needed[49]	Not required
Renal excretion[39]	1% excreted unchanged in the urine	66% renal elimination	50% renal elimination	45% renal elimination	80% renal elimination	Main route of elimination
Interactions	CYP2C9, CYP1A2, CYP3A4 inhibitors Dietary vitamin K[50]	Potent CYP3A4 inhibitors and P-glycoprotein inhibitors[50]	Potent CYP3A4 inhibitors[50]	P-glycoprotein inhibitors[43]	P-glycoprotein inhibitors Proton pump inhibitors[38]	NA
Drug reversal	Vitamin K, fresh frozen plasma, prothrombin complex concentrate, recombinant FVIIa[51]	FVIIa partially reverses rivaroxaban anticoagulant effect[52] Prothrombin complex concentrate completely reverses its anticoagulant effect[53]	No available antidote	No available antidote	It is partially dialyzable[54]	NA
Precautions	Severe active bleeding, pregnancy, breast feeding, documented hypersensitivity[55] Severe renal impairment (glomerular filtration rate <30 mL/min/1.73m^2)[39]	Severe active bleeding; severe renal impairment[39]	Severe active bleeding; severe renal impairment	Severe active bleeding; severe renal impairment	Severe active bleeding, severe renal impairment[39]	NA

Thromboembolic Risk and Treatment

Class I

1. In patients with AF, antithrombotic therapy should be individualized based on shared decision making after discussion of the absolute and RRs of stroke and bleeding, and the patient's values and preferences. *(Level of Evidence: C)*

2. Selection of antithrombotic therapy should be based on the risk of thromboembolism irrespective of whether the AF pattern is paroxysmal, persistent, or permanent (64–67). *(Level of Evidence: B)*

Class I

3. In patients with nonvalvular AF, the CHA2DS2-VASc score is recommended for assessment of stroke risk (68-70). *(Level of Evidence: B)*

4. For patients with AF who have mechanical heart valves, warfarin is recommended and the target international normalized ratio (INR) intensity (2.0 to 3.0 or 2.5 to 3.5) should be based on the type and location of the prosthesis (71-73). *(Level of Evidence: B)*

Class I

5. For patients with nonvalvular AF with prior stroke, transient ischemic attack (TIA), or a CHA2DS2-VASc score of 2 or greater, oral anticoagulants are recommended. Options include:

warfarin (INR 2.0 to 3.0) *(Level of Evidence: A), dabigatran (Level of Evidence: B),* rivaroxaban *(Level of Evidence: B), or apixaban . (Level of Evidence: B)*

Class I

6. Among patients treated with warfarin, the INR should be determined at least weekly during initiation of antithrombotic therapy and at least monthly when anticoagulation (INR in range) is stable (77-79). ***(Level of Evidence: A)***

7. For patients with nonvalvular AF unable to maintain a therapeutic INR level with warfarin, use of a direct thrombin or factor Xa inhibitor (dabigatran, rivaroxaban, or apixaban) is recommended. ***(Level of Evidence: C)***

Class I

8. Re-evaluation of the need for and choice of antithrombotic therapy at periodic intervals is recommended to reassess stroke and bleeding risks. *(Level of Evidence: C)*
9. Bridging therapy with unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) is recommended for patients with AF and a mechanical heart valve undergoing procedures that require interruption of warfarin. Decisions regarding bridging therapy should balance the risks of stroke and bleeding. *(Level of Evidence: C)*

Class I

10. For patients with AF without mechanical heart valves who require interruption of warfarin or newer anticoagulants for procedures, decisions about bridging therapy (LMWH or UFH) should balance the risks of stroke and bleeding and the duration of time a patient will not be anticoagulated. ***(Level of Evidence: C)***

Class I

11. Renal function should be evaluated prior to initiation of direct thrombin or factor Xa inhibitors and should be re-evaluated when clinically indicated and at least annually (80-82). ***(Level of Evidence: B)***

12. For patients with atrial flutter, antithrombotic therapy is recommended according to the same risk profile used for AF. ***(Level of Evidence: C)***

Class IIa

1. For patients with nonvalvular AF and a CHA2DS2-VASc score of 0, it is reasonable to omit antithrombotic therapy . *(Level of Evidence: B)*

2. For patients with non valvular AF with a CHA2DS2-VASc score of 2 or greater and who have end stage CKD (creatinine clearance [CrCl] <15 mL/min) or are on hemodialysis, it is reasonable to prescribe warfarin (INR 2.0 to 3.0) for oral anticoagulation . *(Level of Evidence: B)*

Class IIb

1. For patients with nonvalvular AF and a CHA2DS2-VASc score of 1, no antithrombotic therapy or treatment with an oral anticoagulant or aspirin may be considered. *(Level of Evidence: C)*

2. For patients with nonvalvular AF and moderate-to-severe CKD with CHA2DS2-VASc scores of 2 or greater, treatment with reduced doses of direct thrombin or factor Xa inhibitors may be considered (e.g., dabigatran, rivaroxaban, or apixaban), but safety and efficacy have not been established. *(Level of Evidence: C)*

Class IIb

3. In patients with AF undergoing percutaneous coronary intervention,* bare-metal stents may be considered to minimize the required duration of dual antiplatelet therapy*. *Anticoagulation may* be interrupted at the time of the procedure to reduce the risk of bleeding at the site of peripheral arterial puncture. *(Level of Evidence: C)*

4. Following coronary revascularization (percutaneous or surgical) in patients with AF and a CHA2DS2-VASc score of 2 or greater, it may be reasonable to use clopidogrel (75 mg once daily) concurrently with oral anticoagulants but without aspirin . *(Level of Evidence: B)*

Class III: No Benefit

1. The direct thrombin inhibitor, dabigatran, and the factor Xa inhibitor, rivaroxaban, are not recommended in patients with AF and end-stage CKD or on hemodialysis because of the lack of evidence from clinical trials regarding the balance of risks and benefits . *(Level of Evidence: C)*

Class III: Harm

1. The direct thrombin inhibitor, dabigatran, should not be used in patients with AF and a mechanical heart valve (87). *(Level of Evidence: B)*

Considerations in Selecting Anticoagulants

For patients with CKD, dose modifications of the new agents are available ; however, for those with severe or end-stage CKD, warfarin remains the anticoagulant of choice, as there are no or very limited data for these patients.

Among patients on hemodialysis, warfarin has been used with acceptable risks of hemorrhage

Dose Selection of Oral Anticoagulant Options for Patients with Nonvalvular AF and CKD

Renal Function	Warfarin (92)	Dabigatran† (74)	Rivaroxaban† (75)	Apixaban† (76)
Normal/Mild Impairment	Dose adjusted for INR 2.0–3.0	150 mg BID (CrCl >30 mL/min)	20 mg QD with the evening meal (CrCl >50 mL/min)	5.0 or 2.5 mg BID‡
Moderate Impairment	Dose adjusted for INR 2.0–3.0	150 mg BID or 75 mg BID§ (CrCl >30 mL/min)	15 mg QD with the evening meal (CrCl 30–50 mL/min)	5.0 or 2.5 mg BID‡
Severe Impairment	Dose adjusted for INR 2.0–3.0‖	75 mg BID§ (CrCl 15–30 mL/min)	15 mg QD with the evening meal (CrCl 15–30 mL/min)	No recommendation, See section 4.2.2.2.¶
End-Stage CKD Not on Dialysis	Dose adjusted for INR 2.0–3.0‖	Not recommended¶ (CrCl <15 mL/min)	Not recommended¶ (CrCl <15 mL/min)	No recommendation, See section 4.2.2.2.¶
End-Stage CKD on Dialysis	Dose adjusted for INR 2.0–3.0‖	Not recommended¶ (CrCl <15 mL/min)	Not recommended¶ (CrCl <15 mL/min)	No recommendation, See section 4.2.2.2.¶#

Cardiac Surgery—LAA Occlusion/Excision: Recommendation

Class IIb

1. Surgical excision of the LAA may be considered in patients undergoing cardiac surgery. *(Level of Evidence: C)*

THANK YOU