# Βασικές αρχές διαχείρισης συννοσηροτήτων σε ασθενείς με χρόνια φλεγμονώδη νοσήματα
# **Αντιθρομβωτική αγωγή**

# Basic principles of antithrombotic therapy in patients with chronic inflammatory diseases

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Conflicts of interest: (-)

# Indications of anticoagulation treatment

1. **AF**
2. **Deep vein thrombosis (DVT)**
3. Pulmonary embolism
4. Mechanical valves
5. Antiphospholipid syndrome

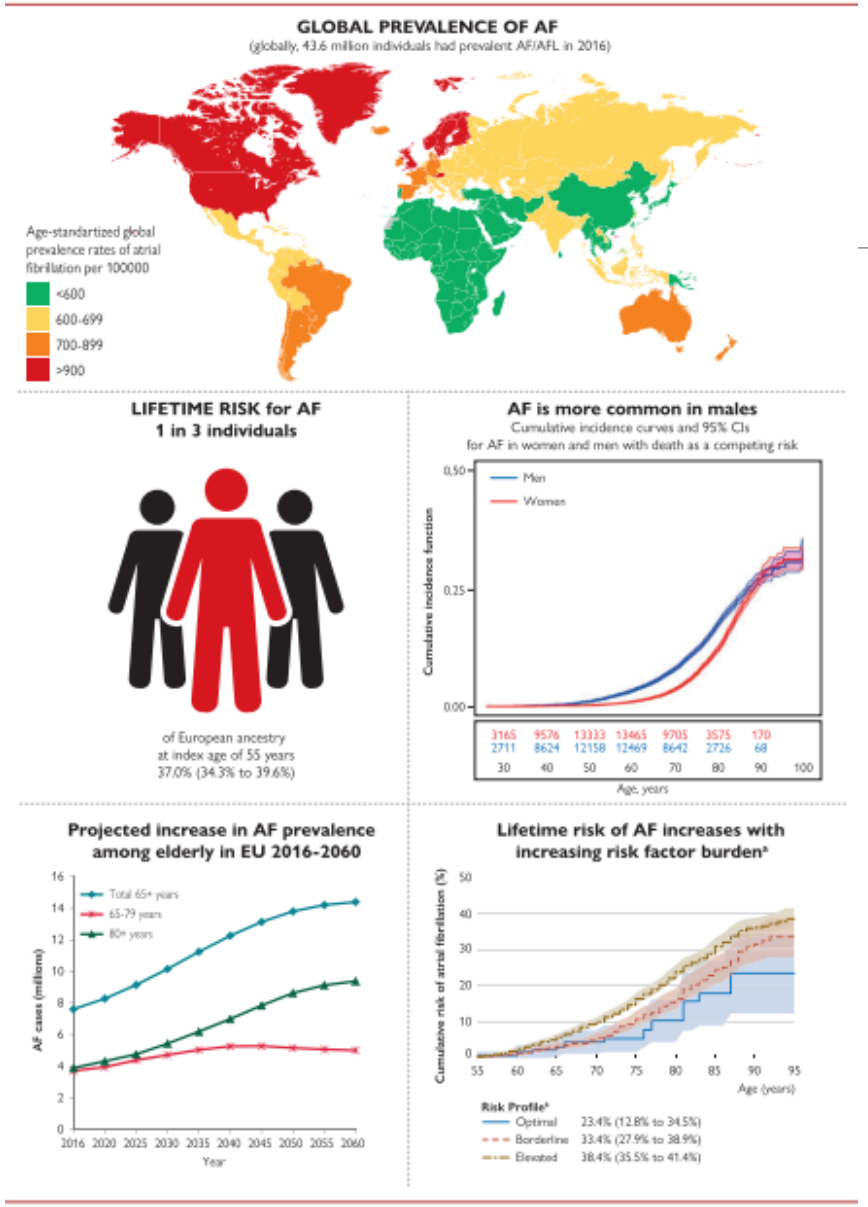
# Available anticoagulants

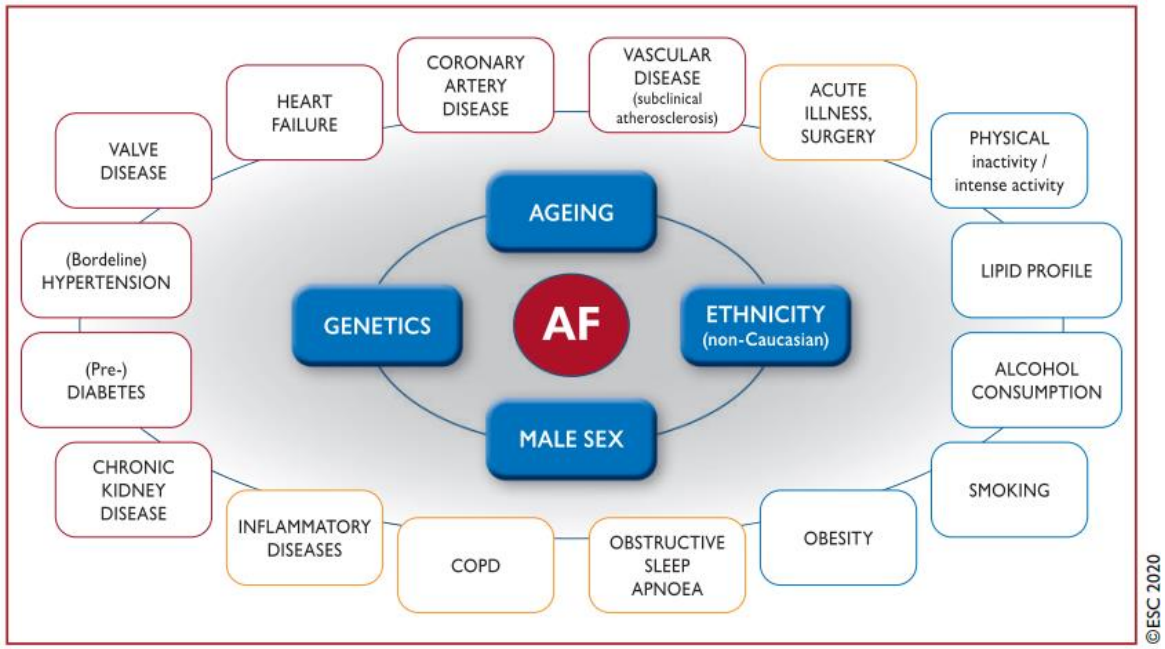
**Direct oral anticoagulants (DOACs)**

Vitamin K antagonists (VKAs)

Heparins

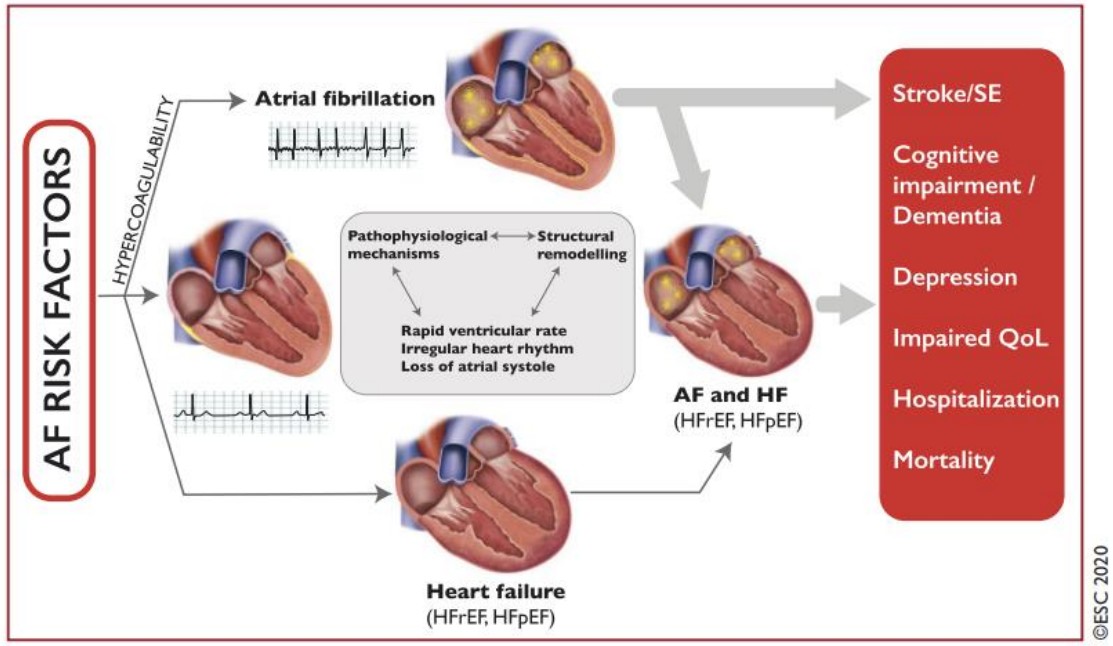
Fondaparinux




EHJ 2020, doi:10.1093/eurheartj/ehaa612

| AF-Related Outcome | Frequency in AF | Mechanism(s) |
|---|---|---|
| Death | 1.5 - 3.5 fold increase | Excess mortality related to:<br>• HF, comorbidities<br>• Stroke |
| Stroke | 20-30% of all ischaemic strokes, 10% of cryptogenic strokes | • Cardioembolic, or<br>• Related to comorbid vascular atheroma |
| LV dysfunction / Heart failure | In 20-30% of AF patients | • Excessive ventricular rate<br>• Irregular ventricular contractions<br>• A primary underlying cause of AF |
| Cognitive decline / Vascular dementia | HR 1.4 / 1.6 (irrespective of stroke history) | • Brain white matter lesions, inflammation,<br>• Hypoperfusion,<br>• Micro-embolism |
| Depression | Depression in 16-20% (even suicidal ideation) | • Severe symptoms and decreased QoL<br>• Drug side effects |
| Impaired quality of life | >60% of patients | • Related to AF burden, comorbidities, psychological functioning and medication<br>• Distressed personality type |
| Hospitalizations | 10-40% annual hospitalization rate | • AF management, related to HF, MI or AF related symptoms<br>• Treatment-associated complications |




EHJ 2020, doi:10.1093/eurheartj/ehaa612

ESC European Society of Cardiology
European Heart Journal (2024) **45**, 3314–3414
https://doi.org/10.1093/eurheartj/ehae176

ESC GUIDELINES

# 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

# $CHADS_2$ ,$CHA_2DS_2$-VASc and $CHA_2DS_2$-VA score

## $CHADS_2$ -> $CHA_2DS_2VASc$

| CHADS2 Risk | Score |
|---|---|
| CHF | 1 |
| Hypertension | 1 |
| Age > 75 | 1 |
| Diabetes | 1 |
| Stroke or TIA | 2 |

*From ESC AF Guidelines http://escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf*

| CHA2DS2-VASc Risk | Score |
|---|---|
| CHF or LVEF ≤ 40% | 1 |
| Hypertension | 1 |
| Age ≥75 | 2 |
| Diabetes | 1 |
| Stroke/TIA/ Thromboembolism | 2 |
| Vascular Disease | 1 |
| Age 65 - 74 | 1 |
| Female | 1 |

## $CHA_2DS_2$-VA

| CHA2DS2-VASc Risk | Score |
|---|---|
| CHF or LVEF ≤ 40% | 1 |
| Hypertension | 1 |
| Age ≥75 | 2 |
| Diabetes | 1 |
| Stroke/TIA/ Thromboembolism | 2 |
| Vascular Disease | 1 |
| Age 65 - 74 | 1 |

**Recommendation Table 6 — Recommendations to assess and manage thromboembolic risk in AF (see also Evidence Table 6)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.[239,240] | I | A |
| A $CHA_2DS_2$-VA score of 2 or more is recommended as an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation. | I | C |
| Oral anticoagulation is recommended in all patients with AF and hypertrophic cardiomyopathy or cardiac amyloidosis, regardless of $CHA_2DS_2$-VA score, to prevent ischaemic stroke and thromboembolism.[270–276] | I | B |
| Individualized reassessment of thromboembolic risk is recommended at periodic intervals in patients with AF to ensure anticoagulation is started in appropriate patients.[277–280] | I | B |
| Antiplatelet therapy is not recommended as an alternative to anticoagulation in patients with AF to prevent ischaemic stroke and thromboembolism.[242,283] | III | A |
| Using the temporal pattern of clinical AF (paroxysmal, persistent, or permanent) is not recommended to determine the need for oral anticoagulation.[284,285] | III | B |

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| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Direct oral anticoagulants are recommended in preference to VKAs to prevent ischaemic stroke and thromboembolism, except in patients with mechanical heart valves or moderate-to-severe mitral stenosis.[25–28,292–294] | I | A |
| A target INR of 2.0–3.0 is recommended for patients with AF prescribed a VKA for stroke prevention to ensure safety and effectiveness.[295–298] | I | B |
| Switching to a DOAC is recommended for eligible patients that have failed to maintain an adequate time in therapeutic range on a VKA (TTR <70%) to prevent thromboembolism and intracranial haemorrhage.[299–303] | I | B |

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Maintaining VKA treatment rather than switching to a DOAC may be considered in patients aged ≥75 years on clinically stable therapeutic VKA with polypharmacy to prevent excess bleeding risk.[309] | IIb | B |

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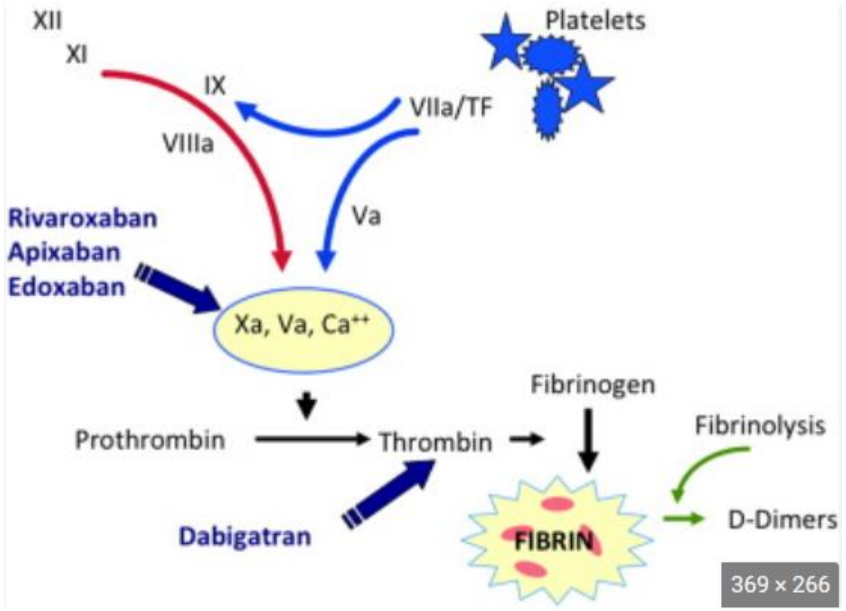
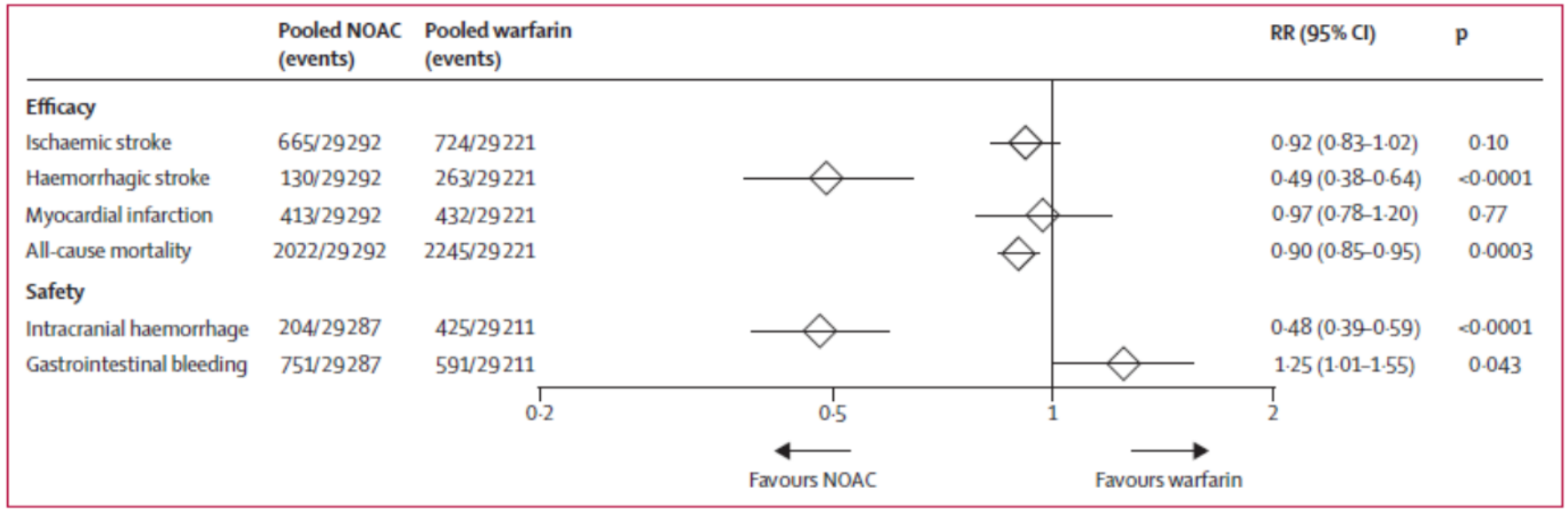
# Choosing among different anticoagulants




| | VKA | NOACs |
|---|---|---|
| • Oral | ✅ | ✅ |
| • Reversible | ✅ | ✅ |
| • No significant food/drug interactions | ❌ | ✅ |
| • Predictable response | ❌ | ✅ |
| • No requirement for coagulation dosing | ❌ | ✅ |
| • Fixed dosing | ❌ | ✅ |
| • Cost | *Low* | *High* |

# Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

*Christian T Ruff, Robert P Giugliano, Eugene Braunwald, Elaine B Hoffman, Naveen Deenadayalu, Michael D Ezekowitz, A John Camm, Jeffrey I Weitz, Basil S Lewis, Alexander Parkhomenko, Takeshi Yamashita, Elliott M Antman*




**NOACs are associated with**:

- A significant reduction in hemorrhagic stroke (with a strong trend towards lower rates of ischemic stroke); all-cause mortality; ICH
- A significant reduction in intracranial hemorrhage
- A trend towards lower rates of MI
- An 25% increase in the risk of gastrointestinal bleeding

Lancet 2014; 383: 955–62

**Table 1** Differences between rheumatic AF and nonrheumatic valvular atrial fibrillation

| Parameter | Rheumatic AF | Nonrheumatic valvular AF |
|---|---|---|
| Presentation | Mitral stenosis, mitral regurgitation, mixed mitral valve disease | Mitral regurgitation, mitral stenosis |
| Age, y | 20-50 | >60 |
| Geographic distribution | Low- and middle-income countries | High-income countries |
| Pathology | Fibrosis and commissural fusion | Myxomatous valve (mitral regurgitation)<br>Calcification of annulus and leaflets (mitral stenosis) |
| Comorbidities | Lesser | Higher |
| Atrial fibrillation | Common (52%) | Less common (16%) |
| Left atrial volume | Larger | Moderate enlargement |
| $CHA_2DS_2$-VASc Score | Untested, not applied | Applicable |

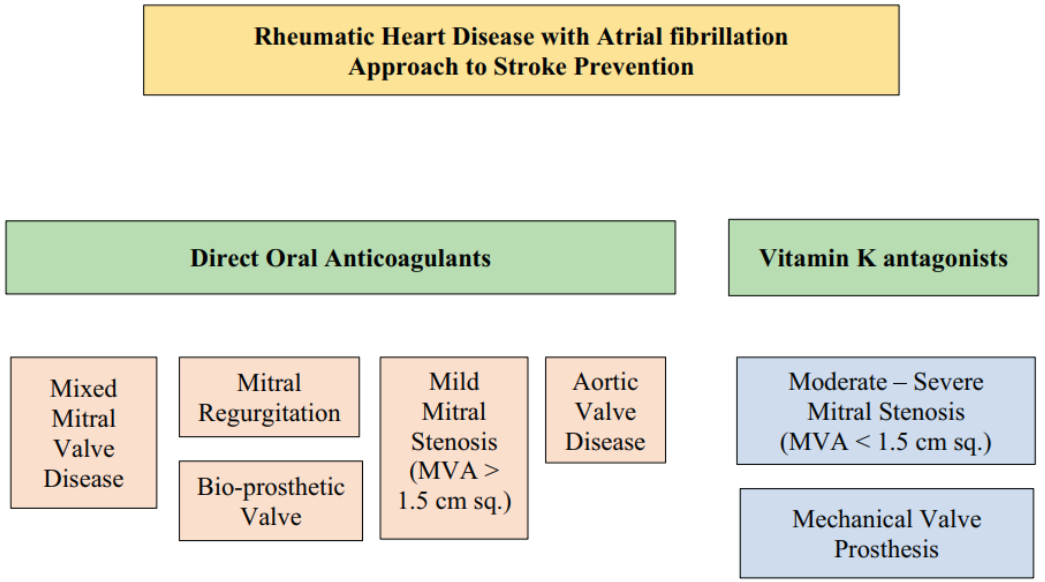



**Figure 1** Stroke prevention in rheumatic atrial fibrillation. MVA = mitral valve area.

Heart Rhythm 2022;3:752-759

# HAS-BLED Score ≥ 3 indicates high bleeding risk

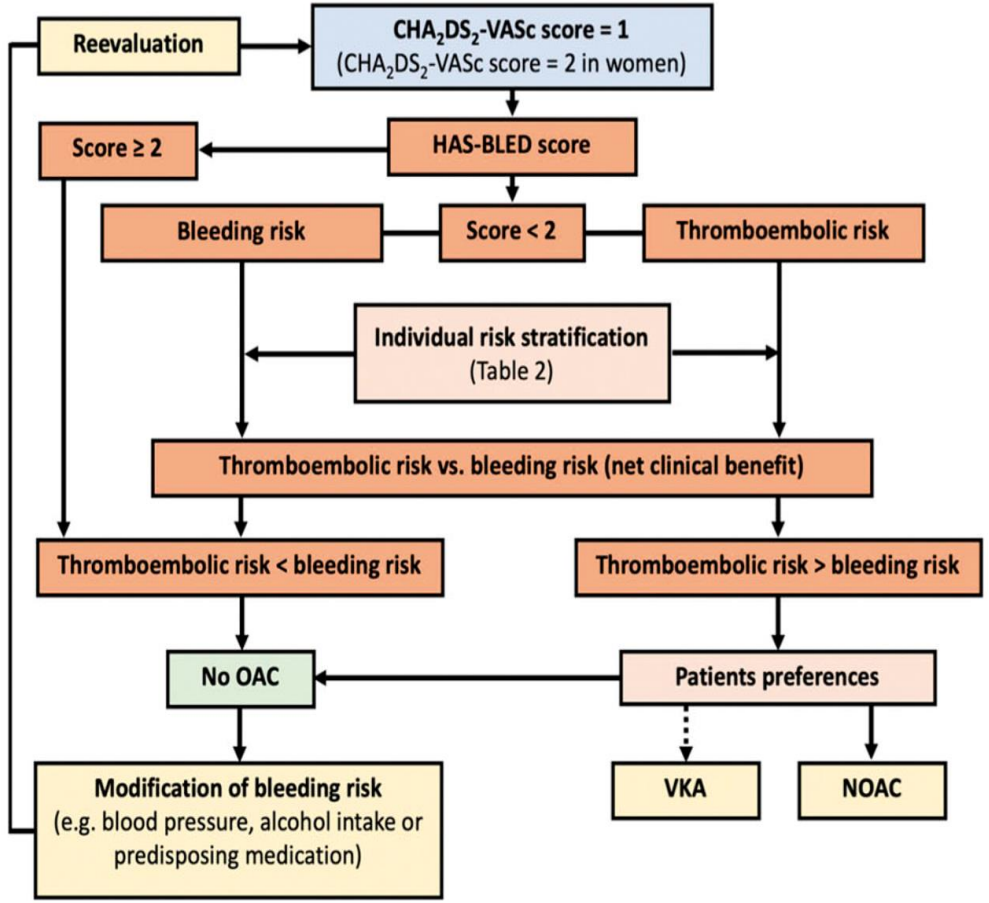
**Table 3** Clinical Characteristics Comprising the HAS-BLED Bleeding Risk Score

| Letter | Clinical Characteristic* | Score | HAS-BLED Score | Bleeds per 100 Patient-years† |
|---|---|---|---|---|
| H | Hypertension | 1 | 0 | 1.13 |
| A | Abnormal renal and liver function (1 point each) | 1 or 2 | 1 | 1.02 |
| S | Stroke | 1 | 2 | 1.88 |
| B | Bleeding | 1 | 3 | 3.74 |
| L | Labile INRs | 1 | 4 | 8.70 |
| E | Elderly | 1 | | |
| D | Drugs or alcohol (1 point each) | 1 or 2 | | |
| | | Maximum 9 points | | |

# Decision tree for oral anticoagulation in patients with atrial fibrillation and a $CHA_2DS_2$-VASc score of 1

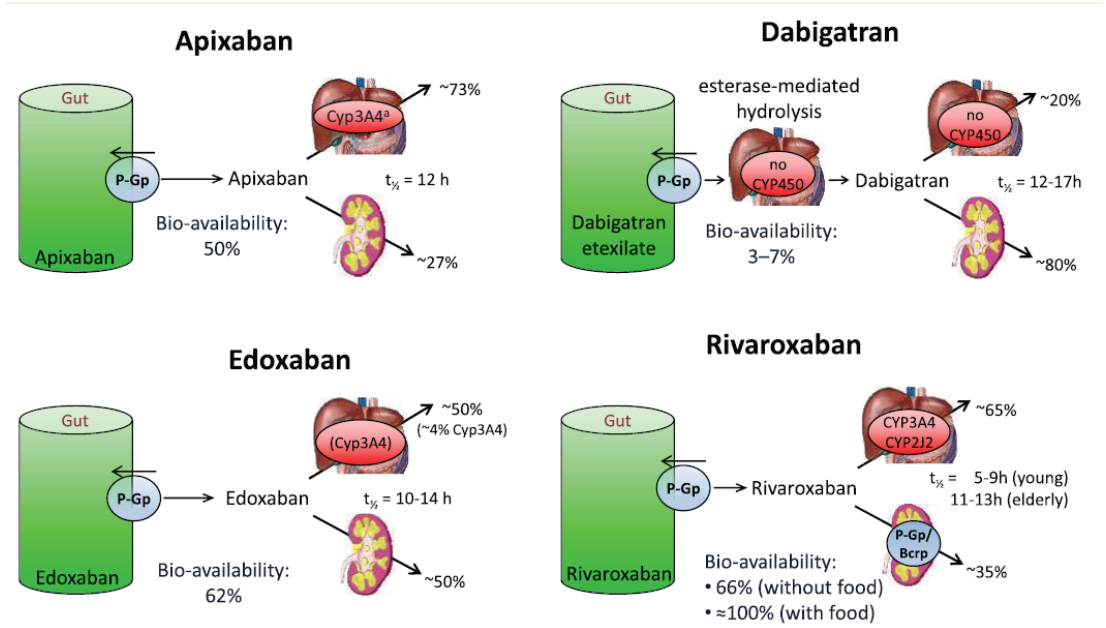
| Favors oral anticoagulation (in case of low bleeding risk) |
|---|
| Age (>65 years) |
| Type II diabetes mellitus |
| Atrial fibrillation (not atrial flutter) |
| Persistent/permanent atrial fibrillation |

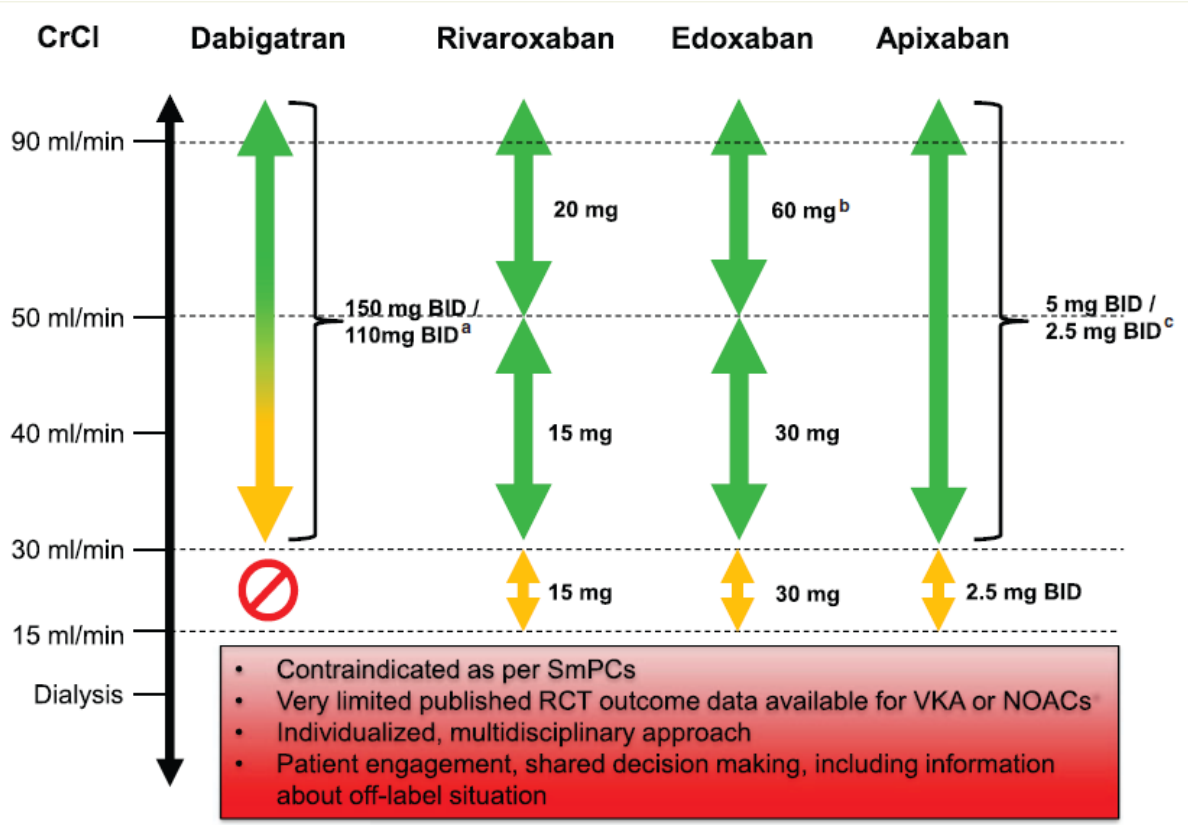
| Additional factors for thromboembolic risk modification |
|---|
| Obesity (body mass index ≥30) |
| Proteinuria (>150mg/24h or equivalent) |
| eGFR (<45ml/h) |
| NT-proBNP (>1400ng/l) |
| Positive cardiac troponin T and I |
| Enlarged LA volume (≥73mL) or diameter (≥4.7cm) |
| LAA emptying velocity (<20cm/s) |
| ABC (Age/Biomarker/Clinical history) score |




Eur Heart J 2019: 40;3010-3012

# DOACs and renal function



# DOACs and renal function

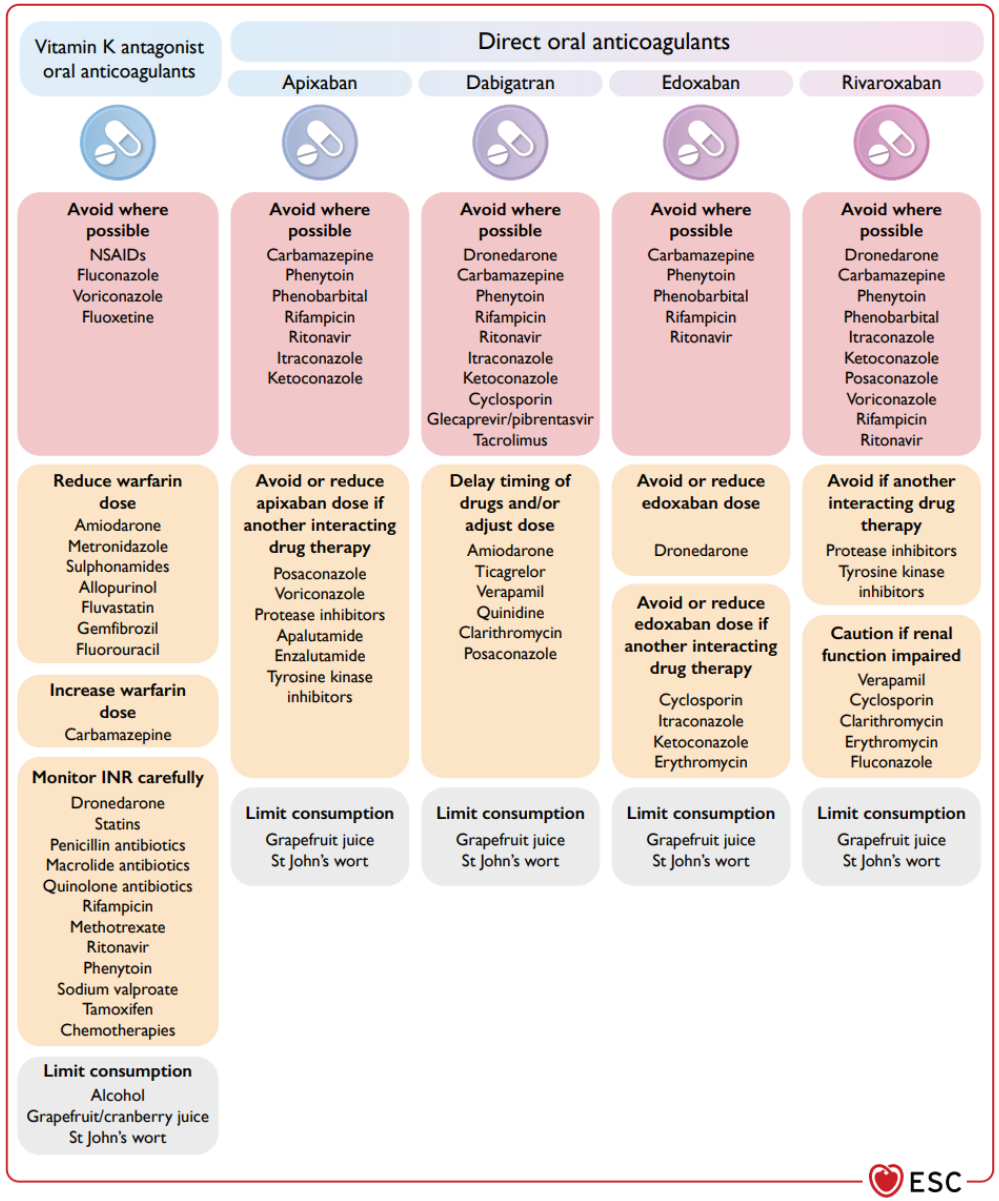
**Table 2** **OACs and approved/studied doses across indications**

**Stroke prevention in atrial fibrillation (SPAF)**

| | Standard dose | Comments/dose reduction |
|---|---|---|
| Apixaban[47] | 5 mg BID | 2.5 mg BID if two out of three fulfilled: weight ≤60 kg, age ≥80 years, serum creatinine ≥133 μmol/L (1.5 mg/dL) (*or* single criterion: if CrCl 15–29 mL/min) |
| Dabigatran[48] | 150 mg BID/110 mg BID | No pre-specified dose-reduction criteria in phase III trial[a] |
| Edoxaban[49] | 60 mg QD | 30 mg QD if: weight ≤60 kg *or* CrCl 15–49 mL/min *or* concomitant therapy with strong P-Gp inhibitor (see 'Pharmacokinetics and drug-drug interactions of NOACs' section) |
| Rivaroxaban[46] | 20 mg QD | 15 mg QD if CrCl ≤15–49 mL/min |

Dabigatran 110 mg b.i.d. in patients with:

- Age ≥80 years
- Concomitant use of verapamil, or
- Increased bleeding risk





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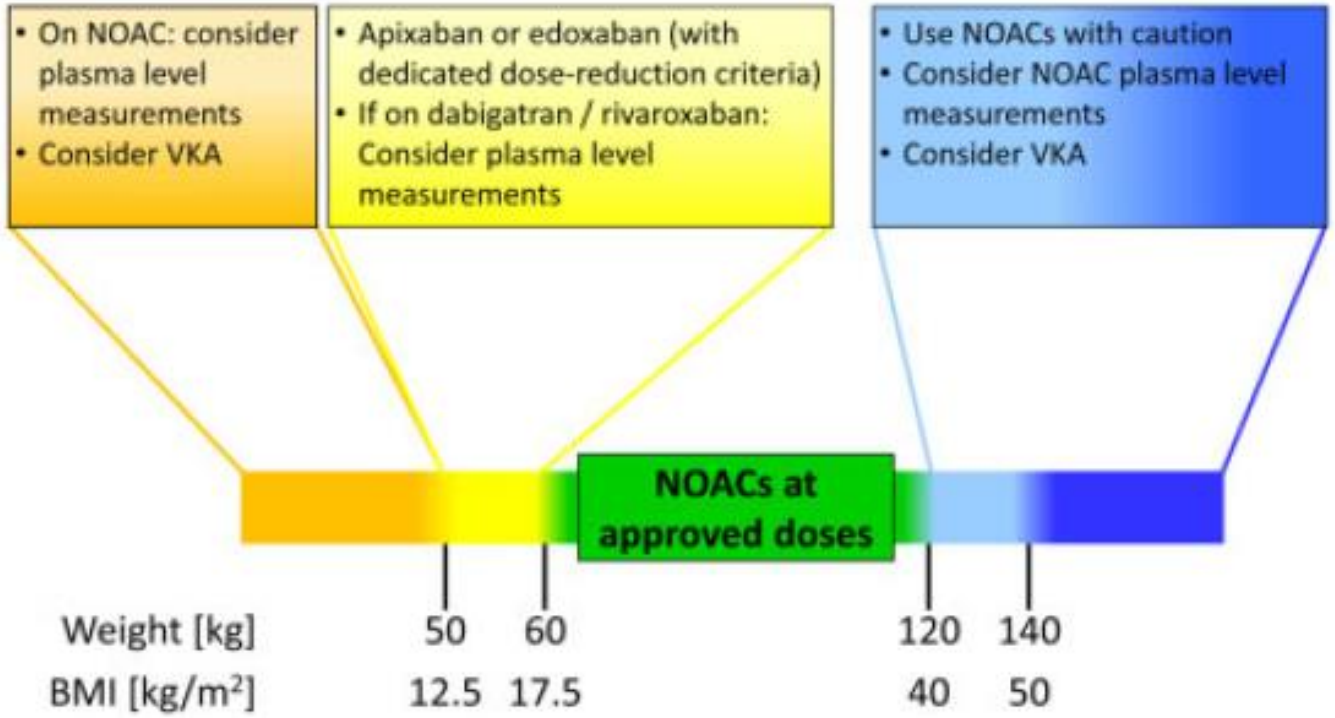
doi:10.1093/europace/euab065



**2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation**

# NOACs in under- and overweight patients



JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 76, NO. 12, 2020


# Mortality in Patients With Atrial Fibrillation Receiving Nonrecommended Doses of Direct Oral Anticoagulants

Alan John Camm, MD,[a] Frank Cools, MD,[b] Saverio Virdone, MSc,[c] Jean-Pierre Bassand, MD,[c,d] David Andrew Fitzmaurice, MD,[e] Keith Alexander Arthur Fox, MBChB,[f] Samuel Zachary Goldhaber, MD,[g] Shinya Goto, MD, PhD,[h] Sylvia Haas, MD, PhD,[i] Lorenzo Giovanni Mantovani, MSc,[j,k] Gloria Kayani, BSc,[c] Alexander Graham Grierson Turpie, MD,[l] Freek Willem Antoon Verheugt, MD, PhD,[m] Ajay Kumar Kakkar, MBBS, PhD,[c,n] for the GARFIELD-AF Investigators*

**OBJECTIVES** The impact of DOAC dosing, according to the recommended guidance on all-cause mortality, stroke/SE, and major bleeding, was assessed at 2-year follow-up in patients with newly diagnosed AF.

**METHODS** Of a total of 34,926 patients enrolled (2013 to 2016) in the prospective GARFIELD-AF (Global Anticoagulant Registry in the FIELD-AF), 10,426 patients received a DOAC.

**FIGURE 1** DOAC Dosing Prescribed at Diagnosis

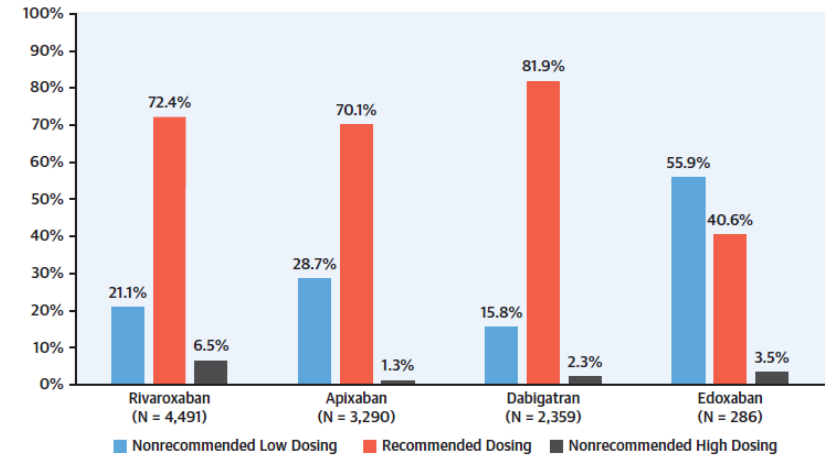
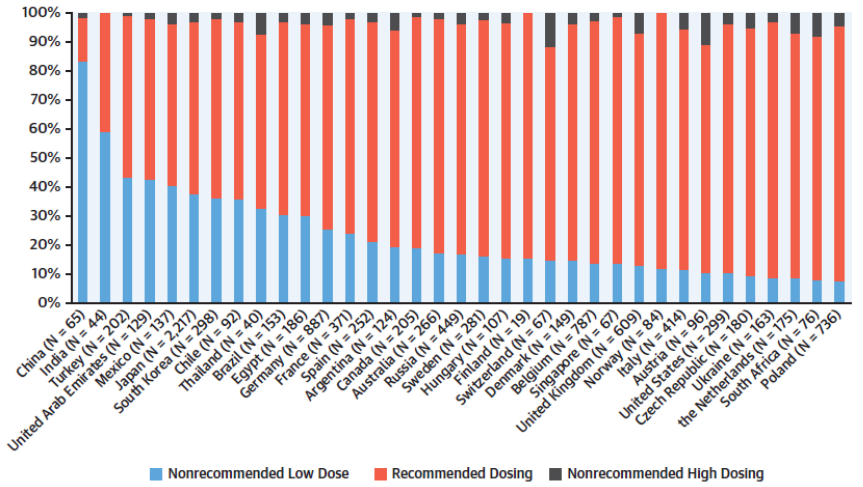



**FIGURE 2** DOAC Dosing Distribution by Country



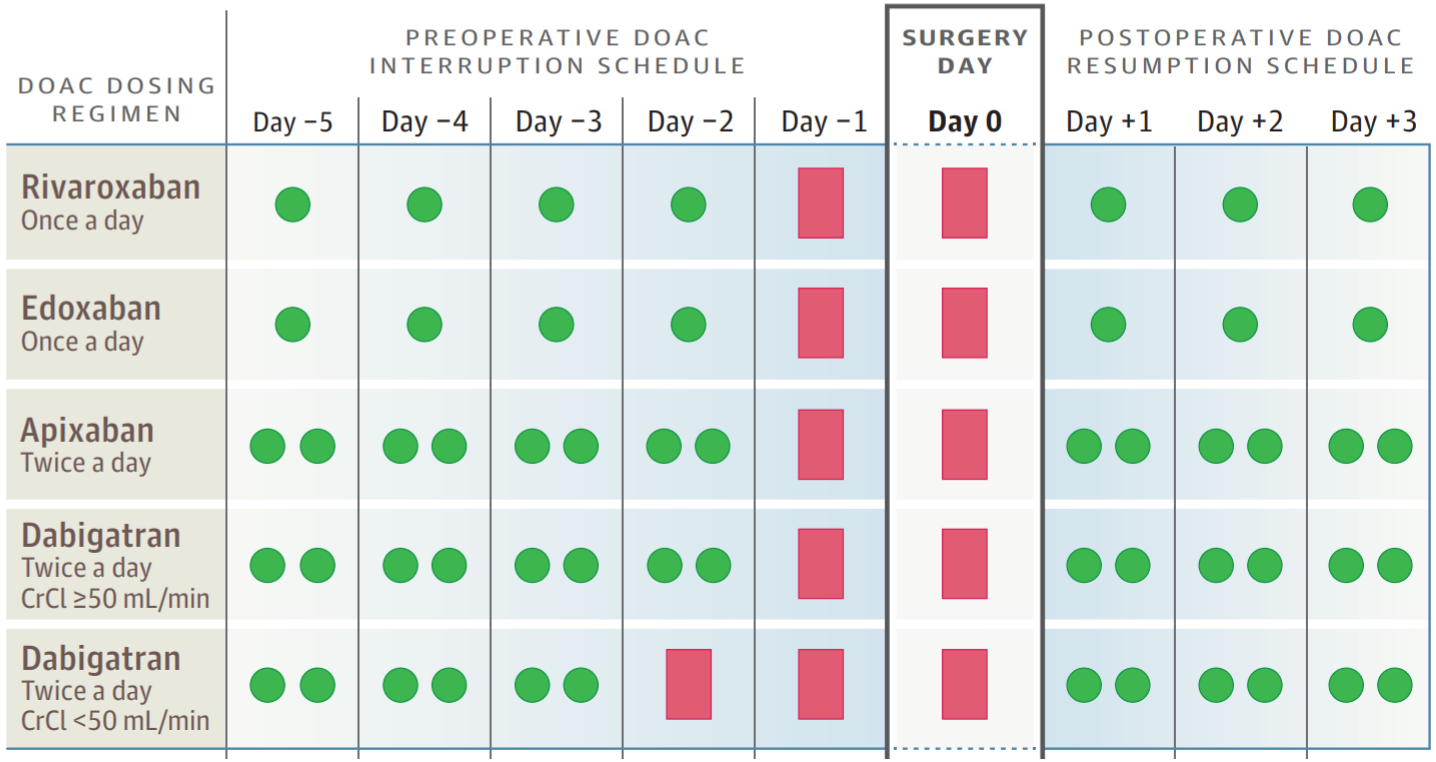
## Figure 1. Perioperative Direct Oral Anticoagulant (DOAC) Dosing Schedule

**Surgical and nonsurgical procedures associated with minimal bleeding risk**

- Cardiac device implantation (eg, pacemaker or cardioverter-defibrillator device)
- Coronary angiography using radial artery access
- Minor dermatologic procedures (eg, excision of basal and squamous cell skin cancers, actinic keratoses, or premalignant or cancerous skin nevi)
- Phacoemulsification (cataract) procedures
- Minor dental procedures (eg, dental extractions, restorations, cleanings, or fillings)

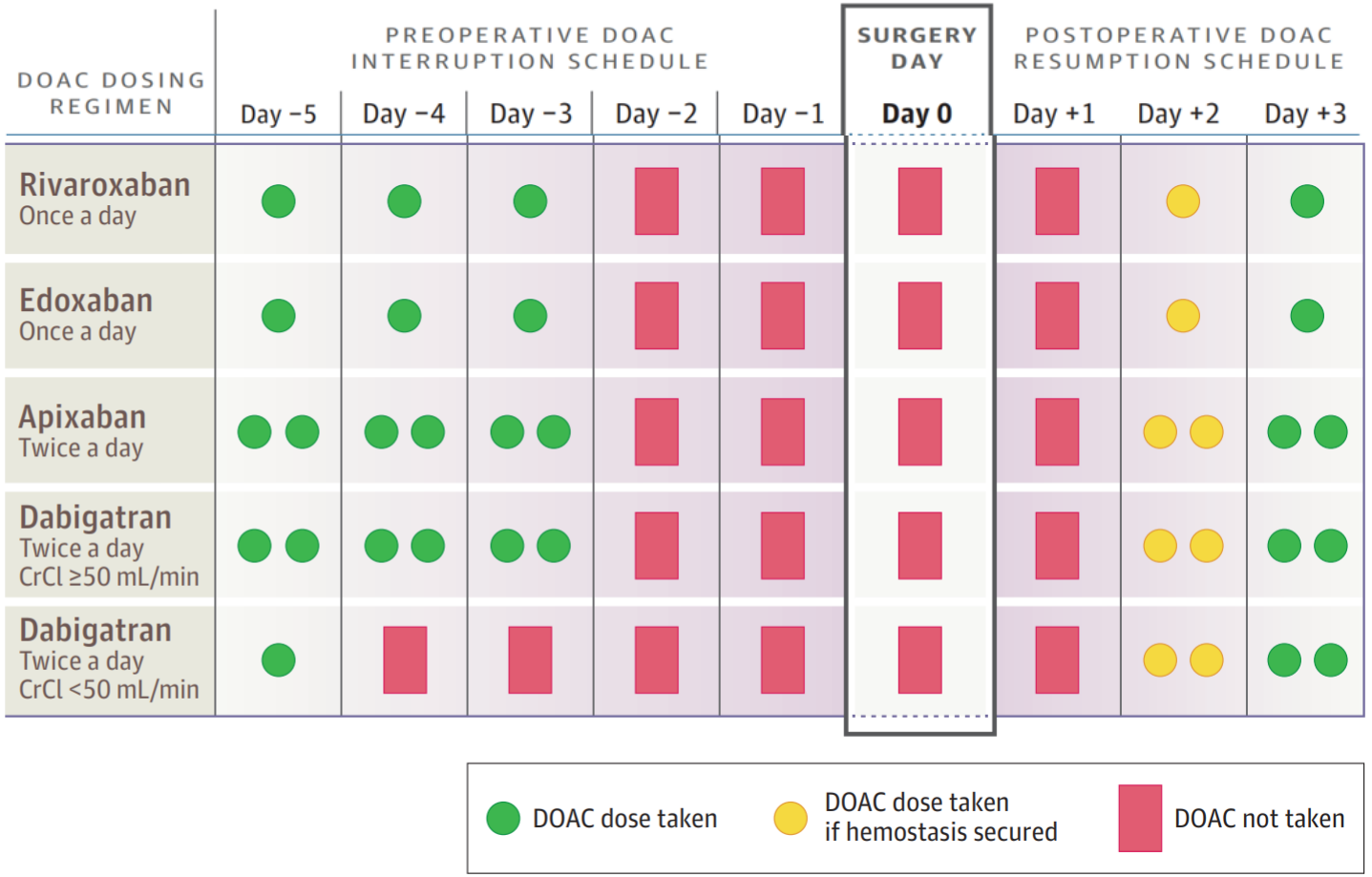
**Procedures associated with low or moderate bleeding risk**

- Laparoscopic cholecystectomy
- Abdominal hernia repair
- Abdominal hysterectomy
- Lymph node biopsy
- Foot or hand surgery
- Coronary angiography using femoral artery access
- Gastrointestinal endoscopy with or without biopsy
- Colonoscopy with or without biopsy
- Hemorrhoidal surgery
- Bronchoscopy with or without biopsy



**Procedures associated with high bleeding risk**

- Any surgery with spinal or epidural anesthesia
- Major cancer surgery (eg, lung, esophagus, gastric, colon, kidney, or hepatobiliary)
- Major orthopedic surgery (eg, hip or knee replacement)
- Major reconstructive plastic surgery (eg, cancer resection)
- Noncancer major thoracoabdominal surgery (eg, colectomy)
- Transurethral prostate or bladder resection
- Selected biopsies (eg, kidney)
- Selected gastrointestinal procedures (eg, endoscopic retrograde cholangiopancreatography)
- Surgery involving highly vascular organs (eg, kidneys)
- Surgery involving closed space areas (eg, cardiac)
- Deep nerve block procedures



# What if a patient has a stroke on OAC?

**Investigate the etiology of stroke!!!**

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**DOI:10.1212/WNL.0000000000207422**

Association of Alternative Anticoagulation Strategies and Outcomes in Patients With Ischemic Stroke While Taking a Direct Oral Anticoagulant

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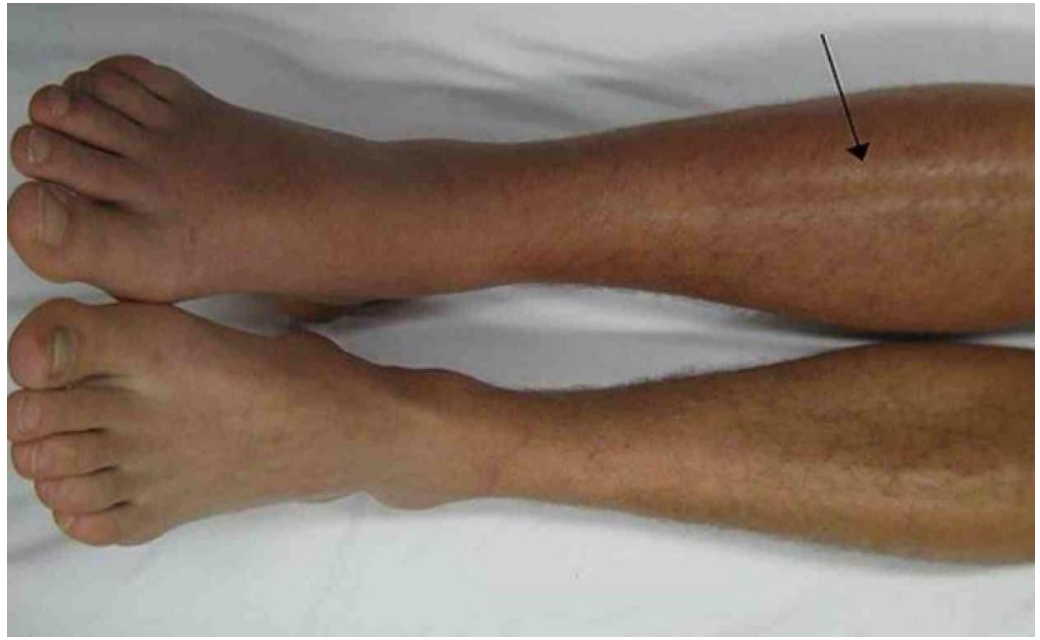
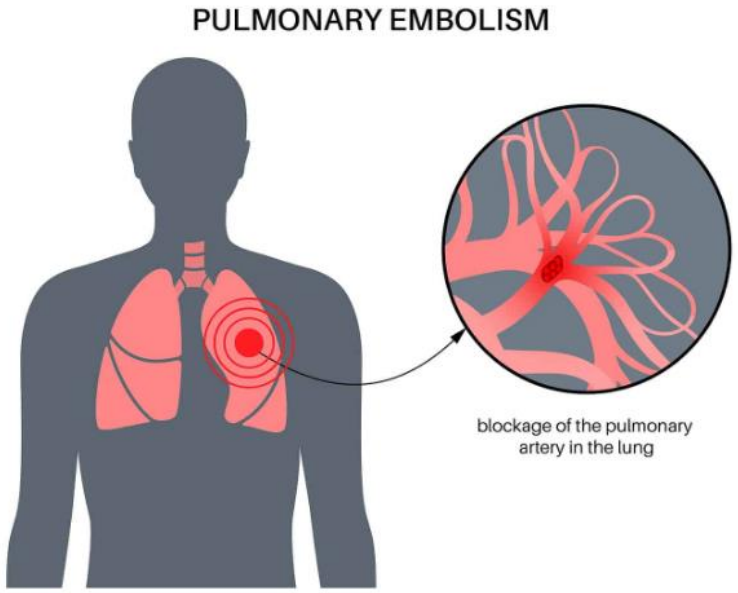
This study provides Class II evidence that in patients with non-valvular AF suffering an ischemic stroke while being treated with a DOAC, **continuing treatment with that DOAC is more effective** at preventing recurrent ischemic stroke than switching to a different DOAC or to warfarin.



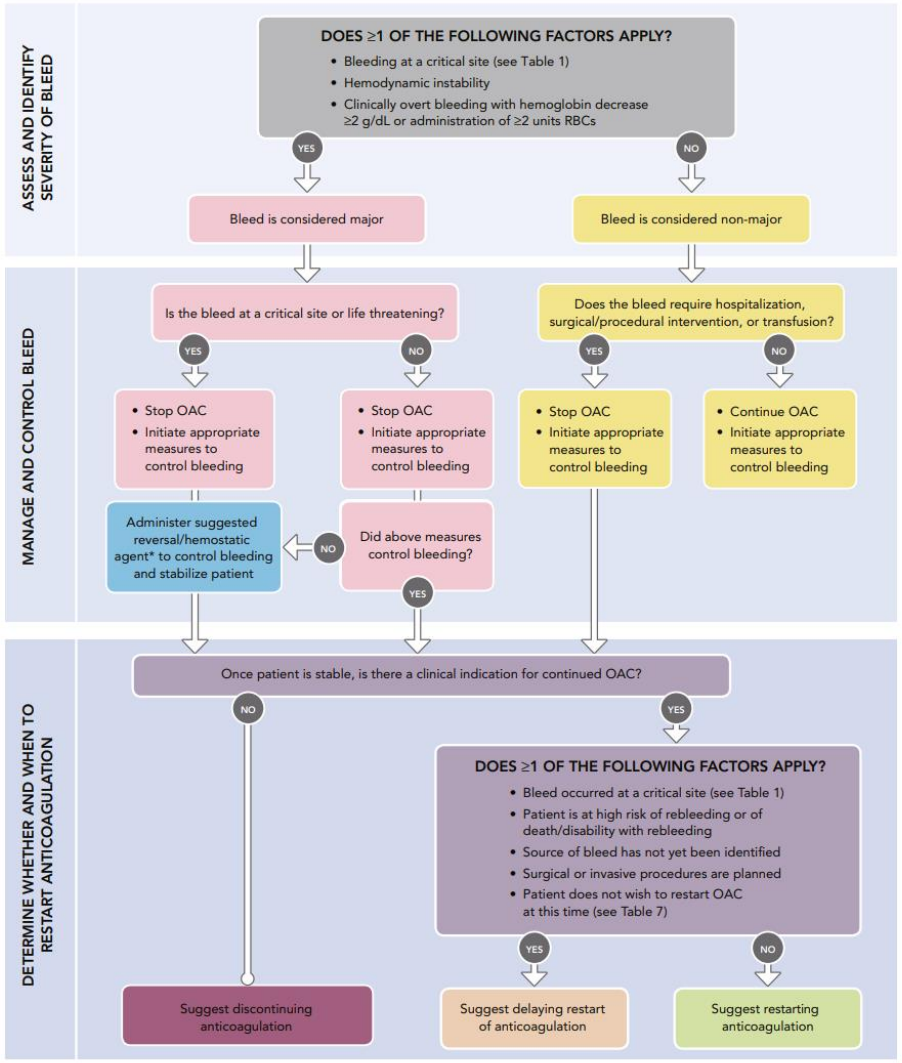

PULMONARY EMBOLISM
blockage of the pulmonary artery in the lung

# DOAC Dosing for VTE Treatment

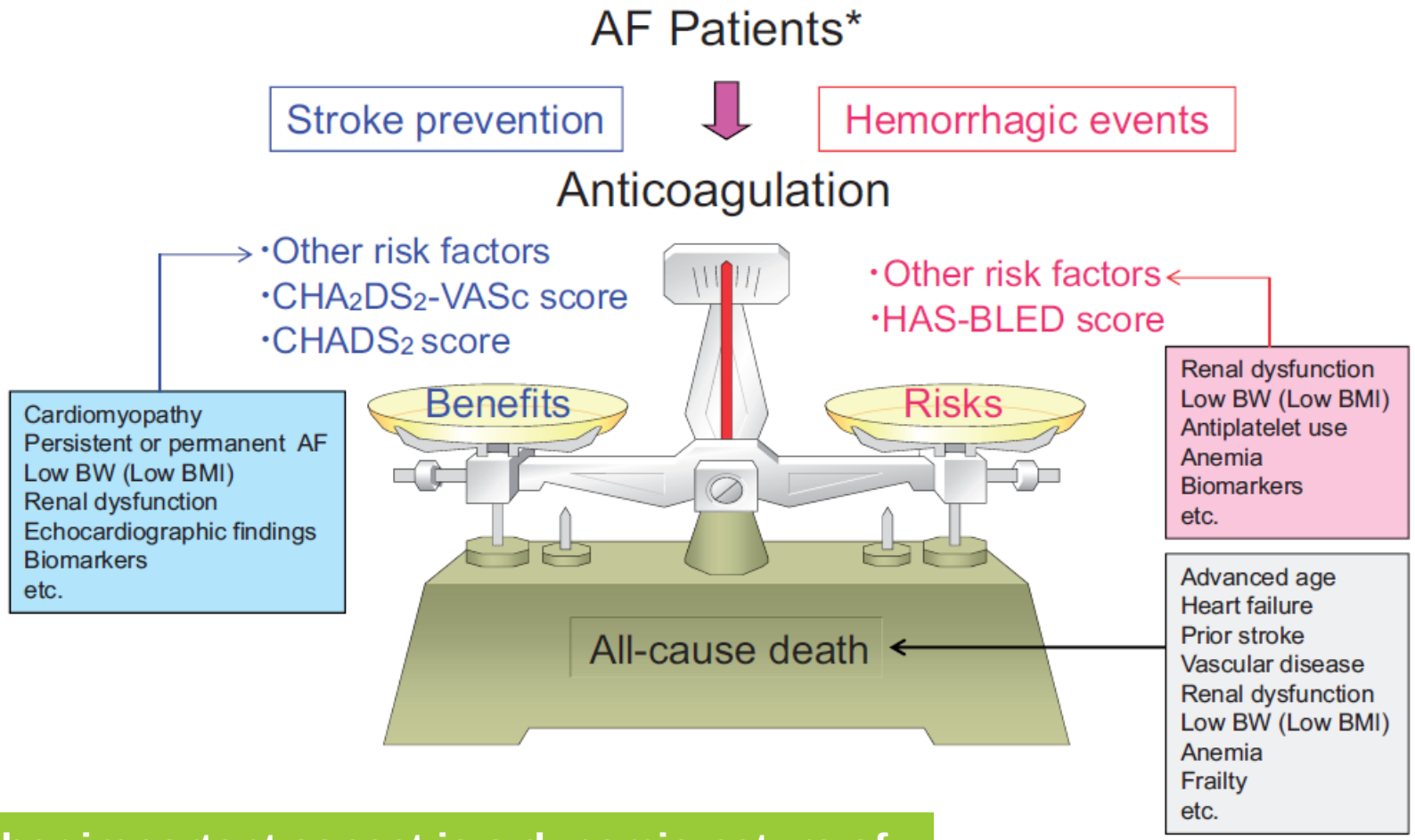
| | Dabigatran (Pradaxa®) | Rivaroxaban (Xarelto®) | Apixaban (Eliquis®) |
|---|---|---|---|
| Treatment of VTE | 150 mg PO BID after 5 – 10 days of parenteral anticoagulation | 15 mg PO BID with food for 21 days, ↓ then 20 mg PO daily with food | 10 mg PO BID for 7 days, ↓ then 5 mg PO BID |
| Renal Adjustment | Clcr ≤ 30 mL/min: no dosing recommendation | Clcr < 30 mL/min: avoid use | None |
| Hepatic Adjustment | None | Moderate or severe hepatic impairment: not recommended | Severe hepatic impairment: not recommended |
| Drug Interactions | Clcr < 50 mL/min with concomitant P-gp inhibitor: avoid concomitant use<br><br>P-gp inducers: avoid concomitant use | Strong dual CYP3A4/P-gp inhibitors/inducers: avoid concomitant use | Strong dual CYP3A4/P-gp inhibitors: ↓ dose by 50%<br><br>Strong dual CYP3A4/P-gp inducers: avoid concomitant use |

Clcr = creatinine clearance, CYP = cytochrome P450, P-gp = P-glycoprotein

**FIGURE 1** Summary Graphic




JACC VOL. 76, NO. 5, 2020




**Another important aspect is a dynamic nature of risk profiles. The stroke risk in patients with AF does not remain static, and with time, patients get older and accumulate more comorbidities.**

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*The Heart of the Matter*
doi:10.1093/eurheartj/suaa176

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# Conclusions

$CHA_2DS_2$-VA and HAS-BLED score determination
DOACs preferable to VKA
Dosage (eGFR, body weight, drug interactions)
Frequent monitoring of patients
Good co-operation among different specialties

# THANK YOU FOR YOUR ATTENTION