■ R E V I E W

Optimal anticoagulation in elderly patients with atrial fibrillation: Which drug at which dose?

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A B S T R A C T

Aging is an important risk factor for adverse events in elderly patients with atrial fibrillation (AF) and complicates the management of anticoagulation. Underuse of oral anticoagulants (OACs) is common in elderly patients because of comorbidities, the altered physiological function of multiple organs, frailty, risk of falls, and the lack of randomized controlled trials (RCTs) specifically for elderly patients. Nevertheless, current data still support OACs use for reducing ischemic stroke with positive net clinical benefits. Sub-analyses of RCTs and real-world cohort studies showed that non-vitamin K antagonist OACs (NOACs) would be more favorable choices compared to warfarin for stroke prevention in the elderly. This review will discuss important data on stroke prevention and the use of NOACs in elderly AF patients.

Key words: anticoagulation, atrial fibrillation, elderly, NOAC, stroke

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide and the prevalence has been increasing with the aging of the population worldwide [1, 2]. AF increases the risks of ischemic stroke and systemic embolism (IS/SE), and the CHA_2DS_2-VASc score is recommended to guide the use of oral anticoagulant (OAC) for stroke prevention [3–6]. Age itself is one of the components of the CHA_2DS_2-VASc score, with 1 score assigned for age 65–74 years and 2 scores for age ≥75 years. The analysis of the Atrial Fibrillation Investigators database observed a 45% increase of risk of ischemic stroke per decade in age (hazard ratio [HR], 1.45; 95% confidence interval [CI], 1.26–1.66) [7]. Even in patients aged ≥65 years, a gradual increase of ischemic stroke with an increase of aging is still evident (Figure 1) [10–13]. Aging also increases the risk of intracranial hemorrhage (ICH) and major bleeding and contributes to

the HAS-BLED score [8, 9] together with other risk factors (Figure 1) [10–13]. Besides, aging alters the physiological functions of multiple organs and might affect medication concentrations and exposure [14]. Therefore, OAC use in elderly AF patients, especially those aged ≥75 years, is a complex issue involving the balance between efficacy and safety.

"Old age" should not be the only reason to withhold oral anticoagulants for AF patients

In real-world practice, underuse of OAC is common in elderly AF patients because of the fear of bleeding and the lack of specific guidelines. However, a nationwide cohort study by Chao et al. demonstrated a decreased risk of stroke (HR, 0.69; 95% CI, 0.49–0.96) and a similar risk of ICH with warfarin compared to no antithrombotic treatment in AF patients aged ≥90 years. Warfarin was still associated with a positive net clinical benefit compared
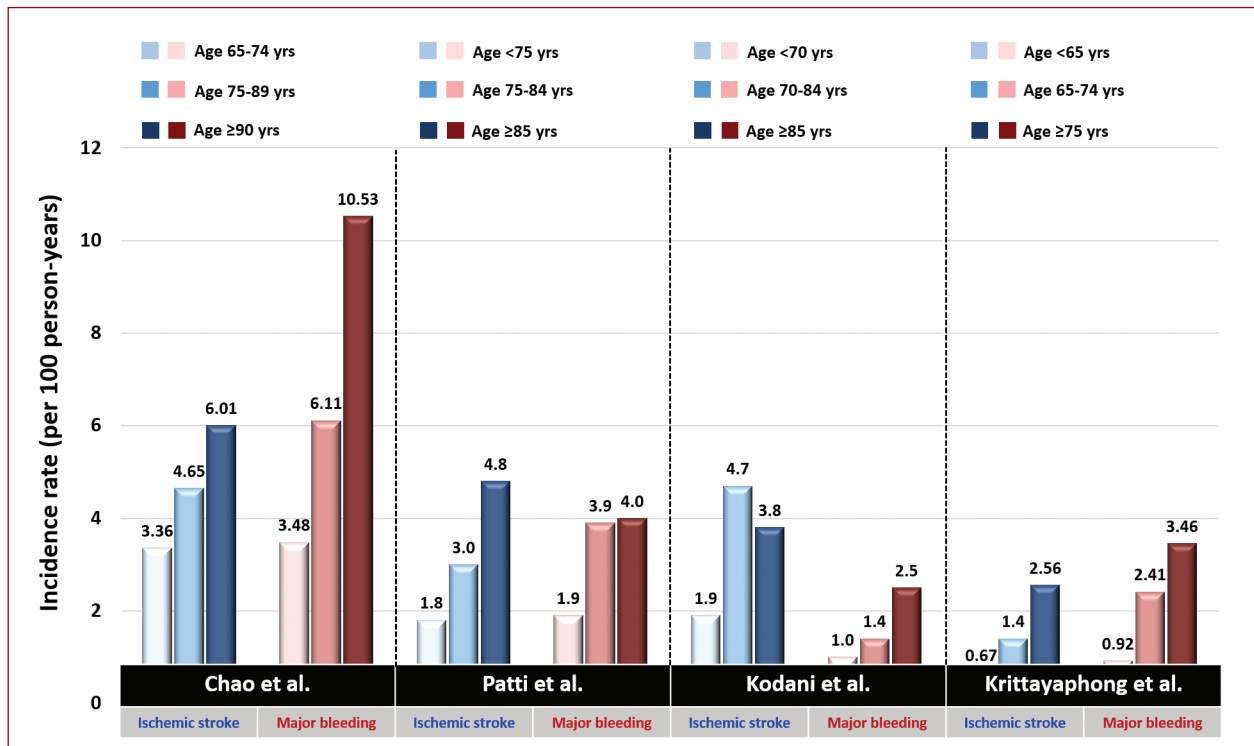
Figure 1. Risks of ischemic stroke and major bleeding in elderly patients with AF. Elderly patients are at increased risks of ischemic stroke and major bleeding, and the risks continues to rise at even advanced age. Data used in the figure were adapted from the papers by Chao et al., Patti et al., Kodani et al., and Krittayaphong et al. [10–13]

Abbreviations: AF, atrial fibrillation

to antiplatelet treatment [15]. The sub-analysis from the prospective PREFER in AF study (PREvention oF Thrombo-embolic Events-European Registry in Atrial Fibrillation) re-ported the presence of a significant gradient of net clinical benefit according to age strata with warfarin use, with the oldest patients deriving the greatest advantage [11]. Even among the very elderly (>90 years) AF patients perceived to be at high risk for bleeding, for example, those with a history of ICH, gastrointestinal (GI) bleeding, or chronic kidney disease, non-vitamin K antagonist OACs (NOACs) were associated with a lower composite risk of ischemic stroke, ICH, major bleeding, or mortality (HR, 0.763; 95% CI, 0.702–0.830) compared to non-OACs [16]. Therefore, old age should not be the only reason not to prescribe OAC in patients with AF.

NOACs would be more favorable choices over warfarin in elderly AF patients

Although NOACs are recommended over warfarin as the preferred choice for stroke prevention in AF in current guidelines [3–6], randomized controlled trials (RCTs) spe-cifically comparing NOACs to warfarin in elderly AF patients are lacking. In landmark trials of NOACs, patients ≥75 years accounted for 30%–40% of all study population [17–20], and patients ≥85 years were even fewer. A meta-analysis including 5 phase-III RCTs reported higher risks of IS/SE and major bleeding in elderly (≥75 years) patients compared to non-elderly patients despite the treatment, but the benefi-

cial effects of NOACs compared with warfarin in reducing IS/SE and major bleeding remained in the elderly group [21]. Sub-analyses from other landmark trials demonstrated a lower (apixaban and edoxaban) or similar (dabigatran and rivaroxaban) risks of major bleeding with NOACs compared to warfarin for AF patients aged ≥75 years (Figure 2) [22––25]. However, it should be emphasized that the enrollment criteria differ in various NOAC trials, and, therefore, these observations should not be interpreted as an indication that one NOAC is better than others for stroke prevention in the elderly with AF.

Real-world cohort studies might partly make up for the paucity of RCTs regarding NOACs use in elderly AF patients (Table 1) [10, 15, 26–31]. A nationwide cohort study showed that NOACs were associated with a lower risk of ICH and a similar risk of ischemic stroke compared to warfarin in AF patients aged ≥90 years [15]. Subgroup analysis at differ-ent age strata (age 65–74, 75–89, ≥90 years) in elderly AF patients supported the overall beneficial roles of NOACs compared to warfarin, but there was heterogeneity in treatment effects in different age strata (Figure 3) [10]. Aging seems to be a more dominant factor for ischemic stroke than types of OACs (NOACs or warfarin), but NOACs remained associated with a lower risk of ischemic stroke in patients aged ≥90 years compared to warfarin. In terms of ICH, NOACs behaved better than warfarin irrespective of age strata. Even for patients aged ≥90 years treated with NOACs, their risk of ICH (0.86%/year) was lower than
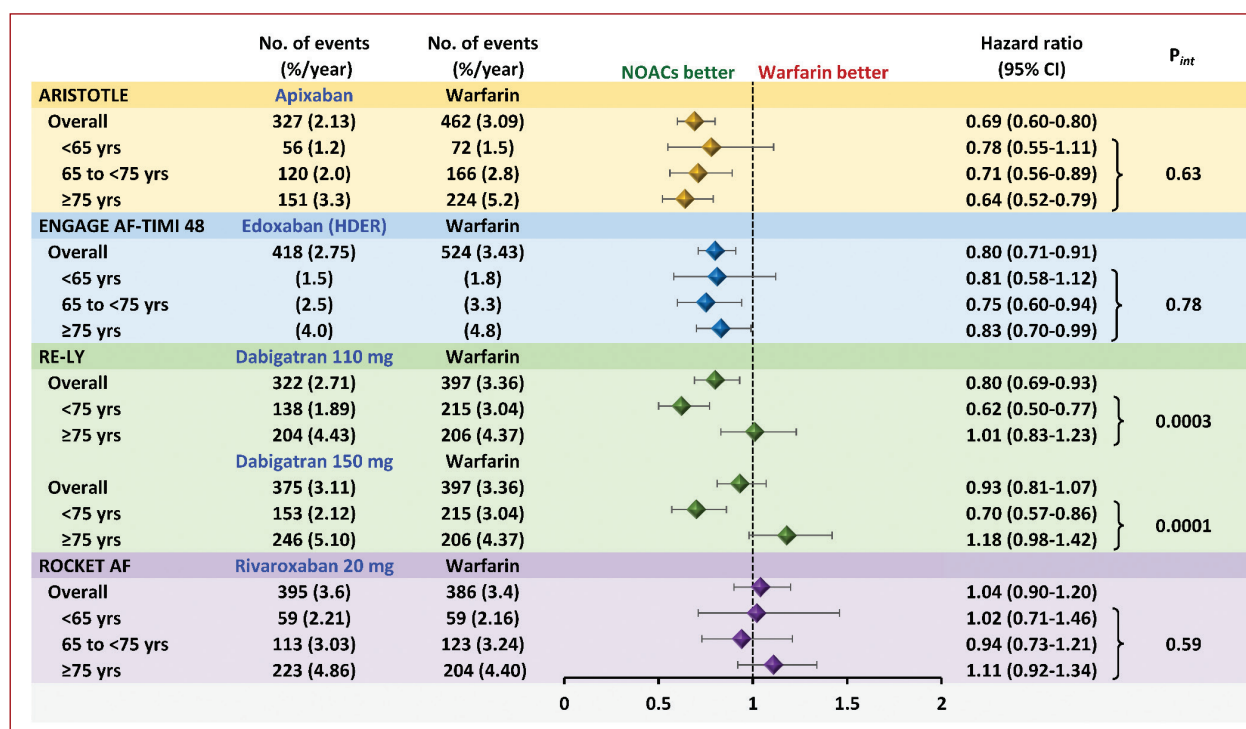
	No. of events (%/year)	No. of events (%/year)	NOACs better	Warfarin better	Hazard ratio (95% CI)	P_int
ARISTOTLE	**Apixaban**	**Warfarin**				
Overall	327 (2.13)	462 (3.09)			0.69 (0.60–0.80)	
<65 yrs	56 (1.2)	72 (1.5)			0.78 (0.55–1.11)	
65 to <75 yrs	120 (2.0)	166 (2.8)			0.71 (0.56–0.89)	0.63
≥75 yrs	151 (3.3)	224 (5.2)			0.64 (0.52–0.79)	
ENGAGE AF-TIMI 48	**Edoxaban (HDER)**	**Warfarin**				
Overall	418 (2.75)	524 (3.43)			0.80 (0.71–0.91)	
<65 yrs	(1.5)	(1.8)			0.81 (0.58–1.12)	
65 to <75 yrs	(2.5)	(3.3)			0.75 (0.60–0.94)	0.78
≥75 yrs	(4.0)	(4.8)			0.83 (0.70–0.99)	
RE-LY	**Dabigatran 110 mg**	**Warfarin**				
Overall	322 (2.71)	397 (3.36)			0.80 (0.69–0.93)	
<75 yrs	138 (1.89)	215 (3.04)			0.62 (0.50–0.77)	0.0003
≥75 yrs	204 (4.43)	206 (4.37)			1.01 (0.83–1.23)	
	Dabigatran 150 mg	**Warfarin**				
Overall	375 (3.11)	397 (3.36)			0.93 (0.81–1.07)	
<75 yrs	153 (2.12)	215 (3.04)			0.70 (0.57–0.86)	0.0001
≥75 yrs	246 (5.10)	206 (4.37)			1.18 (0.98–1.42)	
ROCKET AF	**Rivaroxaban 20 mg**	**Warfarin**				
Overall	395 (3.6)	386 (3.4)			1.04 (0.90–1.20)	
<65 yrs	59 (2.21)	59 (2.16)			1.02 (0.71–1.46)	
65 to <75 yrs	113 (3.03)	123 (3.24)			0.94 (0.73–1.21)	0.59
≥75 yrs	223 (4.86)	204 (4.40)			1.11 (0.92–1.34)	

(Axis: 0   0.5   1   1.5   2)

Figure 2. Risks of major bleeding of NOACs compared to warfarin across different age strata in landmark RCTs. Sub-analyses from landmark trials demonstrated a lower (apixaban and edoxaban) or similar (dabigatran and rivaroxaban) risks of major bleeding with NOACs compared to warfarin for AF patients aged ≥75 years. Data used in the figure were adapted from the papers by Kato et al., Eikelboom et al., Halvorsen et al., and Goodman et al. [22–25].

Abbreviations: CI, confidence interval; HDER, higher-dose edoxaban regimen; NOACs, non-vitamin K antagonist oral anticoagulants; P_int, P for interaction; RCTs, randomized controlled trials

Table 1. Real-world cohort studies in elderly patients with atrial fibrillation: NOACs compared to warfarin

Studies	Year	Country	Definition of elderly	NOACs	Warfarin	IS or IS/SE HR (95% CI)	Major bleeding HR (95% CI	ICH (HR, 95% CI)
Lai et al. [26]	2018	Taiwan	≥85 years	Dabigatran (n = 1180)	n = 1180	1.25 (0.75–2.09)	(GI bleeding) 1.21 (0.76–1.91)	0.31 (0.10–0.97)
				Rivaroxaban (n = 1207)	n = 1207	1.02 (0.64–1.65)	(GI bleeding) 0.81 (0.47–1.38)	0.47 (0.17–1.26)
Tsai et al. [27]	2020	Taiwan	≥85 years	Dabigatran (n = 3893)	n = 3893	0.932 (0.811–1.114)	0.906 (0.769–1.031)	0.496 (0.357–0.688)
				Rivaroxaban (n = 3913)	n = 3913	0.781 (0.649–0.941)	0.868 (0.753–1.001)	0.453 (0.309–0.663)
				Apixaban (n = 574)	n = 574	0.540 (0.277–1.054)	0.874 (0.526–1.456)	0.182 (0.022–1.475)
Chao et al. [15]	2018	Taiwan	≥90 years	NOACs (37% Dabigatran; 57% Rivaroxaban; 6% Apixaban) (n = 978)	n = 768	1.16 (0.61–2.22)	0.95 (0.63–1.44)	0.32 (0.10–0.97)
Chao et al. [10]	2020	Taiwan	75–89 years	NOACs (50% Dabigatran; 5% Apixaban; 45% Rivaroxaban) (n = 28179)	n = 10609	0.825 (0.758–0.897)	0.857 (0.796–0.923)	0.564 (0.474–0.670)
Chan et al. [28]	2019	Taiwan	≥75 years	Edoxaban		0.65 (0.44–0.96)	0.47 (0.29–0.76)	0.40 (0.18–0.88)
				Apixaban		0.56 (0.39–0.79)	0.30 (0.19–0.49)	0.35 (0.17–0.69)
				Rivaroxaban		0.70 (0.51–0.97)	0.56 (0.39–0.82)	0.44 (0.24–0.81)
				Dabigatran		0.71 (0.51–0.98)	0.68 (0.47–0.97)	0.52 (0.29–0.94)
Hanon et al. [29]	2021	France	≥80 years	Rivaroxaban (n = 995)	n = 908	0.44 (0.15–1.30)	0.53 (0.33–0.85)	0.26 (0.09–0.80)
Deitelzweig et al. [30]	2019	US	≥80 years	Apixaban (n = 18897)	n = 18897	0.57 (.47–0.70)	0.53 (0.48–0.58)	0.44 (0.34–0.57)
				Dabigatran (n = 6698)	n = 6698	0.87 (0.65–1.16)	0.90 (0.77–1.05)	0.50 (0.33–0.77)
				Rivaroxaban (n = 25917)	n = 25917	0.73 (0.63–0.85)	0.81 (0.67–0.99)	0.77 (0.63–0.94)
Russo et al. [31]	2020	Italy	≥80 years	NOACs (n = 252)	n = 504	1.00 (0.46–2.19)	0.82 (0.50–1.34)	0.29 (0.07–1.25)

Abbreviations: AF, atrial fibrillation; GI, gastrointestinal; ICH, intracranial hemorrhage; IS/SE, ischemic stroke/system embolism; NOACs, non-vitamin K antagonist oral anticoagulants
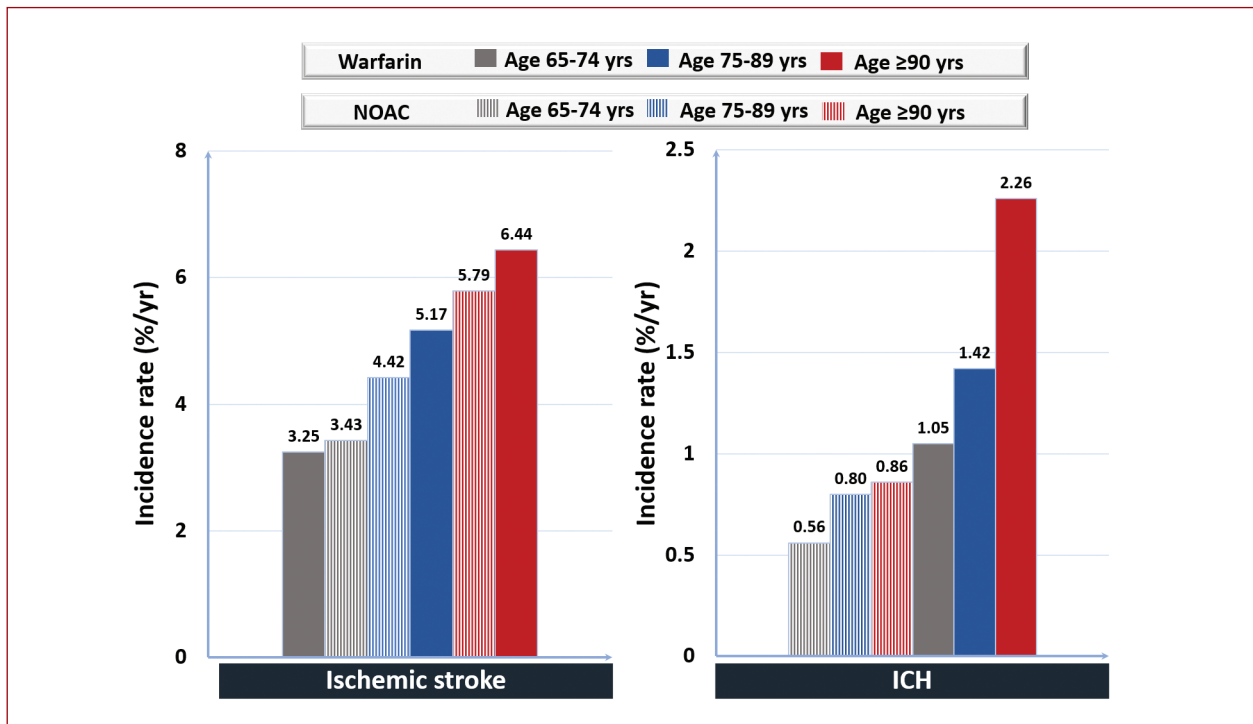
Figure 3. Annual risks of ischemic stroke and ICH in patients treated with NOACs or warfarin in different age strata. Aging seems to be a more dominant factor of ischemic stroke than types of OACs (NOACs or warfarin), but NOACs remained associated with a lower risk of ischemic stroke in patients aged ≥90 years compared to warfarin. In terms of ICH, NOACs behaved better than warfarin irrespective of age strata. Even for patients aged ≥90 years treated with NOACs, their risk of ICH (0.86%/year) was lower than in "younger" patients, aged 65–74 years, receiving warfarin (1.05%/year). Data used in the figure were adapted from the papers by Chao et al. [10]

Abbreviations: ICH, intracranial hemorrhage; OAC – oral anticoagulants; other — see Figure 2

"younger" patients aged 65–74 years receiving warfarin (1.05%/year) (Figure 3) [10]. The patterns of the associations between the risk of ICH and age seem to be different for warfarin and NOACs (Figure 4) [10]. For warfarin, the risk of ICH increased in parallel to the increase in age, while the curve of ICH risk seemed to be relatively flat with NOACs when age increased. Therefore, the absolute risk reduction in ICH with NOACs, compared with warfarin, would be more evident in the elderly AF population. Results from the meta-analysis of 11 RCTs and observational studies also favored NOAC use over VKAs in patients aged >75 years based on improved overall outcomes [32].

In daily practice, the introduction of NOACs did change the landscape of stroke prevention in the elderly AF population. In a recent nationwide report from Taiwan, the introduction of NOACs increased the initiation rates of OACs in elderly AF patients, which were related to the lower risk of ischemic stroke and mortality over time (Figure 5) [33].

DOSING OF NOACS IN THE ELDERLY

There are different dose reduction criteria for each NOAC. Although age had not been a dose reduction criterion in RE-LY (Randomized Evaluation of Long-term Anticoagulation Therapy) [17], dabigatran 150 mg is not recommended for patients aged ≥80 years in Europe, and a lower dose (110 mg) should be considered for patients aged 75–

–79 years. In the ROCKET AF trial (Rivaroxaban Once-Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) [18], dose reduction is mainly driven by renal function, and age had not been a dose-reduction criterion. Nevertheless, renal function is more often impaired in elderly patients in whom a reduced dose might be justified. Like in the ROCKET AF trial, old age was not a dosage-reduction criterion for edoxaban in the ENGAGE AF-TIMI 48 trial (Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48) [20]. In the ARISTOTLE trial (Apixaban for Reduction in Stroke and Other Thromboembolic Events in AF) [19], age directly influenced apixaban dosing as age ≥80 years was one of the three dose-reduction criteria, and the dose of apixaban should be reduced once another dosage reduction criterion was present.

Since renal function is a crucial factor to determine NOAC dosing under most circumstances, accurate evaluation of renal function is important. The most commonly used formulas for estimating renal function include the Cockcroft-Gault (CG) formula, Modified Diet in Renal Disease (MDRD) formula, and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. The CG formula is adopted in most RCTs while the MDRD and CKD-EPI formulas are usually applied in real-world practice. Chao
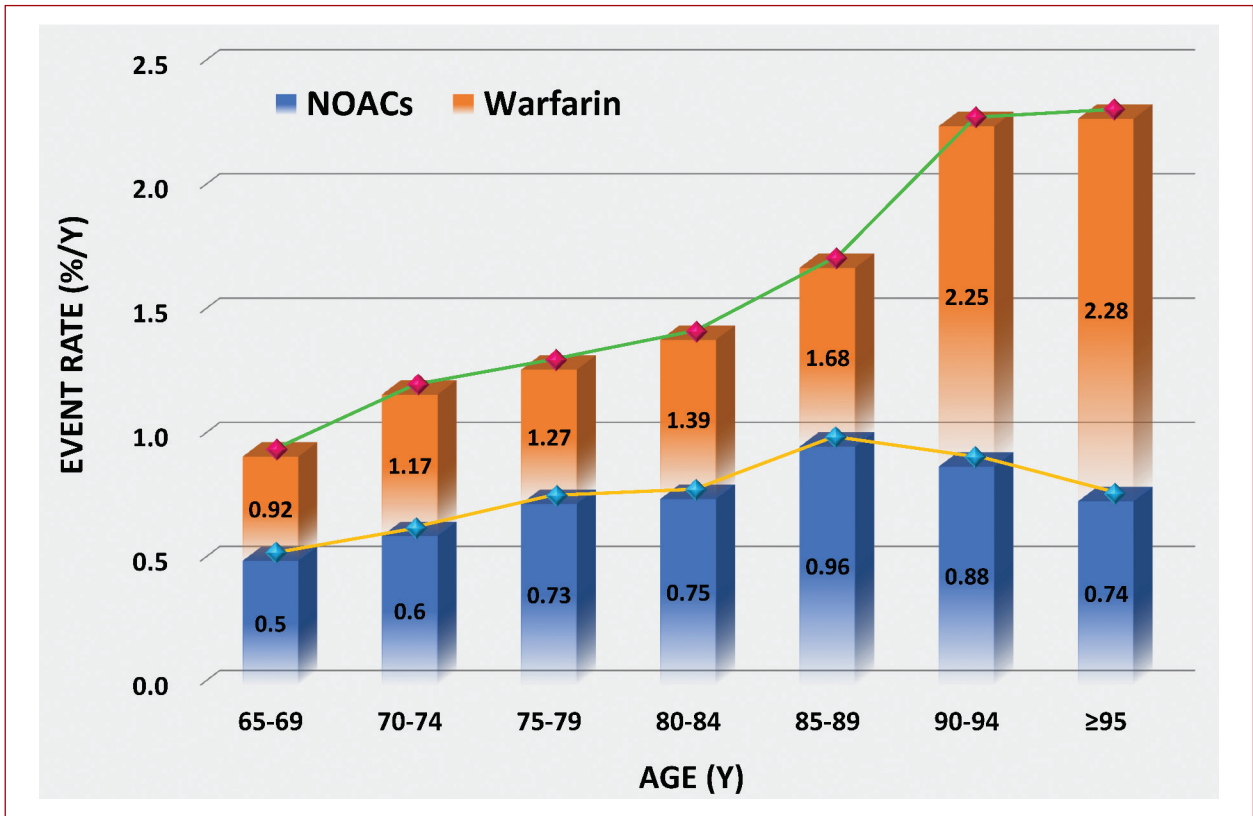
Figure 4. The differences of the risk of ICH between NOACs and warfarin in different age strata. The patterns of the associations between risk of ICH and age seem to be different for warfarin and NOACs. For warfarin, the risk of ICH increased in parallel to the increase in age, while the curve of ICH risk seemed to be relatively flat with NOACs when age increased. Therefore, the absolute risk reductions in ICH with NOACs, compared with warfarin, would be more evident in the elderly AF population. Data used in the figure were adapted from the papers by Chao et al. [10]

Abbreviations: see Figures 2 and 3
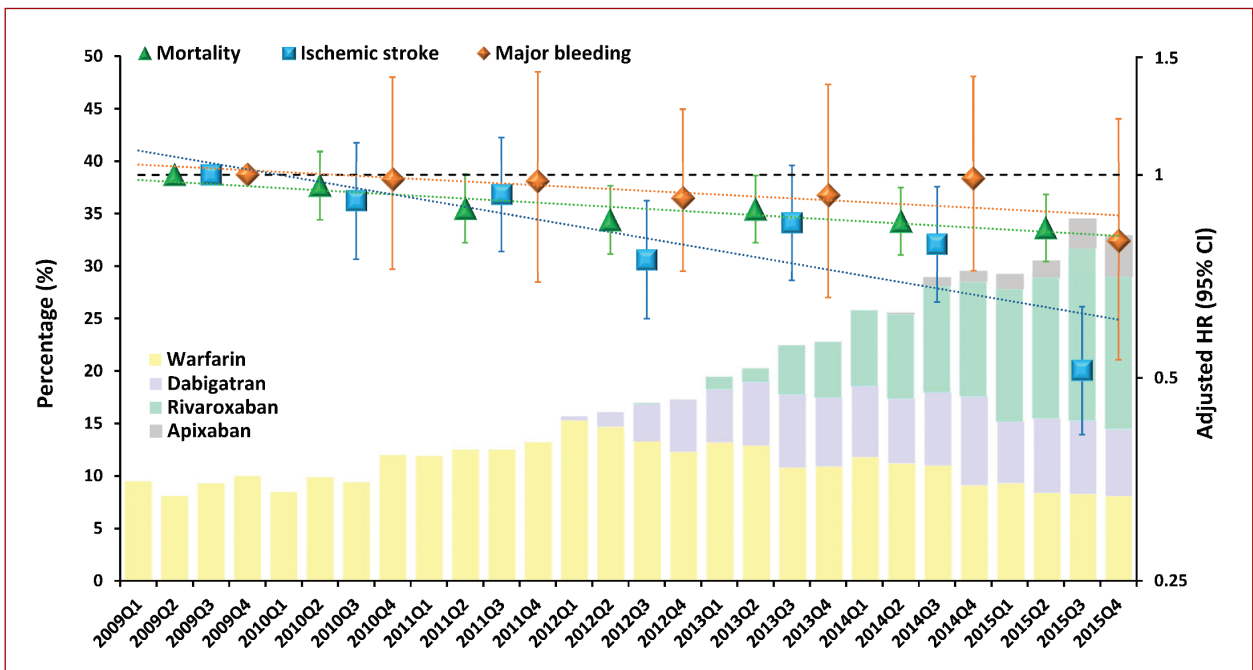
Figure 5. Temporal trends of OACs prescription in elderly AF patients in relation to risks of adverse events. The introduction of NOACs increased the initiation rates of OACs in elderly AF patients which were temporally related to the lower risk of ischemic stroke and mortality over time. The figure was redrawn, and data were adapted from the paper by Cheng et al. [33]

Abbreviations: see Figures 1–3

et al. [34] found the estimated glomerular filtration rate (eGFR) was overestimated in older patients (>75 years) and low body weights (<50 kg) using the MDRD and CKD-EPI compared to the CG equation, which might result in inappropriate dosing (mainly overdosing) of NOACs. Importantly, the overdosing may attenuate the benefits of NOACs regarding the risk of major bleeding compared to warfarin [35]. Therefore, the CG equation should be the preferred equation to calculate eGFR and determine the dosing of NOACs. This issue is particularly important for elderly AF patients.

WHAT IS THE OPTIMAL CHOICE AND DOSE OF NOACS IN ELDERLY AF PATIENTS?

Head-to-head comparisons among different NOACs in elderly patients with AF are still lacking, and only some indirect comparisons are available. A meta-analysis including 5 phase-III RCTs (ARISTOTLE, ENGAGE AF-TIMI48, Japanese-ROCKET AF [J-ROCKET AF], RE-LY, ROCKET AF) showed that standard-dose NOAC exhibited superior efficacy in the elderly (≥75 years) group, whereas low-dose NOACs showed equivalent efficacy compared to warfarin [21]. The efficacy of NOACs was consistent after excluding results from the edoxaban 30 mg-based regimen and the J-ROCKET AF trial. With regard to safety issues, although the overall major bleeding rate was significantly lower in the NOAC group than in the warfarin group, the benefit is observed mainly in non-elderly patients in whom both standard-dose and low-dose regimens of NOACs exhibited superior safety. In the elderly group, NOACs and warfarin exhibited equivalent safety, regardless of the NOAC dosage. The risk of ICH was significantly lower in the NOAC group than in the warfarin group, regardless of age or NOAC dosage. Moreover, the risk of GI bleeding was significantly higher in the standard-dose NOACs group than in the warfarin group in both elderly and non-elderly groups; low-dose NOACs showed a similar risk of GI bleeding in the elderly group and a lower risk in the non-elderly group. NOACs exhibited better net clinical outcomes than warfarin for both elderly and non-elderly patients in standard-dose, but not in elderly patients in low-dose regimens. Further analysis in extremely old patients (aged ≥80 years) demonstrated that standard-dose NOACs, but not low-dose NOACs, reduced IS/SE compared to warfarin [21]. Briefly, in elderly patients, standard-dose NOACs showed better efficacy and similar safety as compared to warfarin except for a trend toward more GI bleeding, whereas low-dose NOACs exhibited similar efficacy, and equivalent or better safety than warfarin. For the trend toward more GI bleeding with certain NOACs, some studies suggest avoiding concomitant antiplatelet treatment and probably considering proton pump inhibitor in elderly anticoagulated patients [36].

Some indirect comparisons among different NOACs in elderly patients were reported. A nationwide cohort study including 15361 patients aged ≥85 years showed a lower risk of ICH, mortality, and composite adverse events with dabigatran; a lower risk of ischemic stroke, ICH, mortality, and composite adverse events with rivaroxaban; and a lower risk of mortality and composite adverse events with apixaban when compared to warfarin [27]. Alnsasra et al. reported the greatest net clinical benefit in elderly AF patients treated with warfarin with time in therapeutic range ≥60% or high dose NOACs (dabigatran 150 mg twice a day, apixaban 5 mg twice a day, rivaroxaban 20 mg once a day). Schäfer et al. [36] calculated the net clinical benefit of 4 landmark trials of NOACs using the annualized rate of thromboembolic events prevented minus the annualized rate of major bleedings induced, along with ICH multiplied by different weighting factors in AF patients aged ≥75 years. Compared to warfarin, the highest and most significant benefit was demonstrated in the case of apixaban, followed by edoxaban, whereas rivaroxaban or either dose of dabigatran only provided a slight numerical benefit. They reported that the higher benefit of apixaban and edoxaban was mainly driven by fewer events of major bleeding compared to warfarin. Furthermore, the increased bleeding risks with dabigatran and rivaroxaban, compared to warfarin, were mostly limited to extracranial bleeding [37].

The ELDERCARE-AF trial included elderly AF patients (≥80 years of age) who were ineligible for OAC use at doses approved for stroke prevention and showed that edoxaban 15 mg once daily was superior to placebo for preventing IS/SE without significant increase of major bleeding [38]. Subsequently, Chao et al. [39] performed a cohort study including 15 183 elderly AF patients aged ≥80 years with enrollment criteria similar to the ELDERCARE-AF trial. They showed that use of NOACs at either the full dose or reduced dose lowered ischemic strokes by 23%, all-cause mortality by 61%, and composite outcomes by 58%, while the risks of ICH and major bleeding were similar as compared to the non-OAC group. In this cohort study, 40% of patients were taking dabigatran, 49% rivaroxaban, and 11% apixaban.

Notably, the optimal choice and dose of NOACs in elderly AF patients remain undetermined yet because of the absence of head-to-head comparisons in RCTs. Besides, the currently available trials differ in terms of inclusion and exclusion criteria, as well as of underlying stroke risks of study populations [37]. Therefore, it is too early to draw a robust conclusion regarding the choice of certain NOACs, and shared decision-making remains the most important step before NOACs are prescribed for elderly AF patients.

IMPORTANT CLINICAL FACTORS ABOUT THE ANTICOAGULATION MANAGEMENT IN ELDERLY PATIENTS WITH AF

Aging is usually accompanied by a gradual decline of renal function [40] and might influence the decision of OAC use. Khan et al. [41] observed that in the 36% of patients aged ≥75 years with eGFR <59 ml/min/1.73 m^2 at the time of NOAC initiation, all major bleeding episodes were associated with a decline in eGFR compared to baseline. Thus,
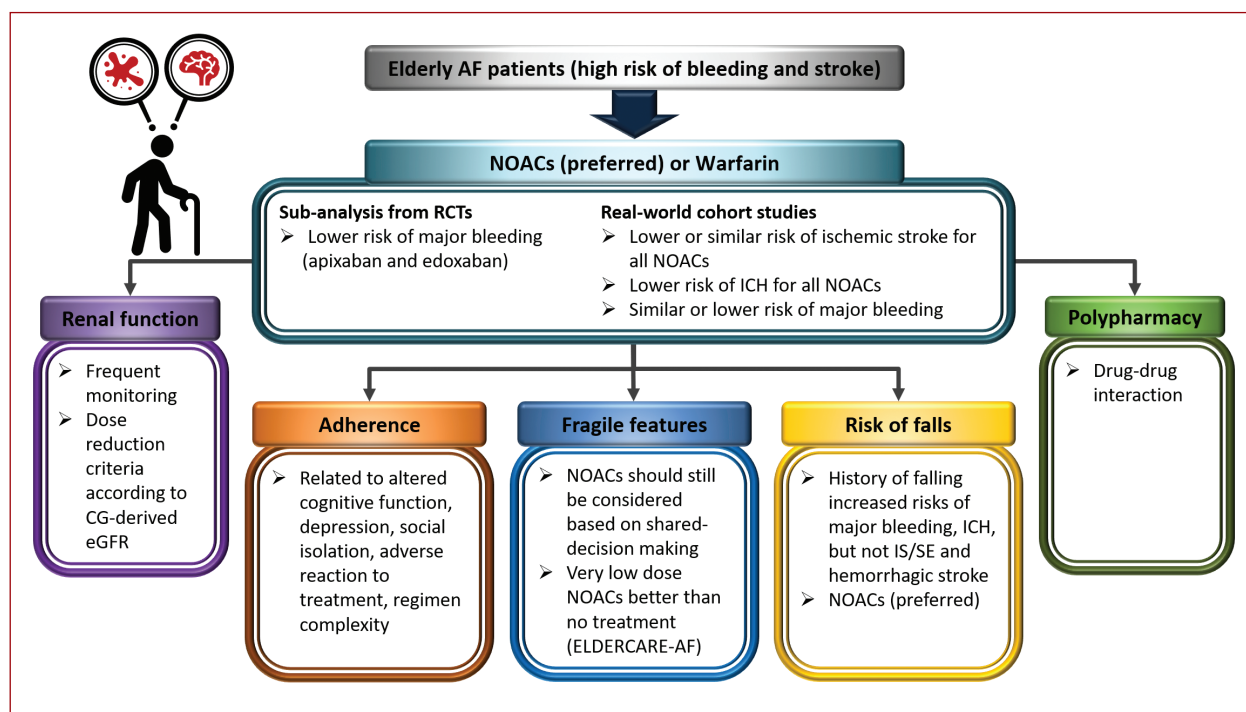
Figure 6. Considerations about the anticoagulation management in elderly patients with AF

Abbreviations: CG-derived eGFR, estimated glomerular filtration rate derived from the Cockcroft-Gault formula; IS/SE, ischemic stroke/system embolism; other — see Figures 1–3

regular monitoring of renal function is recommended in elderly anticoagulated patients to adjust the dosages of NOACs once indicated by dosage reduction criteria of each NOAC and to correct modifiable causes for patients whose renal function declines rapidly [41, 42]. A meta-analysis showed that in elderly patients, both NOACs without dose reduction in patients with creatinine clearance (CrCl) ≥50 ml/min and reduced-dosed NOACs meeting appropriate dose reduction criteria in those with a CrCl <50 ml/min behaved equivalently to warfarin for safety endpoints, which highlights the importance of following dose reduction criteria even for patients with impaired renal function [21]. The risk of falls with consequent bleeding is a common reason for not prescribing OACs in elderly AF patients [43]. In the subgroup analysis from the ARISTOTLE trial, about 5% of patients had a history of falling, and they had a more than the three-fold increased risk of fall and a more than the two-fold increased risk of any bone fracture during the trial period. Patients with a history of falling had higher rates of major bleeding and ICH, but similar rates of IS/SE and hemorrhagic stroke compared to those without a history of falls. The superiority of apixaban over warfarin in relation to efficacy and safety was consistent, irrespective of the history of falls [44]. In a secondary analysis of the ENGAGE AF-TIMI 48 trial, in patients with an increased risk of falling (but not specifically a history of falls), treatment with edoxaban resulted in a greater absolute risk reduction in severe bleeding events and all-cause death as compared to warfarin [45]. Therefore, NOACs might be an attractive choice for stroke prevention in elderly patients at risk of falling.

In a meta-analysis including patients aged 63.8– –85.9 years from 20 observational studies, frailty was associated with decreased OAC prescription on hospital admission, but not at discharge. It was also associated with the increased risk of stroke, all-cause mortality, symptom severity, and length of hospital stay [46]. Polypharmacy is frequent in elderly patients, and drug-drug interactions, although less common with NOACs, should be considered. Drugs affecting the P-glycoprotein transport system may potentially interact with NOACs, and dose reductions are sometimes recommended in elderly patients [47]. Adherence to therapy is an issue in elderly patients and possibly relates to altered cognitive function, depression, social isolation, adverse effects of treatment, and regimen complexity [48, 49]. Furthermore, physiological organ changes, malnutrition, and hypoalbuminemia with heterogeneous binding to proteins may be present in a proportion of elderly patients, thus affecting the pharmacokinetics of NOACs [14]. All these risk factors should be comprehensively assessed and taken into consideration when prescribing NOACs for elderly patients (Figure 6).

CONCLUSIONS

Aging increases the risk of adverse events in elderly AF patients, but OAC use provides clinical benefits, with the oldest patients deriving the greatest advantage. Thus, the age and fear of bleeding should not be the reasons for withholding OACs. Sub-analyses and real-world cohort studies generally favor the use of NOAC over warfarin in elderly patients, but the optimal choice and dose of NOACs

have not been determined yet. Therefore, dose adjustment according to the dose reduction criteria of each NOAC is crucial. Other risk factors potentially affecting anticoagulation treatment should be assessed carefully, such as renal function impairment, risk of falls, frailty, nutritional status, adherence to therapy, etc. More data from RCTs are urgently needed for optimal stroke prevention strategies in elderly AF patients.

Article information

Conflict of interest: None declared.

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