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Benefits and Complications of Using New Oral Anticoagulants (NOACS) in Elderly and Very Elderly Patients with Non-Valvular Atrial Fibrillation. A Comparative Study.

Agapi Fournaraki[1,2*], Mina Apostola[1,2], Ilias Katsogiannis[3], Maria Bonou[1,2]

[1]Department of Social Sciences, Hellenic Open University, Patras, Greece.

[2]Department of Medicine, University of Thessaly, Larisa, Greece.

[3]Laboratory of Hygiene and Environmental Protection, Department of Medicine, Democritus University of Thrace, Alexandroupolis, Greece.

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*** CORRESPONDING AUTHOR:**
Agapi Fournaraki, e-mail: pharmagapi@gmail.com

ABSTRACT

Atrial fibrillation (AF) is the most common arrhythmia, with an increased frequency of occurrence in older age groups. AF can cause thromboembolic events with ischemic strokes being the most common. Therefore, the role of anticoagulant therapy is central. Until a few years ago, vitamin K antagonists (VKAs) represented the most used anticoagulant drugs for the prevention of thromboembolic complications of AF. However, VKAs had many problems in use, mainly due to their narrow therapeutic range, as well as multiple drug and food interactions. The increased requirements for frequent monitoring and dose adjustments led to decreased compliance and underuse. In recent years, new oral anticoagulant drugs (NOACs) have been developed, which have radically changed the management of patients with AF. NOACs include dabigatran, which is a direct thrombin inhibitor, and rivaroxaban, apixaban and edoxaban, which are direct inhibitors of factor Xa. Phase 3 studies, as well as subsequent analyses and real-world evaluations, have shown that NOACs are more effective in preventing stroke and systemic thrombosis in olders and are considered as the best choice for elderly (>65) and very elderly (>80) patients with AF, with clear clinical benefit against warfarin, while demonstrating at least an equivalent safety profile. There are of course several differences between them, with apixaban appearing as the drug with the best efficacy and safety profile in the elderly over 75 years of age. However, the choice of the most appropriate anticoagulant treatment should take into account the individual clinical profile of each patient, evaluating each time the benefits and risks of its use.

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice, affecting up to 33.5 million people worldwide. AF is not commonly found in people under the age of 65 years (<2%), but its frequency increases with age. The demographic aging of the population and the increase in the prevalence of other conditions that predispose to AF (obesity, hypertension, diabetes) have increased its impact, with about 9% of people aged 80 years and older developing the disease. AF can cause the formation of blood clots in the left atrium, which can then embolize into the systemic circulation and most commonly the cerebral arteries (ischemic stroke). These serious complications increase the rates of morbidity and mortality in elderly patients with AF[1-7].

The administration of anticoagulant therapy is a cornerstone and urgent need for the prevention and treatment of thromboembolic events in AF. However, it carries the risk of complications, with the most significant being bleeding, sometimes life-threatening, with the elderly and very elderly being more vulnerable[8-10]. For decades, the anticoagulant therapy of choice in AF for the prevention of thromboembolic events has been the vitamin K antagonists (VKAs), as well as suboptimal treatment with aspirin. However, the disadvantages they present have led to the development of new oral anticoagulants (NOACs). These drugs have been shown to be at least as effective as VKAs in preventing thromboembolism in non-valvular AF and maintain a favorable safety profile. NOACs include dabigatran, which is a direct thrombin inhibitor, and rivaroxaban, apixaban, edoxaban, which are direct factor Xa inhibitors. NOACs were designed to achieve anticoagulation therapy in a broad range of AF patients [1,2,11]. Despite the availability of these safer alternative drugs, the use of anticoagulant therapy remains suboptimal in elderly patients with AF, at risk for bleeding events[12].

The purpose of this review is to highlight the effectiveness and safety of NOACs compared to VKAs, as well as to present comparative studies aimed at selecting the most appropriate anticoagulant in the vulnerable group of elderly patients with non-valvular AF, taking into account the individual needs of each patient.

2. Method of Literature Search

The following keywords were used to search the MEDLINE database via the PubMed search engine for the writing of this review:

- NOACS AND atrial fibrillation
- NOACS AND olders
- Atrial fibrillation AND olders
- Risks of Noacs AND elderly
- Noacs AND (complicationsORbleeding)

Articles that concerned clinical trials, meta-analyses, reviews, and systematic reviews published in the last 5 years in the English language and referring to AF and the newer anticoagulant treatment, mainly in elderly patients, were selected.

3. Results

3.1 Stratification of Thromboembolic Risk in Patients with AF (Table 1)

European guidelines recommend the use of the CHA2DS2-VASc score for categorizing thromboembolic risk when making treatment decisions for patients with AF. Using this score helps identify low-risk patients who can be excluded from anticoagulant therapy, as well as those who have an indication for anticoagulant therapy. With a CHA2DS2-VASc score of 0 in men or 1 in women, the initiation of anticoagulant therapy is not recommended due to the absence of risk factors. With a score of 1 in men or 2 in women, the use of anticoagulant therapy should be considered, weighing individual bleeding risk against the risk of stroke. In men with a score of 2 or women with a score of 3, strong recommendation is given for anticoagulant therapy, as the benefits of its use significantly outweigh the risk [4,13,14].

3.2 Antiplatelet Therapy with Aspirin

In the past, prescribing aspirin to low-risk patients for stroke prevention was common practice, as it

Table 1: CHA2DS2-VASc Scale for Estimating Thromboembolic Risk
Scoring: Low risk (0), Moderate risk (1), High risk (2-9) [4,13,14]

Risk factor	CHA2DS2 -VASc
Syncope	1 point
Hypertension	1 point
Age	1 point (65–74 years old) 2 points (≥75 years old)
Diabetes	1 point
Previous stroke or systemic embolism	2 points
Vascular disease	1 point
Female gender	1 point (only as an additional risk)

reduced the risk of stroke to some extent and was considered safer for hemorrhagic events. However, in current European guidelines, it is clearly stated that "antiplatelet monotherapy is not recommended for stroke prevention in patients with AF, regardless of the risk of stroke." It has been proven that VKAs are superior to aspirin in stroke prevention and the rates of major bleeding are similar to aspirin, both in elderly and very elderly vulnerable patients [11,15].

3.3 Vitamin K Antagonists (VKAs) (Table 2)

Vitamin K antagonists (VKAs) (warfarin, acenocoumarol) have been the recommended oral anticoagulant protection against thromboembolic complications of AF for over 50 years. However, they have several disadvantages and limitations. They have a narrow therapeutic window, resulting in even minor deviations from therapeutic levels putting patients at

Table 2: Pharmacological characteristics of warfarin[6].

PROPERTIES	VITAMIN K ANTAGONISTS
TYPE	**Warfarin**
MECHANISM OF ACTION	It inhibits the synthesis of vitamin K-dependent clotting factors
TMAX (H)	90 minutes
HALF LIFE TIME	36-42 hours
MAXIMUM ANTICOAGULANT EFFECTIVENESS	5-7 days
EXCRETION	Liver
REDUCED DOSE	It should be avoided in liver failure
LABORATORY MONITORING	INR
ANTIDOTE	Vitamin K

Table 3: Pharmacological characteristics of NOACs [16,19,20].

PROPERTIES	DABIGATRAN	RIVAROXABAN	APIXABAN	EDOXABAN
MECHANISM OF ACTION	Direct inhibitor of thrombin	Factor Xa inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
PRODRUG	Yes	No	No	No
HALF LIFE TIME (H)	12 - 14	6-13	12	12
TMAX (H)	1.5	2.5	3	1-5
BIOAVAILABILITY	7%	60%-80%	66%	60%
KIDNEY'S EXCRETION	80%	1/3 of the dose	Kidney clearance only 25%	Medium
LIVER METABOLISM	Low Does not get metabolized in CYP450	Medium (2/3 of the dose in the liver CYP (CYP3A4)	Medium CYP (CYP3A4)	Medium
INTERACTIONS WITH OTHER MEDICINES	P-gp inhibitors (ketoconazole, verapamil) P-gp inducers (rifampicin, carbamazepine)	Strong inducers and inhibitors of CYP3A4 Strong inhibitors of P-gp	Strong inducers and inhibitors of CYP3A4 and P-gp	Inducers and inhibitors of P-gp. Erythromycin, azithromycin, clarithromycin, ketoconazole, itraconazole
DOSE	150mg x 2 or 110mg x 2 and 75mg x 2 in case of kidney failure	20 mg daily 15 mg daily CrCl < 50 mL/min	5mg x 2 and 2,5mg x 2 if 2 of the following apply: age >80 years, weight< 60 kg, serum creatinine > 1,5 mg/dL	60 mg daily or 30 mg daily if CrCl< 50 mL/min or body weight <60kg
SPECIFIC REVERSAL AGENTS	Idarucizumab Aripazine	Andexanet alfa Aripazine	Andexanet alfa Aripazine	Andexanet alfa Aripazine

risk for serious complications (bleeding). Especially the elderly have an increased risk of bleeding (intracranial, gastrointestinal, etc.) due to age, comorbidities and polypharmacy. Therefore, regular monitoring of clotting with measurement of international normalized ratio (INR) and frequent dose adjustments are required to maintain a balance between effectiveness and safety in clinical practice. VKAs have slow onset of action and long half-life (dangerous when urgent surgery is needed). Genetic polymorphisms exhibited by each patient cause variable response. In addition, multiple interactions with other drugs and foods affect their activity and increase the demand for dose adjustment. All these limitations result in variable patient compliance and overall underutilization for the prevention of stroke [1,6,16].

3.4 Novel Oral Anticoagulants (NOACs) (Table 3)

NOACs (Novel Oral Anticoagulants) were designed to address the challenges of maintaining therapeutic anticoagulation in a broad range of patients with atrial fibrillation. NOACs are not antagonists of Vitamin K and include the drugs dabigatran, rivaroxaban, apixaban and edoxaban.

Most of clinical practice guidelines worldwide recommend NOACs over warfarin for the majority of non-valvular atrial fibrillation patients, as they have shown a favorable balance between efficacy and safety compared to VKAs, with significant reductions in stroke, intracranial hemorrhage and mortality. [1,2,15,17].

Advantages of NOACS in clinical practice are: [1,2,3,18]

- They are effective and safe for preventing thromboembolic events.
- Easy to use, with oral administration in a fixed dosing regimen once or twice a day.
- Have wide therapeutic windows.
- No need for laboratory monitoring of anticoagulant activity.
- Improved patient compliance, especially in the elderly.
- Rapid onset of action and short half-life after discontinuation.
- Half-life is well-defined (considering age-related increase due to renal function decrease).
- Predictable pharmacokinetics and pharmacodynamics with low inter-individual variability, even at an individual level.
- Fewer drug and food interactions.
- Cost-effectiveness for stroke prevention in non-valvular atrial fibrillation has been demonstrated in some studies.

Four large Phase III trials evaluated the non-inferiority of NOACs compared to VKAs in terms of further reducing the combined risk of stroke and systemic embolism by 19% and all-cause mortality[3].

DABIGATRAN

In the RE-LY trial, dabigatran was compared to warfarin. In the overall trial, dabigatran administered at a dose of 150mg twice daily, reduced the rate of stroke or systemic embolism by 34% with a similar rate of major bleeding. Dabigatran administered at a dose of 110mg twice daily, reduced the rate of major bleeding by 20% compared to warfarin and showed a similar rate of stroke or systemic embolism[11]. In the RE-LY trial, 7.258 (40%) of the participants were aged ≥75 years and the representation of this age group was well balanced in the three treatment categories (adjusted dose warfarin, dabigatran 110mg twice daily and dabigatran 150mg twice daily). Additionally, a subgroup analysis compared the safety and efficacy of dabigatran versus warfarin in four age groups (<75, 75 to <80, 80 to <85 and ≥85 years)[5]. The administration of dabigatran 110mg twice daily, reduced thromboembolic events by 12%, and the administration of dabigatran 150mg twice daily reduced the incidence of stroke or systemic embolism by 33%[11]. Age did not significantly affect these outcomes. However, this study showed a clear interaction between age and the risk of major bleeding in the three therapeutic categories[5]. Dabigatran 110mg twice daily was associated with major bleeding rates similar to warfarin (4.43% vs. 4.37%; p=0.89), while the dose of 150mg twice daily showed a higher risk of major bleeding (5.10% vs. 4.37% in the warfarin arm; p=0.07). This risk was related to extracranial major bleeding and was age dependent. Thus, the use of dabigatran 110mg twice daily was supported in patients aged ≥80 years, rather than dabigatran 150mg. The risk of intracranial bleeding was lower with both doses of dabigatran, regardless of age[12]. Both doses of dabigatran reduced mortality in patients aged <75 years, but were similar to warfarin in patients >85 years old[5].

RIVAROXABAN

The ROCKET-AF trial compared once-daily rivaroxaban 20mg with warfarin. In the overall trial, rivaroxaban was found to be equally effective as warfarin in preventing thromboembolic events, with a similar rate of major bleeding. In this study, 44% of patients were aged ≥75 years old. In this age group,

Table 4: Assessment of hemorrhagic risk according to the HAS-BLED scale: low risk (0), moderate risk (1-2), high risk (≥3). [13,22]

HAS-BLED	Points
Hypertension (syst>160 mmHg)	1
Kidney/liver failure (1 point each)	1 or 2
History of cerebrovascular accident (CVA) or stroke	1
Bleeding history	1
INR out of normal range	1
Age >65	1
Medicines (NSAIDs, antiplatelets) / alcohol (1 point each)	1 or 2

rivaroxaban was found to be non-inferior to warfarin in preventing thromboembolism, with a thromboembolic event rate of 2.3% (rivaroxaban) versus 2.9% (warfarin). As for bleeding events, the rates were similar, with a major bleeding rate of 4.9% in the rivaroxaban group versus 4.4% in the warfarin group. The difference in the above rate did not concern intracranial hemorrhage, which was lower in the rivaroxaban group, but rather extracranial hemorrhage, especially gastrointestinal bleeding, which was more frequent in elderly patients receiving rivaroxaban [5,11,12].

APIXABAN

The ARISTOTLE trial compared apixaban 5mg twice daily (or 2.5mg twice daily in patients with two or more of the following factors: age ≥ 80 years, body weight ≤ 60 kg, serum creatinine ≥ 1.5 mg/dL) with warfarin. In the overall trial, apixaban reduced the rate of thromboembolic events by 21% and the rate of major bleeding by 31%. In this study, 31% of patients were aged ≥ 75 years old. In this age group, apixaban reduced the incidence of stroke or systemic embolism by 29% and major bleeding by 36%. Both in the overall trial and in the subgroup of patients aged ≥ 75 years, the net clinical benefit favored apixaban, which reduced both thrombotic and major bleeding events [5,11,12].

EDOXABAN

The ENGAGE-AF trial compared edoxaban (at a full dose of 60mg or a reduced dose of 30mg once daily based on clinical criteria) with warfarin. In the overall trial, edoxaban reduced thromboembolic events by 13% and major bleeding by 20% compared to warfarin. In the study, 40% of patients were aged ≥ 75 years old. In this age group, the percentage of thromboembolic events was 1.9% in the edoxaban arm compared to 2.3% in the warfarin arm, and the percentage of major bleeding was 4% in the edoxaban arm compared to 4.8% in the warfarin arm. Therefore, edoxaban was at least as effective as warfarin in preventing stroke or systemic embolism regardless of age, while it had an additional benefit for patients aged ≥ 75 years due to the reduction in major bleeding [5,11].

3.5 Complications of NOACs in Elderly Patients

A bleeding event related to anticoagulant therapy is classified as major or non-major or minor, both of which are attributed to bleeding without a history of

prior injury or intervention[7]. A major bleeding event is characterized by extensive and/or symptomatic clinically significant bleeding, located in a critical organ/region that is potentially life-threatening, such as intracranial, intraspinal, pericardial, intraperitoneal/peritoneal, gastrointestinal, traumatic splenic rupture, and/or a decrease of at least 2 g/dl in hemoglobin or requires blood transfusion of at least 2 units[9], whereas, a minor (non-major) bleeding refers to a smaller extent of bleeding that is clinically apparent and requires management, such as hematuria, hemoptysis, epistaxis, intramuscular hematoma of the rectus abdominis muscle, etc.[7].

Specific factors have been implicated in the increased risk of bleeding in elderly patients with non-valvular atrial fibrillation, either related to the administered medication (type, dose) or non-pharmacological causes. Specifically, pre-existing comorbidities of the elderly (renal and hepatic dysfunction, diabetes, hypertension, COPD), geriatric syndromes (frailty, falls, cognitive impairment), hematologic disorders, systemic collagen diseases, thrombocytopenia, use of anti-inflammatory drugs (steroids or non-steroidal), antiplatelet agents (clopidogrel), history of bleeding (intracranial, gastrointestinal), smoking and alcohol use have been positively correlated[7].

The dual role of chronic kidney disease in the mechanism of hemorrhagic events in elderly patients with atrial fibrillation is noteworthy. On the one hand, the progressive reduction in glomerular filtration rate can affect the pharmacokinetics of NOACs due to their renal excretion, necessitating dose adjustments. On the other hand, renal dysfunction negatively affects platelet function (adhesion, aggregation), leading to disturbances in hemostasis that result in increased rates of intracranial and gastrointestinal bleeding[5,9,21].

3.6 Stratification for Hemorrhagic Risk (Table 4)

The assessment of hemorrhagic risk is performed using stratification models that include either clinical variables, such as the widely used HAS-BLED scale or biomarkers such as the ABC scale [age, biomarkers (GDF-15, cTn-hs, hemoglobin), history of bleeding]. Recently, the incorporation of new biomarkers related to cardiovascular function and the clotting process (fibrinogen plasma thrombus) is being investigated in order to improve the prognostic value of assessment models [7,13,22].

3.7 Management of Complications of NOACs in Elderly Patients (Figure 1)

The management of NOAC-associated bleeding poses a particular challenge for clinicians, as it is mainly characterized by internal bleeding with subtle clinical symptoms that can become life-threatening and the levels of anticoagulant therapy are not determined by routine coagulation laboratory tests. Specifically, the management of bleeding consists of measures for hemodynamic stabilization, blood product transfusion, and the use of specific or non-specific reversal agents. The approved specific reversal agents are idarucizumab, a monoclonal antibody that reverses dabigatran and Andexanet alfa, a recombinant coagulation factor Xa, with official approval for the reversal of rivaroxaban and apixaban. In addition, the effectiveness of new reversal agents, such as FXa(116L) and PER977 (arapazine/chiraparantag), as factor Xa reversals, is being investigated. Non-specific reversal agents that are administered adjunctively or in the absence of specific agents, include activated or non-activated prothrombin complex concentrate (4F-PCC or aPCC), antifibrinolytics such as tranexamic acid and desmopressin. Finally, it should be noted that reversal agents can sometimes have prothrombotic effects and should be strictly administered in life-threatening bleeding or pre-/perioperative in an urgent interventional procedure. It is important to closely follow the recommendations and guidelines of the treating physicians for the management of bleeding associated with NOACs [7,23,24,25].

3.8 Effectiveness of NOACS in Elderly Patients

The best available data support that NOACs have

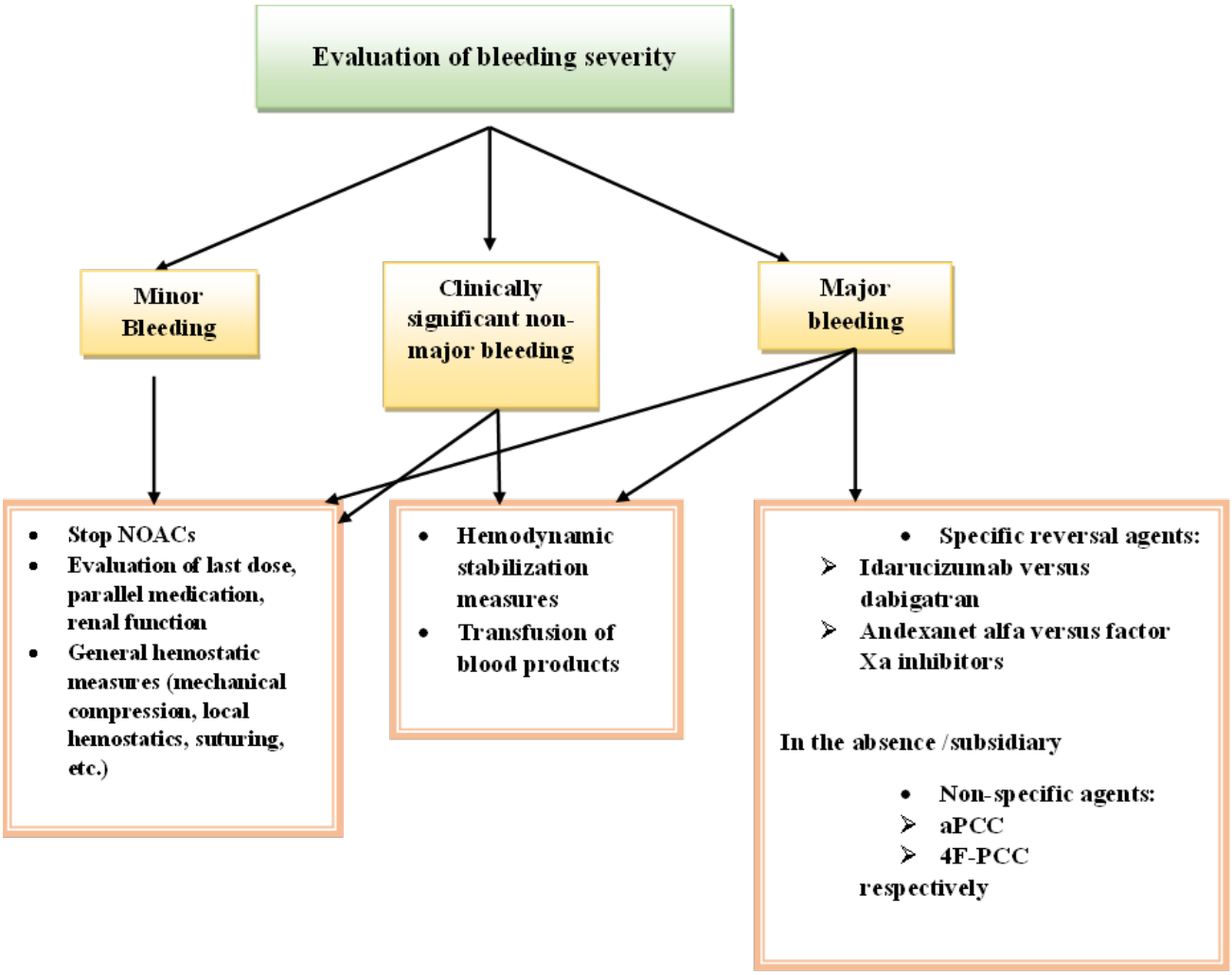

Figure 1: *Management of bleeding according to severity* [23,24,25.]

better effectiveness in the prevention of stroke and systemic thromboembolic events in elderly patients and are considered the preferred choice for elderly (over 65 years old) and very elderly (over 80 years old) patients with non-valvular atrial fibrillation, with a clear clinical benefit over warfarin [17,18].

The systematic review by Hulle et al. examined the impact of bleeding in 24,455 patients treated with NOACs compared to vitamin K antagonist and concluded that newer anticoagulants have a superior safety profile regarding all categories of bleeding events. A statistically significant difference was found in the rates of intracranial hemorrhage [7,26].

These results are also confirmed by the systematic review by Chai-Adisaksopha et al., which included randomized trials in a sample of 102,607 individuals with a median age of 70-73 years for individuals with atrial fibrillation. Specifically, a comparable safety profile was observed between NOACs and warfarin, with a significant 50% reduction in the frequency of intracranial hemorrhage in patients receiving NOACs compared to warfarin. However, the frequency of major gastrointestinal bleeding was increased with NOACs at a rate of 2.09% compared to 1.70%

with warfarin [7,9,27].

Regarding very elderly patients (over 80 years old), the meta-analysis by Bonanad et al., which included 16 studies and a sample of over 100,000 patients, revealed that newer anticoagulants were more effective and safer compared to warfarin for thromboembolic risk prevention. A statistically significant reduction of 43% in intracranial hemorrhage was observed, while the risk of major and gastrointestinal bleeding was at least equivalent, indicating that advanced age should not be a primary reason to withhold prescription of NOACs [28].

The latest review by Franco et al., examined 205 patients with an average age of 78 years old, who were under anticoagulant treatment, with respect to the occurrence of non-major bleeding. It was found that patients receiving NOACs had higher rates of gastrointestinal and genitourinary bleeding compared to those on warfarin[29].

A retrospective study by Khan et al., focused on the hemorrhagic complications of elderly patients undergoing treatment with NOACs. In total, it included 142 patients over the age of 75, of whom 36% had moderate/severe renal dysfunction. The results revealed that newer anticoagulants were a safe option for elderly individuals over the age of 75, with a hemorrhagic event rate of 1.37 per 100 person-years, while apixaban was found to be the safest among all [7,30].

The meta-analysis by Wolfe et al., examined over 100,000 patients in terms of the risk of intracranial hemorrhage comparing the four NOACs among themselves and with warfarin. Treatment with NOACs was found to be the safer option, while among the NOACs, dabigatran at a reduced dose (110 mg) was identified as superior in safety in the head-to-head comparative study, with a 56% reduction in risk compared to rivaroxaban, for this specific hemorrhagic complication[31].

In the retrospective study by Hou et al., the effect of rivaroxaban was evaluated in 299 patients over the age of 60, where adequate effectiveness against thromboembolic events was observed, while a moderate non-major bleeding occurred in 8.4% of patients, with a significant proportional increase in bleeding risk with age and dose[32].

In the NAXOS observational study by Ganse et al., involving a sample of 321,501 patients, it was observed that apixaban was superior in terms of safety, effectiveness, and mortality compared to vitamin K antagonists. Additionally, in the comparative study of NOACs, similar levels of effectiveness were attributed to all NOACs, with apixaban showing superior safety compared to rivaroxaban, while exhibiting at least a similar level of safety compared to dabigatran[33].

Lastly, according to a recent published literature review by Pazal et al., in which a comprehensive comparative study of NOACs was conducted in elderly patients with AF, apixaban was classified as the most suitable (effective/safe) for long-term treatment, ranking it in the highest category A of the FORTA scale, while other NOACs and warfarin were classified as beneficial alternatives in category FORTA B[34].

In conclusion, compared to older oral anticoagulants, NOACs are superior in preventing thromboembolic complications, while demonstrating at least an equivalent safety profile in elderly patients, even in those with moderate renal impairment[18].

Specifically:

- All NOACs are associated with similar or reduced risks of major bleeding compared to warfarin [2,35].
- Significant reduction in intracranial hemorrhage associated with the use of NOACs compared to warfarin[2,15,35].
- NOACs are associated with a higher rate of gastrointestinal bleeding compared to warfarin (the percentage varies depending on the selected NOAC and its dosage)[19,35].
- Especially for individuals aged 75 and older, the use of apixaban and edoxaban shown to be safer against gastrointestinal bleeding risk[7,9].
- There is no significant difference in the rates of fatal bleeding for any NOAC compared to warfarin[35].

Furthermore, the use of NOACs does not increase cardiovascular risk[35]. Finally, discontinuation of NOACs is easy and safe in case procedures such as sur-

gery, cardioversion, or catheter ablation are required in patients with AF[1].

4. Conclusion

The administration of anticoagulant therapy to elderly patients with non-valvular AF presents a challenge, due to the increased risk of both ischemic and hemorrhagic events. According to the recent scientific data, NOACs are an appropriate treatment option in this specific patient population, as they are superior in preventing thromboembolic complications compared to VKAs, while demonstrating at least an equivalent safety profile. However, there are several differences between them, with apixaban appearing as the drug with the best efficacy and safety profile in the elderly over 75 years of age.

Nevertheless, the clinical benefit that elderly patients with AF have from using NOACs is often undermined by clinicians due to the risk of hemorrhagic complications, mainly because of the absence of a laboratory method to determine anticoagulant activity, resulting in under-prescription. Additionally, despite the fact that the elderly are the majority users of anticoagulant therapy, they are underrepresented in clinical trials, particularly those over 80 years old, making it difficult to draw safe conclusions. Finally, the optimal recommended anticoagulation treatment in elderly patients is a combination of benefit/risk assessment through approved scoring scales (CHA2DS2 -VASc, HAS-BLED) as well as the patient's individual clinical profile (comorbidities, preferences). □

Οφέλη και Επιπλοκές από τη Χρήση Νεότερων από του Στόματος Αντιπηκτικών Φαρμάκων (NOACS) σε Ηλικιωμένους και πολύ Ηλικιωμένους Ασθενείς με Μη Βαλβιδική Κολπική Μαρμαρυγή. Συγκριτική Μελέτη.

Αγάπη Φουρναράκη[1,2*], Μίνα Αποστόλα[1,2], Ηλίας Κατσόγιαννης[3], Μαρία Μπόνου[1,2]

[1]Τμήμα Κοινωνικών Επιστημών, Ελληνικό Ανοικτό Πανεπιστήμιο, Πάτρα, Ελλάδα.

[2]Τμήμα Ιατρικής, Πανεπιστήμιο Θεσσαλίας, Λάρισα, Ελλάδα.

[3]Εργαστήριο Υγιεινής και Περιβαλλοντικής Προστασίας, Τμήμα Ιατρικής, Δημοκρίτειο Πανεπιστήμιο Θράκης, Αλεξανδρούπολη, Ελλάδα.

ΛΕΞΕΙΣ-ΚΛΕΙΔΙΑ: Κολπική μαρμαρυγή, NOACS, βαρφαρίνη, θρομβοεμβολή, ηλικιωμένοι

ΠΕΡΙΛΗΨΗ

Η κολπική μαρμαρυγή (ΚΜ) είναι η πιο συχνή αρρυθμία, με αυξημένη συχνότητα εμφάνισης σε μεγάλες ηλικιακές ομάδες. Η ΚΜ δύναται να προκαλέσει θρομβοεμβολικά συμβάντα με συνηθέστερα τα ισχαιμικά εγκεφαλικά επεισόδια. Ως εκ τούτου, ο ρόλος της αντιπηκτικής αγωγής είναι κεντρικός. Μέχρι πριν από λίγα χρόνια, οι ανταγωνιστές της βιταμίνης Κ (VKAs) αντιπροσώπευαν τα πιο συχνά χρησιμοποιούμενα αντιπηκτικά φάρμακα για την πρόληψη των θρομβοεμβολικών επιπλοκών της ΚΜ. Όμως, οι ανταγωνιστές της βιταμίνης Κ (VKAs) εμφάνιζαν πολλά προβλήματα στη χρήση, εξαιτίας κυρίως του στενού θεραπευτικού τους εύρους, αλλά και των πολλαπλών αλληλεπιδράσεων με

φάρμακα και τροφές. Οι αυξημένες απαιτήσεις για συχνή παρακολούθηση και προσαρμογές της δόσης οδηγούσε σε μειωμένη συμμόρφωση και υποχρησιμοποίηση. Τα τελευταία χρόνια αναπτύχθηκαν τα νέα από του στόματος αντιπηκτικά φάρμακα (NOACs), τα οποία άλλαξαν ριζικά τη διαχείριση των ασθενών με ΚΜ. Στα NOACs συμπεριλαμβάνονται η νταμπιγκατράνη που είναι άμεσος αναστολέας θρομβίνης και η ριβαροξαμπάνη, η απιξαμπάνη και η εντοξαμπάνη που είναι άμεσοι αναστολείς του παράγοντα Xa. Οι μελέτες φάσης 3, καθώς και μεταγενέστερες αναλύσεις και πραγματικές αξιολογήσεις έχουν αποδείξει ότι τα NOACs έχουν καλύτερη αποτελεσματικότητα στην πρόληψη του εγκεφαλικού και των συστηματικών θρομβοεμβολικών επεισοδίων σε ηλικιωμένους και θεωρούνται ως η καλύτερη επιλογή για ηλικιωμένους (άνω των 65) και πολύ ηλικιωμένους (άνω των 80) ασθενείς με ΚΜ, με καθαρό κλινικό όφελος έναντι της βαρφαρίνης, ενώ καταδεικνύουν ένα τουλάχιστον ισοδύναμο προφίλ ασφάλειας. Υπάρχουν βέβαια αρκετές διαφοροποιήσεις μεταξύ τους, με την απιξαμπάνη να εμφανίζεται ως το φάρμακο με το καλύτερο προφίλ αποτελεσματικότητας και ασφάλειας στους ηλικιωμένους άνω των 75 ετών. Ωστόσο, η επιλογή της καταλληλότερης αντιπηκτικής αγωγής θα πρέπει να λαμβάνει υπόψιν το ατομικό κλινικό προφίλ του εκάστοτε ασθενούς, αξιολογώντας κάθε φορά τα οφέλη και τους κινδύνους από τη χρήση της.

***ΣΥΓΓΡΑΦΕΑΣ ΓΙΑ ΕΠΙΚΟΙΝΩΝΙΑ:**
Αγάπη Φουρναράκη, e-mail: pharmagapi@gmail.com

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