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ORIGINAL RESEARCH ARTICLE

A Structured Literature Review and International Consensus Validation of FORTA Labels of Oral Anticoagulants for Long-Term Treatment of Atrial Fibrillation in Older Patients (OAC-FORTA 2019)

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Abstract

Introduction Evidence regarding safety and efficacy of oral anticoagulants for the treatment of atrial fibrillation (AFib) in older adults has been assessed regarding the age appropriateness of oral anticoagulants (OAC) according to the FORTA (Fit fOR The Aged) classification (OAC-FORTA). Three years after its first version (OAC-FORTA 2016), an update was initiated to create OAC-FORTA 2019.

Methods A structured review of randomized controlled clinical trials and summaries of individual product characteristics was performed to detect newly emerged evidence on oral anticoagulants in older patients with AFib. This review was used by an interdisciplinary panel of European experts ($N = 10$) in a Delphi process to label OACs according to FORTA.

Results A total of 202 records were identified and 11 studies finally included. We found four new trials providing relevant data on efficacy and safety of warfarin, apixaban, dabigatran or rivaroxaban in older patients with AFib. In the majority of studies comparing the non-vitamin-K oral anticoagulants (NOACs) with warfarin, NOACs were superior to warfarin regarding at least one relevant clinical endpoint. The mean consensus coefficient significantly increased from 0.867 (OAC-FORTA 2016) to 0.931 ($p < 0.05$) and the proposed FORTA classes were confirmed in all cases during the first round (consensus coefficient > 0.8). Warfarin, dabigatran, edoxaban and rivaroxaban were assigned to the FORTA B label, acenocoumarol, fluindione and phenprocoumon were labeled FORTA C and only apixaban was rated as FORTA A.

Conclusion OAC-FORTA 2019 confirms that AFib can be successfully treated with positively labeled antithrombotics at advanced age.

Key Points

Atrial fibrillation can be successfully treated with positively labeled oral anticoagulants such as apixaban, warfarin, dabigatran, edoxaban and rivaroxaban in older age.

More trials, especially ones aimed at patients with geriatric syndromes, are urgently needed.

1 Introduction

The most common form of cardiac arrhythmia, atrial fibrillation (AFib), affects about 2% of the general population and its prevalence has increased in recent years [1, 2]. AFib represents one of the most relevant public health issues due to its risk for major clinical effects such as stroke and dementia [1–3]. With advancing age, its prevalence increases from < 0.2% in those under the age of 49 years to about 4% in those aged 60–70 years and even rises to 10–17% in those aged 80 years and older [1, 2]. In addition, the stroke risk in patients with AFib increases with age [1]. The use of oral anticoagulants (OACs) in patients with AFib has been shown to reduce the risk of embolic stroke by over 50% [4–6]. Thus, oral anticoagulation therapy in older adults is highly successful and absolutely necessary to reduce the risk for thromboembolic stroke [7]. As for many other medications [8], there is a lack of evidence regarding safety and

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efficacy of some OACs for long-term treatment of AFib in older people [2, 5].

In 2008, the FORTA (Fit fOR The Aged) classification was proposed to improve drug prescribing in older adults [9]. It labels medications regarding their safety, efficacy and age appropriateness for the treatment of a given disease with one of the following four classes: A (indispensable), B (beneficial), C (questionable) and D (avoid) [9–12]. Based on this classification, the FORTA list [11] was developed in German-speaking countries comprising about 300 assessments for 30 age-relevant diagnoses. In a randomized controlled trial (VALFORTA) [13], the quality of medication as determined by the FORTA score (sum of over- and under-treatment errors), the occurrence of adverse drug reactions and some other relevant clinical endpoints (e.g. activities of daily living) were significantly improved by the FORTA intervention [13]. Based on these results, two updates of the FORTA list, several country-/region-specific FORTA lists and a European FORTA list have been developed [12, 14, 15].

In 2016, the appropriateness of common oral OACs for the long-term treatment of AFib in older adults was separately assessed in detail and validated on the basis of a review by an interdisciplinary panel of European experts [OAC-FORTA 2016; 5]. This detailed assessment of individual drugs was not feasible for the full FORTA list to limit its size and enhance usability; thus, the full list often issues statements on drug groups rather than individual drugs. In OAC-FORTA 2016, all non-vitamin-K antagonist oral anticoagulants and warfarin were classified as FORTA-A or -B and three other vitamin-K antagonists (VKAs) as FORTA-C. In between, the recent issue of the FORTA list [12] endorses the OAC-FORTA list at all counts, though developed by a larger and independent panel of geriatric experts.

As for the full FORTA list, updating of OAC-FORTA is deemed to be necessary after 3 years to reflect the rapid progress of evidence in the field.

Here we report on an update of the structured literature review to cover new evidence that has emerged since the first review [6] and on the related Delphi consensus procedure to establish the OAC-FORTA 2019 list.

2 Methods

In general, the procedures used in OAC-FORTA 2019 were the same as used for OAC-FORTA 2016 [5] applied to the period starting from the closing date for OAC-FORTA 2016 up until now. In brief, the process was as follows.

2.1 Structured Literature Review

A new structured literature review was performed in PubMed/MEDLINE from February 1, 2016 to May 28, 2019 using the search terms ((substance name) AND atrial fibrillation)) plus the standard filters: randomized controlled trial (RCT), full text, aged: 65+ years. The substances name was one of the following: warfarin, dabigatran, edoxaban, rivaroxaban, acenocoumarol, fluindione, phenprocoumon, apixaban.

Inclusion and exclusion criteria were identical to those used for OAC-FORTA 2016, including entries until January 31, 2016 [5]. Briefly, only randomized controlled trials with at least 100 participating patients treated by one of the substances for a minimum of 6 months were included. In addition, data on stroke and/or safety of a particular substance were required for inclusion. Secondary analyses were only included if they provided new relevant data on older patients. There were no language exclusions. Besides, only level 1 studies according to the Oxford Centre for Evidence-Based Medicine were included [16]. Abstracts were extracted into a Microsoft Word file and reviewed for appropriateness by MW and FP. The data extracted from the selected papers are depicted in Table 1 and Supplementary Table 1 (see Electronic Supplementary Material [ESM]). As before (OAC-FORTA 2016 [6]), no meta-analysis of data was conducted. The published safety/efficacy parameters were summarized and provided to the expert panel members. Besides, the validity assessment of the clinical trials was calculated by using the Jadad score, which ranges from zero (very poor) to five (rigorous) [17].

2.2 Analysis of Summary of Product Characteristics (SmPCs)

We searched for and analyzed the most recent versions of SmPCs for all drugs ($N = 8$) as previously described [5] and compared them with the 2016 versions. The European Medicines Agency website served as the preferred source for the SmPCs. In addition, we used other sources such as the manufacturers' websites or the Fachinfo-Service® (https://www.fachinfo.de/).

2.3 Recruitment of Raters and Selection of Drugs

MW had previously identified and recruited raters from several European countries based on online information. Experts were chosen if they met the following criteria: "geriatricians or cardiologists with documented clinical experience in the pharmacotherapy of older adults; high academic status; prominent standing in the leading geriatric/cardiology medical associations; substantial number, and the

Table 1 Results of the structured literature review on oral anticoagulants; if not separated, participants may have been counted twice in the age categories

	Abstracts (01 Feb 2016–28 May 2019)	Separate studies/entries fulfilling criteria	New trial	Secondary analysis from a trial contained in OAC-FORTA 2016	Patients aged > 65/70 years	Patients aged > 75/80 years	Information on geriatric syndromes
Vitamin-K antagonists							
Acenocoumarol	2	0	–	–	–	–	–
Fluindione	0	–	–	–	–	–	–
Phenprocoumon	1	0	–	–	–	–	–
Warfarin	93	11	4	7	2162	892	Edoxaban Versus Warfarin in Atrial Fibrillation Patients at Risk of Falling (ENGAGE AF TIMI 48 Analysis): 'Edoxaban is an attractive alternative to warfarin in patients at increased risk of falling, because it is associated with an even greater absolute reduction in severe bleeding events and mortality' [17]
Non-vitamin-K oral anticoagulants							
Apixaban	32	3	1	2	1646	344	–
Dabigatran	23	2	1	1	–	233	–
Edoxaban	26	2	0	2	–	–	Edoxaban Versus Warfarin in Atrial Fibrillation Patients at Risk of Falling (ENGAGE AF–TIMI 48 Analysis): 'Edoxaban is an attractive alternative to warfarin in patients at increased risk of falling, because it is associated with an even greater absolute reduction in severe bleeding events and mortality [17]
Rivaroxaban	35	3	1	2	1025	494	–

quality and relevance of publications" [5]. All raters ($N=10$) who participated in OAC-FORTA 2016 were invited and agreed to take part in this study; therefore, no new raters were required. Extensive training would have been necessary for new raters, as provided before the 2016 rating. The following lead disciplines were represented: cardiology (6 raters), geriatrics (3 raters), stroke (neurology)/geriatrics (1 rater).

The list of oral anticoagulants assessed in this study were the same as in OAC-FORTA 2016 [5].

2.4 Delphi Process

Since all participants were already familiar with the FORTA principle [5], a convention and funding were not required. We sent a summary of the selected studies, all the evidence (Table 1 and Supplementary Table 1, see ESM) and a FORTA questionnaire (Supplementary Table 3, see ESM) to all expert panel members via email. A copy of the original email is provided in Supplementary Material 1 (see ESM). The initiator proposals of FORTA classifications ($N=8$) were identical to the results of OAC-FORTA 2016 [5], confirmed by the FORTA 2018 list [12].

2.5 Statistics

The statistical analysis has been described in detail elsewhere [5, 11]. In brief, the expert panel members evaluated the OACs according to FORTA based on the evidence provided and their own knowledge/experience. The calculations of the consensus coefficient were performed as described by Kuhn-Thiel et al. [11]. In brief, the percentage of raters' FORTA classifications (excluding abstentions) agreeing with the proposed FORTA labels (A, B, C or D) was calculated for each item separately. The resulting percentages were then weighted to calculate a corrected consensus coefficient for each item reflecting the degrees of variation between the experts' individual FORTA ratings. The weights are defined

as follows: range 0: unanimity, no deviation; range 1: neighboring FORTA classes, half weight; range 2: from A to C or B to D, two-thirds weight; range 3: from A to D, full weight [18]. In this study, a second round was not required as the corrected consensus coefficient was higher than 0.8 for all substances in the first round. For the determination of the final FORTA classes, the experts' FORTA labels for each medication were converted into numerical values A = 1, B = 2, C = 3 and D = 4. The arithmetic mean m was then calculated for each drug and reconverted to FORTA labels as follows:

If $1 \leq m < 1.5$: FORTA A

If $1.5 \leq m < 2.5$: FORTA B

If $2.5 \leq m < 3.5$: FORTA C

If $m \geq 3.5$: FORTA D [5, 11]

As well, the Shapiro–Wilk test [19] was utilized to test for normality and the *t* test was used to compare the means of two groups. Statistical analyses were performed using SAS version 9.4 Software for Windows (SAS Institute Inc., Cary, NC, USA).

3 Results

3.1 Structured Literature Review

A total of 202 records were identified in the search and 130 of them were excluded at abstract level (Fig. 1). Thus, 72 articles were further assessed as full papers. Finally, 11 studies [20–30] were identified as meeting our inclusion criteria [5].

Since warfarin was used as a control for non-vitamin-K oral anticoagulants (NOACs), 10 of them had to be considered twice, for the NOAC AND for warfarin. One study by Reddy et al. [28] compared only warfarin with left atrial

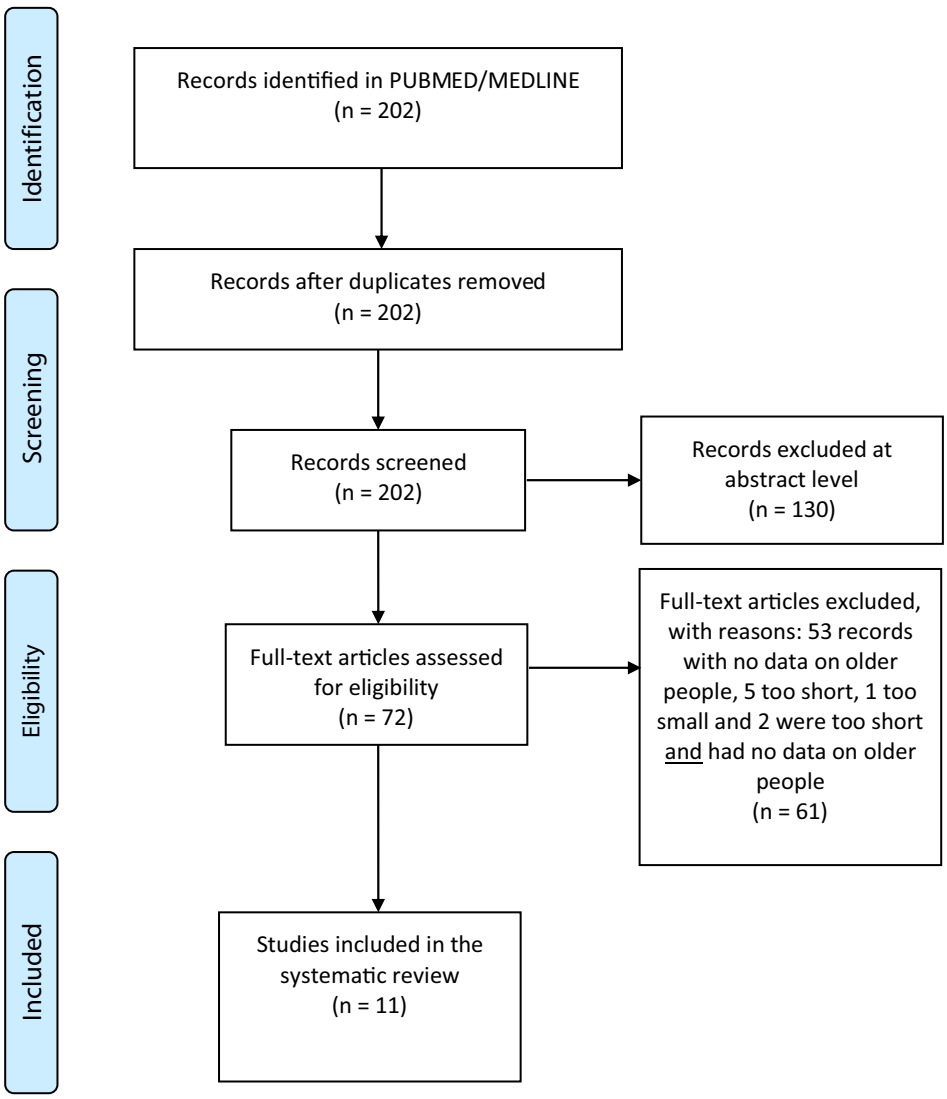

Fig. 1 Flow diagram for the structured literature review according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA)

appendage closure (LAAC) with the Watchman device (Boston Scientific, St. Paul, MN, USA).

We found few new trials ($n=4$) providing relevant data on efficacy and safety of warfarin, apixaban, dabigatran or rivaroxaban in older patients (Table 1). Three of them tested after percutaneous coronary intervention (PCI) anticoagulation in patients with AFib; there was no new trial for edoxaban. As the ENTRUST-AF PCI trial comparing edoxaban with VKAs after successful coronary stenting in AFib patients [31] was published after May 28, 2019, this study was not included here. The other seven studies on NOACS and warfarin were secondary analyses from trials already included in OAC-FORTA 2016. One of them was a secondary analysis of the ENGAGE AF-TIMI 48 trial [32] demonstrating superiority of edoxaban over warfarin in patients at risk of falling regarding severe bleeding events and mortality [30]. This was the only study with information on geriatric syndromes found here.

The total number of abstracts extracted for each substance, the numbers of included studies reporting data on older patients to support drug efficacy and safety, the number of new trials, patient numbers for different age groups and information on geriatric syndromes are provided in Table 1; the details of the studies used for the metrics in Table 1 can be found in Supplementary Table 1 (see ESM).

Again, we found no RCTs on the use of the VKAs acenocoumarol, fluindione and phenprocoumon in older patients. The highest number of patients studied originated from 11 trials assessing the use of warfarin and no new patients were analyzed using edoxaban.

The selected studies, number of patients in various age groups, relevant data on efficacy and safety such as the odds ratio, hazard ratio or event rates, duration of the treatment, methodological quality of the original studies assessed by the Jadad score [17] and relevant information on geriatric syndromes in each study are depicted in Supplementary Table 1 (see ESM). All 11 studies were of high quality according to the Jadad score (≥ 3). Six of the eleven trials even had the highest possible score of 5, indicating the highest methodological quality in these studies. Changes in the SmPCs compared with those available for OAC-FORTA 2016 are provided at the end of each section in Supplementary Table 1 (right two columns: all changes for older people and interpretation of changes regarding geriatric relevance).

Overall, in each study comparing the NOACs with warfarin, NOACs were superior to warfarin regarding at least one relevant clinical endpoint. In brief, rivaroxaban was superior to warfarin with regard to a composite of two major endpoints (all-cause death and recurrent hospitalization); apixaban was superior to warfarin for all ages (including > 75 years) with regard to intracranial hemorrhage; dabigatran was superior to warfarin for older patients (aged 80–84 or < 75 years, not in patients aged 75–79 or ≥ 85 years) with regard to risk for intracranial hemorrhage; dabigatran (110 mg) in dual therapy with a P2Y12 inhibitor was superior to a triple therapy including warfarin with regard to major or clinically relevant non-major bleeding. Finally, edoxaban was superior to warfarin regarding risk for major bleeding and intracranial hemorrhage. However, in a study stratified for increased fall risk, edoxaban was less superior to warfarin regarding one of the composite endpoints (death/stroke/systemic embolic event/major bleeding) in patients at high risk of falling as compared with patients with a low risk of falling [30]. Overall, in that study, edoxaban was generally superior to warfarin with regard to safety, efficacy and all other composite endpoints in patients at increased fall risk.

The most recent SmPCs for all substances were reviewed and changes (as compared with previous versions) relevant to geriatric patients are stated in Supplementary Table 1 (see ESM). In brief, the SmPCs of warfarin (dose-adjustment, renal impairment), fluindione (general caution in elderly patients and lower doses), apixaban (data on pharmacokinetics in older patients) and dabigatran (use of the Cockcroft–Gault method to estimate renal function) were marginally altered.

3.2 Results of the Delphi Process

The individual ratings as well as the results of the Delphi process to classify oral anticoagulants according to FORTA are depicted in Table 2. The mean consensus coefficient significantly increased from 0.867 (OAC-FORTA 2016) [5] to 0.931 ($p < 0.05$) and the proposed FORTA classes were confirmed in all cases during the first round (consensus coefficient > 0.8). The raters' comments (condensed in Table 2) are shown in full in Supplementary Table 2 (see ESM). For fluindione and phenprocoumon, one rater refrained from voting. Half of the substances were assigned to the FORTA B label (warfarin, dabigatran, edoxaban and rivaroxaban), three regionally used oral anticoagulants were labeled FORTA C (acenocoumarol, fluindione and phenprocoumon) due to the lack of appropriate data and only apixaban was rated as FORTA A. In addition, the lowest degree of agreement with the proposed FORTA labels was present for warfarin and edoxaban (consensus coefficient = 0.85 for both) and the proposed FORTA labels for apixaban, rivaroxaban and dabigatran (low intensity) were unanimously confirmed by all ten raters.

Table 2 Results of the Delphi process to label oral anticoagulants according to the Fit-fOR-The-Aged (FORTA) classification

Drug	FORTA class[a]	FORTA-A	FORTA-B	FORTA-C	FORTA-D	Number of raters[b]	Consensus coefficient (cut-off 0.800)	Comments relevant for FORTA classification
Acenocoumarol	C			9	1	10	0.95	No new data; no appropriate data—user experience only
Fluindione	C			8	1	9	0.944	No new data; no appropriate data—user experience only
Phenprocoumon	C		1	7	1	9	0.889	No new data; no appropriate data—user experience only; meanwhile big observational studies comparing phenprocoumon with NOACs are published. The results are similar to the big NOAC trials. No RCTs, but there is no evidence that phenprocoumon is less effective and safe than warfarin; in one retrospective cohort study, rivaroxaban was superior compared with phenprocoumon
Warfarin	B		7	3		10	0.85	No new data; most data indicated inferiority, especially in the elderly. Overall, VKAs should be avoided in pts older than 75 years; wealth of clinical experience, INR provides reliable measurement of anticoagulation effect and suitable for use in valvular and non-valvular atrial fibrillation and in patients with mechanical heart valves but often 'contraindicated' in older patients due to inability to attend clinics regularly, polypharmacy, poor control Risk of ICH almost double that of NOAC agents in older patients, significant dietary and drug interactions and close monitoring required and variable dose scheduling; patients with impaired renal function, depending on the comorbidity, may require lower or higher dose of warfarin; older patients require lower doses
Dabigatran Low-intensity strategy (110 mg BID)	B		10			10	1	Some new subgroup data, but results as before—it is probably safer but less potent than certain alternative DOACs; no relevant new data. However, renal safety issues are highly relevant in older patients and we do have at least one signal that dabi. 110 is not more effective concerning ICB in pts aged > 85 years; is as efficacious in preventing ischemic stroke as warfarin, safer than warfarin in terms of ICH/major bleeding, no significant close monitoring needed compared with warfarin, evidence shows renal function deteriorates faster in patients with CKD on warfarin than on dabigatran 110 mg BID and less drug interactions than warfarin but mainly renally excreted, large capsules to swallow and it cannot be removed from foil to be 'blister packed'

Table 2 (continued)

Drug	FORTA class[a]	FORTA-A	FORTA-B	FORTA-C	FORTA-D	Number of raters[b]	Consensus coefficient (cut-off 0.800)	Comments relevant for FORTA classification
Dabigatran High-intensity strategy (150 mg BID)	B	1	8	1		10	0.9	Some new subgroup data, but results as before—dabi. 150 is probably more potent but less safe than dabi. 110; renal safety issues > low-intensity strategy; high-intensity strategy should be avoided in pts aged > 80 years and should be used with caution. New data demonstrating unsafety in older pts justify downgrade from B to C; more efficacious than warfarin in preventing ischemic stroke at high dose, safer than warfarin in terms of ICH, no significant close monitoring needed compared with warfarin, evidence shows renal function deteriorates faster in patients with CKD on warfarin than on dabigatran 150 mg BID and less drug interactions than warfarin but age interaction evident in RE-LY study on clinical findings with increased major bleeding in older groups compared with VKAs, mainly renally excreted, large capsules to swallow and it cannot be removed from foil to be 'blister packed'
Edoxaban High-intensity strategy only (60 mg OD)	B	3	7			10	0.85	Falls data is reassuring but not generalizable to the real world, frail, older adult population; nor enough new data; once daily, no close monitoring needed compared with warfarin, as efficacious in preventing ischemic stroke as warfarin, reduced ICH and major bleeding compared with warfarin, no age interaction in safety or efficacy and strong safety data compared with warfarin in patients at high risk of falls
Rivaroxaban	B		10			10	1	No new data; overall the available new data do not support an upgrade from FORTA B to A. However, some data demonstrates that the kidney function might be more stable compared with VKA and there are still concerns about GI bleeding events; once daily, no close monitoring needed compared with warfarin, safer than warfarin in terms of ICH and less drug–drug interactions but higher rates of GI bleeding than warfarin and no reduction in overall major bleeding compared with VKA
Apixaban	A	10				10	1	No new data; available data supports FORTA A; as efficacious in preventing ischemic stroke as warfarin, enhanced safety with reduction in ICH and major bleeding compared with warfarin, no close monitoring needed compared with warfarin, no age interaction in trial findings, less drug interactions than warfarin and evidence of safety in patients with history of falls

The FORTA class is depicted as well as the number of raters in each FORTA category. Comments were summarized from data, summary of product characteristics (SmPC) and raters' comments (full versions are provided in Supplementary Tables 1 and 2, see ESM)

BID/BD twice a day, *CKD* chronic kidney disease, *dabi.* dabigatran, *DOAC* direct oral anticoagulant, *FORTA* Fit fOR The Aged, *GI* gastrointestinal, *ICB* intracranial bleeding, *ICH* intracerebral hemorrhage, *INR* International Normalized Ratio, *NOAC* non-vitamin-K oral anticoagulant, *OD* once daily, *pts* patients, *RCT* randomized controlled trial, *VKA* vitamin K antagonist

[a]Proposed FORTA class in parenthesis if different from result

[b]Total number of raters was 10

4 Discussion

4.1 New Evidence

As a result of scientific progress and new clinical studies in geriatrics, triennial updates of FORTA lists have been proven to be necessary and appropriate; this in particular applies to OAC-FORTA as oral anticoagulation in AFib remains of key interest for the geriatric population.

Similar to OAC-FORTA 2016, this new review of literature revealed that most (67%) of the numerous secondary analyses of RCTs do not contain subgroup analyses for older people; therefore, they still do not provide important data on safety and efficacy for the main consumers of OACs who are at highest risk for stroke and bleeding events. For instance, a recent secondary analysis of the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial [33] evaluating the outcomes among users of oral anticoagulants with AFib and a history of falling did not contain a subgroup analysis for older patients [34]. Thus, we do not yet know whether those promising results also apply for patients aged > 80 years. Therefore, the superiority of apixaban over warfarin being robust against a history of falling may only be extrapolated to older patients.

The identical inclusion and exclusion criteria used in both OAC-FORTA processes do not allow for the inclusion of registries, cohort studies or data from insurance companies, as they may be biased and often contradictory. In addition, they do not necessarily provide separate data for the population of interest. Nevertheless, the results of most registries and other data sources for geriatric patients are generally in line with OAC-FORTA and usually favor the use of NOACs over VKAs for the treatment of AFib in older people [35–40]. They do not always include detailed separate analyses for different OACs. However, they may provide data on as yet unstudied VKAs, such as those for phenprocoumon [41]; this registry reports superiority for apixaban and dabigatran, but not rivaroxaban, over phenprocoumon regarding bleeding risk.

4.2 Implications for Daily Practice and Further Research

In the OAC-FORTA 2019 assessment, an increased degree of consensus among the experienced European experts underlines the validity of the process. It is notable that for this process (unlike OAC-FORTA 2016), no funding was obtained.

OAC-FORTA 2019 underlines the opportunities of anticoagulant treatment for AFib in older people: it lists five options of positively labeled drugs (FORTA A or B). Apixaban remains the preferred NOAC in older people (FORTA A) due to an unchanged positive view of all experts on its efficacy and safety data in this population. The B-labeling of warfarin as the only positively labeled VKA probably does not reflect clearly enough the prevailing recommendations to use NOACs in older people with AFib as intermediate labels such as B – are not provided by the FORTA system. Unstudied VKAs should not be used as studied alternatives are available. As studies on OAC specifically designed for compromised, older populations are still largely absent, but urgently needed, the results of the European study of multimorbid frail older subjects with AFib (EUROSAF), a multicenter prospective observational study, are eagerly awaited [42].

4.3 Strengths

This study presents an update of OAC FORTA to include the novel evidence from clinical trials, manufacturers information and the current knowledge and experience of international experts from several European countries. This classification supports therapeutic decisions on anticoagulation in older AFib patients. It includes a variety of VKAs that are specifically used in some European countries while NOACs seem to be generally used. Therefore, OAC-FORTA appears to be applicable to the majority of European countries.

4.4 Limitations

The review may have missed relevant publications due to limitations of search terms and databases, though there were no reports on missed studies in the identical OAC-FORTA 2016 process over the past 4 years. Also, all experts originate from Europe and therefore the results may not be representative for other regions. In addition, there was no general practitioner (GP) on the panel, although GPs may utilize the OAC-FORTA recommendations as well. A face-to-face panel meeting could have facilitated information dissemination and procedural homogeneity. As all raters had participated in the first OAC-FORTA assessment, this was not considered to be necessary, an assumption that is supported by the even greater consensus in this procedure compared with the former one.

Although absent, a second panel to countercheck the ratings may have been helpful as heterogeneity could have increased due to lack of procedural experience. The limited number of FORTA categories may not allow for distinguishing subtle differences between drugs.

5 Conclusion

In summary, OAC-FORTA 2019 confirms that AFib can be successfully treated with positively labeled oral anticoagulants in older age. Emerging evidence underlines that this

recommendation seems to be valid even in patients with geriatric syndromes, in particular falls. More trials, especially aimed at this frail or vulnerable section of an aging population, are urgently needed.

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Compliance with Ethical Standards

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Conflict of interest MW was employed by AstraZeneca R&D, Mölndal, as director of discovery medicine (translational medicine) from 2003 to 2006, while on sabbatical leave from his professorship at the University of Heidelberg. Since returning to this position in January 2007, he has received lecturing and consulting fees from Sanofi-Aventis, Bayer, Berlin-Chemie, Boehringer Ingelheim, Aspen, Novartis, Takeda, Roche, Pfizer, Bristol-Myers, Daichii-Sankyo, Lilly, Otsuka, Novo-Nordisk, Shire and LEO Pharma. FWAV has received honoraria for consulting and presentations from Bayer HealthCare, Boehringer Ingelheim, BMS/Pfizer and Daiichi-Sankyo. RC has received honoraria for consulting and presentations from Bayer HealthCare, Boehringer Ingelheim, BMS/Pfizer and Daiichi-Sankyo. VMG has received honoraria for consulting and presentations from Bayer HealthCare, Boehringer Ingelheim, BMS/Pfizer and Daiichi-Sankyo. TJQ has received research support from BMS/Pfizer alliance. TJQ has received honoraria for giving non-promotional lectures from BMS/Pfizer alliance and Bayer. RH has received lecture fees from Bayer Vital GmbH, BMS, Daichii Sankyo, Novartis, Pfizer, Sanofi MSD Pasteur. DR has received honoraria for consulting from Bayer Vital GmbH, Boehringer Ingelheim and Daiichi-Sankyo. DR has received honoraria for giving non-promotional lectures from BMS/Pfizer alliance, Bayer Vital GmbH, Boehringer Ingelheim and Daiichi-Sankyo. OH received lecturing and consulting fees from Pfizer, Bristol Myers Squibb, Bayer, Novartis, Daiichi Sankyo, Servier, Leo Pharma, Boehringer Ingelheim, Astra Zeneca, Boston Scientific. GS, MH, PM and FP declare that they have no conflict of interest.

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