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AGE APPROPRIATENESS OF ORAL ANTICOAGULANTS

Atrial fibrillation afflicts approximately 13% of patients ages 75 years and older and is the leading cause of morbidity and mortality due to stroke. Atrial fibrillation is also a major risk factor for dementia. Although the risk of stroke can be significantly reduced with anticoagulant use in specific patient populations, concern has risen about whether or not the benefits of anticoagulants in the elderly outweighs the risks. This issue of *CLIPs* briefly summarizes an article that reviews oral anticoagulants for the treatment of atrial fibrillation in older (age > 65 years) patients and to classify appropriate and inappropriate drugs based on efficacy, safety, and tolerability using the Fit fOR The Aged (FORTA) classification. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at chipor@samford.edu.

Wehling M, Collins R, Gil VM, et al. Appropriateness of oral anticoagulants for the long-term treatment of atrial fibrillation in older people: results of an evidence-based review and international consensus validation process (OAC-FORTA 2016). *Drugs Aging*. 2017 May 10. doi: 10.1007/s40266-017-0466-6. [Epub ahead of print]

Introduction

- The Fit fOR The Aged (FORTA) classification was developed to assist physicians in determining the appropriate agents for their elderly patients.
- FORTA provides guidance for medication choices based on the benefit:risk profile of the patients and other factors.
- The FORTA list differs from the Beers Criteria list, which does not require much knowledge of the individual patient.
- FORTA improves medication quality and has been shown to reduce adverse drug effects (number needed to treat [NNT] = 5).
- The purpose of this study was to determine the appropriateness of anticoagulants used in the treatment of atrial fibrillation in patients >65 years of age by using the FORTA classification.
- Eight oral anticoagulants used to treat atrial fibrillation were rated by a panel of experts based on a literature review and two-step Delphi approach using the FORTA classification.

Methods

- A literature search in PubMed/MEDLINE was performed from November 2015 to February 2016 to identify appropriate articles.
- Randomized controlled trials with > 100 patients exposed to the particular drug for at least 6 months were chosen if they included patients aged ≥65 years.
- Geriatricians or cardiologists with documented clinical experience in the pharmacotherapy of older people were included on the panel.
- The medications evaluated in the study were vitamin K antagonists (e.g., warfarin, phenprocoumon, acenocoumarol and fluindione), and all non-vitamin K oral anticoagulants (NOACs; e.g., dabigatran, rivaroxaban, edoxaban, and apixaban).
- Panel members evaluated the medications based on the FORTA classification and provided recommendations for the FORTA classification.
- Medications were classified as FORTA A, B, C, D. This lettering system coincided with absolutely, beneficial, cautious, and don't.

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Results (continued)

- A total of 32 studies met the inclusion criteria.
- There was explicit data on older patients on all drugs except for phenprocoumon, acenocoumarol and fluindione.
- Warfarin had the most patients studied.
- A placebo-controlled trial of warfarin analyzed both efficacy and safety on 616 patients aged >70 years.
- NOACs were only compared to warfarin.
- Refer to Table 1 for the classifications of the anticoagulants.

Table 1: Recommendations for FORTA classification

Drug	FORTA class	Comments relevant for FORTA classification
Acenocoumarol	C	No clinical data, efficacy/safety unknown, high risk of interactions
Fluindione	C	No clinical data, efficacy/safety unknown, high risk of interactions
Phenprocoumon	C	No clinical data, efficacy/safety unknown though high exposure of large patient groups, high risk of interactions
Warfarin	B	Well studied, efficacy highly likely in the elderly, safety concerns, monitoring need, evidence on geriatric syndromes still limited, inferiority to NOACs in certain conditions, high risk of interactions
Dabigatran (low dose)	B	Large study in the elderly, efficacy/safety established with limited indications for superiority, low risk of interactions, significant renal problem, antidote available
Dabigatran (high dose)	B	Large study in the elderly, efficacy/safety established with limited indications for superiority, low risk of interactions, significant renal problem, antidote available
Edoxaban	B	Large study in the elderly, efficacy/safety established with limited indications for superiority, low risk of interactions
Rivaroxaban	B	Large study in the elderly, efficacy/safety established with the least indications for superiority, low risk of interactions
Apixaban	A	Two large studies in the elderly, efficacy/safety established with convincing data on superiority in multiple major endpoints including mortality, low risk of interactions

Discussion

- The results of the FORTA process show that, within a given drug class, the perceived appropriateness can vary greatly.
- There were not many studies that evaluated geriatric conditions. There were two older studies that evaluated the cognitive function or falls in relation to warfarin treatment.
- No relevant data on specific geriatric syndromes or side effects with geriatric relevance other than bleeding have been studied. So, the FORTA assessment was based on the efficacy/safety data, renal function, dosing regimen, etc.
- Weaknesses of this study include: only studies with >100 patients were included in the literature review and the panel of experts was small and did not include any experts form North America.
- Strengths include using the Delphi process to bring opinions from different backgrounds and there was a large degree of consensus between the raters.

Conclusion

- All NOACs and warfarin were classified as beneficial or very beneficial in older persons (FORTA-A or FORTA-B).
- Distinct advantages and disadvantages were not reflected in full for these medications
- There is a lack of evidence for the other VKAs (phenprocoumon, acenocoumarol and fluindione) used in older patients.

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