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Chapter

Anticoagulation in AF and Elderly Frail Patient: How to Face New Challenges

Alba María Costa Grille, Irene Criado Martín and Roberto Petidier Torregrossa

Abstract

Aging is an important risk factor for patients with atrial fibrillation. The estimated prevalence of atrial fibrillation in patients aged ≥80 years is 9–10%, with four- to fivefold increased risk of embolic stroke and with an estimated increased stroke risk of 1.45-fold per decade in aging. Older age is also associated with increased risk of major bleeding with oral anticoagulant (OAC) therapy. In this chapter, we will focus on the role of oral anticoagulation with new oral anticoagulants, non-vitamin K antagonist, in populations with common comorbid conditions, including age; chronic kidney disease; coronary artery disease, on multiple medication; and frailty. In patients 75 years and older, randomized trials have shown new oral anticoagulants to be as effective as warfarin, or in some cases superior, with an overall better safety profile, consistently reducing rates of intracranial hemorrhages. Prior to considering oral anticoagulant therapy in an elderly frail patient, a comprehensive assessment should be performed to include the risk and benefits, stroke risk, baseline kidney function, cognitive status, mobility and falling risk, multiple medication, nutritional status assessment, and life expectancy.

Keywords: anticoagulation, atrial fibrillation, elderly, new oral anticoagulants, frailty

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia in our daily clinical practice, affecting 4.5 million people in Europe and approximately 33.5 million people globally [1]. Estimates suggest a significant increase in AF incidence with age from 4.1/1000 under 75 years to 26.3/1000 in people older than 75 years [2]; in the same way, its prevalence rises from 0.1% in people under 55 years to 9% of those older than 80 [3–5], with an average annual cost of 2.365 € for each patient [6]. Due to the increase in life expectancy, the number of elderly people over 80 years with non-valvular AF (NVAF) will be fourfold in 2050; therefore, this group will represent over the 50% of the total of patients with this arrhythmia [4, 5], and stroke risk will increase 25–36% in elderly individuals between 80 and 89 years old [2, 7, 8].

Although people over 75 years present worse prognosis, higher mortality, and more adverse effects than those with age between 65 and 74 years [8], up to 35% of octogenarians do not receive oral anticoagulant (OAC) therapy [5]. The use of vitamin K antagonists (VKA) is reduced up to 14% for each decade of increase in
age, regardless of other stroke risk factors [5, 9]. Frequent reasons for not initiating antithrombotic treatment in frail older individuals are (1) antiplatelet therapy, (2) more than 90 years, (3) falling risk, and (4) nursing home residents, even though a strong indication and evidence show that frailty increases stroke risk but not major bleeding risk [10].

In Europe, since 2011, there is an available new family of OAC with indication for stroke and venous thromboembolism prevention in patients with NVAF. This new family includes four direct oral anticoagulants (DOACs), dabigatran (an active direct thrombin inhibitor), apixaban, edoxaban, and rivaroxaban (direct factor Xa inhibitors). Different meta-analyses have proved up to 20% reduced stroke risk, 12% reduced mortality, and 50% reduced intracranial bleeding risk, in comparison with warfarin, showing fewer drugs and food interactions, with no control needed [9, 11]. The cost-utility of these drugs has been tested by cost-effectiveness analysis [6], and benefits shown are maintained regardless of age, presenting a greater reduction on all-cause mortality, stroke, and major, intracranial, and total bleedings in older individuals, the ones that present a higher risk [12–14].

Nonetheless, studies specifically designed in elderly population are not yet available, and the current evidence exclude multimorbidity patients, polypharmacy, and geriatric syndromes and just evaluate the benefit using health indicators with low clinical impact in this population [15–17]. In addition, the mean age of the patients included in clinical trials is 5–10 years lower than mean age of real-life patients with NVAF; because of that, the current guidelines are not able to make strong recommendations for individuals of 85 years or more [5, 18]. In order to solve this lack of evidence, data from sub-group phase III pivotal trials have been used, including over 30,000 patients older than 75 years, to demonstrate efficacy of DOACs in comparison to VKA, showing equal safety profile in the older ones than in younger people [9, 19, 20] (Figure 1).

Anticoagulation in elderly patients supposes a huge challenge because of the frequent association with health conditions that can modify not only the therapy indication but also the type and dosage of drug, tolerance, adhesion, safety profile, and the results we seek. Among these health determinants, we highlight frailty, disability, comorbidity, polypharmacy, cognitive impairment, risk of falling, nursing home residents, nutritional status, oral feeding problems, sensory disorder, and personal and social issues [2, 21]. A complete comprehensive geriatric assessment (CGA) focused in identifying all these factors, combined with aging biology knowledge, a good

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6. タイトル．他生体老化的研究 2010; 5–2039432 DOI: 10.1161/JAMA.112.85432.

Figure 1.
Rates of very elderly subjects present in pivotal studies of DOAC.
calculation of global and disability-free life expectancy, and a better knowledge of elderly pharmacology and individuality side effects of OAC in this population including long time to benefit, will allow us to get a better adequacy of this therapy and to reach better health results. More clinical trials including frail aging patients and all these factors are needed in order to achieve real-life elderly population representative samples to better adjust OAC therapy in this group of age [18, 22].

2. Medication considerations in elderly patients

2.1 Thromboembolic and bleeding risk

The thrombotic risk in patients with NVAF is stratified by the CHA2DS2-VASc score: in patients with CHA2DS2-VASc score of 0, the thrombotic risk does not outweigh the risk of bleeding, so OAC is not recommended, but a CHA2DS2-VASc score of 1 or more reverses the risk/benefit balance, and anticoagulation is clearly recommended with class IA indication [23, 24].

The uncertainty arises when the score is 1; as in these patients, the stroke rate varies widely.

The thrombotic risk increase with higher CHA2DS2-VASc score. In elderly patients (75 years or older), OAC is always suitable; however, we may assess each case individually and evaluate bleeding risk, which is the most important complication in the anticoagulation treatment [24, 25].

Bleeding events are the most important complication of antithrombotic treatment, so this requires us to personalize decision-making, especially in elderly patients with multimorbidity, geriatric syndromes, frailty, or disability.

There are several scores that help us to measure bleeding risk [26], which take into account different factors associated with increasing bleeding risk, with no intention of contraindicating OAC but to modify them with our intervention, in order to increase anticoagulation therapy’s security profile.

The most widespread one is HAS-BLED score, which includes different determinants, all of them potentially modifiable, except the age. Other scores, like HEMORR2HAGES score, add some aspects that are usually included in CGA (falls, cognitive impairment) susceptible to evaluation and management by a geriatrician. The ATRIA bleeding risk score takes into account five parameters and stratify the bleeding risk into three levels [27, 28]. The ORBIT risk score proposes five determinants: age, anemia, previous bleeding episodes, renal impairment, and antiplatelet therapy. This one demonstrates similar discrimination with better sizing than HAS-BLED and ATRIA scores, according to ROCKET AF trial [29]. The ABC-bleeding score includes age, previous bleeding episodes, and three serum biomarkers (hemoglobin, troponin T, and GDF15 or cystatin C/creatinine clearance) and obtains more appropriated results than HAS-BLED and the ORBIT, according to ARISTOTLE and RE-LY trials [27], but biomarkers are not standardized, and there is no defined cut point (class IIb indication).

2.2 Suitable control of anticoagulation

Antithrombotic treatment efficacy mostly depends on an adequate maintenance of anticoagulation levels, universally measured in VKA treatment by the “international normalized ratio” or INR (therapeutic range from 2.0 to 3.0).

The poor control of anticoagulation according to INR represents one of the independent predictors most related with thrombotic and bleeding complications showing in several trials [30].
Different methods have been proposed to define VKA anticoagulation quality like control percentage out of therapeutic range, control cross-sectional analysis, and time in therapeutic range (TRT), being the last one the most widely accepted and related with complication incidence (stroke, bleeding, and mortality) [30].

The INR is considered suboptimal when TRT calculated by Rosendaal method [31] (assumes a linear progression between two INR values and calculates the specific INR for each day) is fewer than 65%. Actually, labile INR is one of the items included in HAS-BLED score, and whereas an INR value above 70% is associated with an optimal efficacy and security level, lower values increase stroke risk, major bleeding, and mortality, associating even worse prognosis than patients with NVAF not receiving antithrombotic treatment.

2.3 Frailty and falls

Frail elderly patients with NVAF must be considerately able to receive anticoagulation therapy, because of their increased vulnerability and higher functional worsening risk and disability. It is necessary to properly distinguish in the differentiation between frailty (autonomous elderly with risk of functional impairment) and disability (functional impairment established with a greater or lesser degree of autonomy) of dependency (established disability). Frailty might precede by several years the development of disability and other clinical outcomes and is a major risk factor for non-catastrophic disability [32].

The comprehensive geriatric assessment (CGA) associated with performance status test, like short performance physical battery (SPPB) or gait speed measurement, is the suitable tool to assess an individualized therapeutic decision [33–35]. Once we identify a frailty elderly, we must initiate multicomponent exercise intervention that has demonstrated reduction of multimorbidity, disability, dependence, and, thus, institutionalization and death.

Oral anticoagulation has been proposed to increase intracranial bleeding risk due to traumatic brain injury related with falls, and this has been used as a contraindication to initiate anticoagulation, increasing its under prescription as the result [36]. The evidence is limited because patients with falls are excluded from trials and also there are papers that deny that patients with OAC and higher risk of falls have increased risk of severe bleedings [37]. However, the benefit in patients with high risk (CHA2DS2-VASC >3) exceeds the risk of falls [38]. It has been estimated that a patient with anticoagulation treatment has to fall 295 times in a year so that the risk exceeds benefit of treatment [39]. Between DOACs, only edoxaban was assessed in patients with atrial fibrillation judged to be at increased risk of falling. No treatment interaction was observed between either dosing regimens of edoxaban and warfarin for the efficacy and safety outcomes. Treatment with edoxaban resulted in a greater absolute risk reduction in severe bleeding events and all-cause mortality compared with warfarin [40].

2.4 Polypharmacy

Polypharmacy is defined as the chronic administration of five or more drugs, and this may determine OAC’s choice, because risk of interactions is higher with a bigger number of medicines.

VKA treatments have frequent pharmacological interactions that require strict monitoring in disease exacerbating phases, treatment modifications, or hospital admission.

DOACs interact with fewer drugs and offer a more stable level of anticoagulation, being indicated in patients with polypharmacy. All of them are dependent on
P-glycoprotein (Pgp) transport for intestinal absorption. So concomitant use of inhibitors of this transport (amiodarone, ketoconazole, quinidine and verapamil) is expected to increase absorption and plasma concentration of DOACs, and inducers (rifampicin and carbamazepine) led to a decrease of its. Rivaroxaban and apixaban are partially metabolized by cytochrome P450 (CYP3A4), so agents considered inhibitors (azolic antifungals, ritonavir, and macrolides) increase the effect, and inducers (rifampicin, phenytoin, carbamazepine, and phenobarbital) reduce it [8, 41].

2.5 Nutritional status

Attention to nutrition is fundamental to good clinical practice. Nutrition care improves patient outcomes and reduces healthcare costs. The feed MEGlobal Group on Nutrition in Healthcare proposed Nutrition Care Pathway recommending the steps: screen always, intervene promptly when needed, and supervise routinely [42].

The nutritional status may affect OAC activity; thus, protein deficit and hypoalbuminemia in malnutrition patients raise plasma OAC concentration and, therefore, bleeding risk. Because of that, every elderly patient with NVAF may undergo nutritional status assessment before to initiate oral anticoagulation. As a screening tool, Mini Nutritional Assessment Short Form (MNA-SF) is the one recommended to identify malnutrition patients and the ones in risk for it [43].

2.6 Cognitive impairment

Dementia is not an anticoagulation contraindication by itself. Factors as severity, life expectancy, and adherence to therapy must be taken into account before indicating antithrombotic treatment [28].

Elderly patients with mild to moderate cognitive impairment (“Global Deterioration Scale” or GDS <5) have not increased bleeding risk and may receive OAC [2].

Labile INR in patients with VKA is related with progression of cognitive impairment; thus, we should consider to change DOACs in patients with moderate impair of cognitive function [8].

We do not know the bleeding risk or the benefit of anticoagulation therapy in patients with NVAF and severe cognitive impairment (GDS 6–7), but this phase of dementia is related with greater mortality and poor quality of life [33]. Therefore, not initiating OAC is an option if we reach an agreement with family/caregiver.

Cognitive impairment determines poor therapy adherence, so OAC should be initiated in patients with a responsible caregiver [2].

2.7 Mobility and disability

To evaluate the instrumental activities of daily life is useful to assess the independence to manage the medication, and to evaluate basic activities of daily life determines the access to INR control. These are two essential tools that may help to choose DOACs because they can improve adherence and security [2].

Although there is no evidence about OAC therapy risk/benefit ratio in patients with severe/total functional dependence, this situation is related with increase short- and long-term mortality and poor quality of life [30]; thus, it is fair to not indicate anticoagulation in these patients.

2.8 Life expectancy

The total life expectancy and free of disability may modify anticoagulation attitude in the elderly with NVAF. Currently, life expectancy varies a lot around the
world from the higher one of 84.1 years in Japan to the lowest one of 52.2 years in Sierra Leone. Because of that, different tools have been designed and validated to assess life expectancy in order to take the right decision, not only based on age but also considering function, frailty, and comorbidity, among other factors. Some of the most used ones are Schonberg index and Lee index, both of them available in http://ePrognosis.ucsf.edu, and Studentski tables of life expectancy according to gait speed published in 2011 [44].

The time that an intervention takes until it shows efficacy (lag time to benefit) may be taken into account as well. Managing anticoagulation therapy, this time to benefit is really short, so life expectancy over 6 months is enough to justify anti-thrombotic drug use.

3. Dosage and profile of anticoagulant agent

Different meta-analyses [19, 20, 45, 46] have evaluated clinical randomized trials in patients over 75 years and have shown that DOACs are as effective in ictus prevention as warfarin; however, there are differences between type of OAC and dosage in the case of ictus/thromboembolism rate, major bleeding, and intracranial bleeding [47, 48]. Apixaban and edoxaban demonstrated less incidence of major bleeding in comparison with VKA; nevertheless, rivaroxaban and dabigatran 110 mg have similar risk. Apixaban, edoxaban, and dabigatran were associated with lower rates of intracranial bleeding compared to VKA [46].

Regarding gastrointestinal bleeding, in patients over 75 years, dabigatran and edoxaban 60 mg have demonstrated increased gastrointestinal bleeding risk in comparison with VKA, and there is no enough evidence in regard to apixaban and rivaroxaban [14, 45].

A recent review establishes that in patients older than 75 years, apixaban 5 mg twice a day is a first choice and rivaroxaban 20 mg once daily, edoxaban 60 mg once daily, and dabigatran 110 mg twice a day are second choices [49]. Given the increasing complexity of drug prescription in the elderly, in 2008 “Fit FOR The Aged (FORTA) classification” was born with intent to guide clinicians to optimize it. Recently, a systematic review of scientific evidence plus the application of Delphi method and FORTA classification has been published assessing oral anticoagulation in elderly patients with AF taking into account efficacy, security, and tolerability. Among DOACs, only apixaban was included in category A (very beneficial) because it shows superiority in every endpoint, including major and intracranial bleeding, ictus prevention, and mortality [50]. Furthermore, real-life anticoagulation [51–53] use trials have been published recently showing similar results to pivotal trials.

4. Special considerations for dosing in the elderly

There are no randomized clinical trials evaluating anticoagulation effectiveness and safety of the DOACs versus VKA in the clinical situations outlined below. The following recommendations are based on pivotal analyses of each of the new anticoagulants.

4.1 Elderly patient with renal failure

Chronic renal failure is a risk factor for both stroke and systemic embolism and in patients with atrial fibrillation (AF) [54]. Some studies using VKA have
demonstrated the overall benefit of anticoagulation in patients with moderate to severe renal insufficiency (creatinine clearance 15–49 ml/min) despite the increased risk of bleeding [55].

In patients with mild to moderate renal failure, direct anticoagulants have been shown to decrease the incidence of systemic thromboembolism and major bleeding compared to VKA [56].

Regarding safety in patients with moderate renal insufficiency (CrCl 30–49 ml/min), apixaban has been shown to significantly reduce the risk of bleeding against VKA. No significant differences were found between dabigatran and rivaroxaban versus VKA [57]. Severe renal failure (CrCl <30 ml/min) was an exclusion criterion in the pivotal clinical trials of DOACs.

Analyzing pharmacokinetic properties, it is important to point out that 80% of dabigatran is eliminated by the kidneys, while in the case of rivaroxaban, apixaban, and edoxaban, the renal clearance is 35, 25, and 50, respectively. Based on this, dabigatran is contraindicated in patients with CrCl<30 ml/min and all “anti-factor X” when the CrCl is less than 15 ml/min [15].

In patients with severe renal failure (CrCl <15 ml/min), including dialysis patients, clinical guidelines suggest not to anticoagulate [15].

4.2 Elderly patient with liver failure

Metabolism through cytochrome P450 (CYP3A4) is null or insignificant in dabigatran and edoxaban, about 25% in apixaban and 30% in rivaroxaban.

In mild hepatic insufficiency with no alteration of coagulation, the use of DOACs is safe, although it is recommended to avoid concomitant use with other drugs that are metabolized by CYP or glycoprotein P [58]. Moderate to severe hepatic failure (Child-Pugh B or C) is a contraindication for anticoagulation with both VKA and DOACs.

4.3 Elderly patient with malnutrition or dysphagia

Unlike VKA, DOACs do not interact with elements of the diet. Data available for elderly people with low weight and corporal mass index are poor. Current recommendations subscribe not to modify the doses of rivaroxaban or dabigatran in patients with low weight. In patients with <60 kg, the dose of edoxaban should be set (30 mg/24 h) and is one of the two criteria necessary to recommend the dose reduction of apixaban (2.5 mg/12 h) [48].

The DOAC binding-protein coefficient is variable: 35% dabigatran, 50% edoxaban, 90% apixaban, and > 90% rivaroxaban [58]. There are no specific recommendations in this regard, and the published data do not indicate to modify the doses [15].

4.4 Elderly patient with a history of bleeding

In elderly patients with an episode of major bleeding, whether intracranial or digestive, in treatment with anticoagulants, it is recommended to individualize the decision of restarting anticoagulation, based on several conditions such as age, control of blood pressure, the origin of bleeding, suitable anticoagulation at the time of the bleeding, the need for antiplatelet therapy, the risk of ischemic stroke, and, in the case of intracranial origin, the location and severity of it. Anticoagulation should be initiated after treatment of the cause, with anticoagulants with a low risk of bleeding, waiting 4–8 weeks if the origin was intracranial [49].
4.5 Elderly patient with cancer or terminal organ disease

There is no available evidence to establish recommendations on anticoagulant therapy in elderly patients with atrial fibrillation and cancer or terminal organ disease. In cancer patients with atrial fibrillation, the low efficacy and safety of VKA have been documented given the interactions with cancer treatment [55]. In this scenario, DOACs could provide great advantages due to their predictable action at fixed doses. Possible limitations would come from the hemorrhagic risk, especially in gastrointestinal and central nervous system tumors, and the potential interactions with antineoplastic treatment, especially if metabolized via CYP or glycoprotein P. In the case of terminal organ disease, the prescription of drugs that prolong life or prevent disability should be avoided or interrupted, especially if the time necessary to obtain the benefit exceeds life expectancy. With regard to anticoagulants, it is recommended to suspend whenever the life expectancy is less than 6 months and is not a case of high thromboembolic risk [2, 59, 60].

4.6 Elderly patient during the perioperative period and surgery

DOACs, unlike VKA, can be maintained perioperatively, without the need for bridging therapy with heparin, given that their half-life is short, and the anticoagulant effect decreases rapidly after stopping the drug. Taking into account renal function and the risk of bleeding from surgery, a safety time period prior to the intervention can be established without the need for biological control [61].

In invasive procedures with low or moderate risk of bleeding, the anti-factor Xa must be suspended 24 hours before the intervention and 36 hours, in the event of severe renal insufficiency (CrCl <30 ml/min). In the case of dabigatran, the withdrawal should be 24–48 hours before, depending on the glomerular filtration rate. In high-risk bleeding procedures, anti-factor Xa must be discontinued 48 hours before the intervention and dabigatran 48–96 hours according to the glomerular filtration rate.

If urgent intervention is required, the procedure should be delayed at least the half-life of the drug (approximately 12 hours average) provided there is an end of effect parallel to the half-life (dabigatran, apixaban, and edoxaban) and considering the degree of renal elimination (25% apixaban, 50% edoxaban, and 80% dabigatran).

If this is not possible, there is an increased risk of bleeding that must be assessed against the urgency of the intervention. Prothrombin complex concentrates or recombinant factor VIIa should be used only in the event of significant hemorrhage, and not for prophylactic reversal [62]. In 2015, the European Medicine Agency approved the use of idarucizumab, a humanized monoclonal antibody, to reverse the effects of dabigatran in life-threatening bleeding episodes. Although not yet commercialized in Europe [63], the use of andexanet alfa has been tested for the reversal of the effects of the factor Xa inhibitors with favorable and promising results in elderly patients, still awaiting approval [64].

The resumption of treatment will depend on the postoperative hemorrhagic risk. In the case of major or urological abdominal surgery, we should wait for the absence of active hemorrhage visualized by the drainages. In procedures with good hemostasis, it can be restarted 6 hours after the intervention, but normally the indications are to restart anticoagulation 24 hours after the intervention; unless there is a high risk of bleeding, then it is suitable to wait 48/72 hours [65].

In dental extractions and other dental procedures, there is currently no knowledge enough to establish recommendations with a high level of evidence. In the bibliography, being a low-risk procedure, it recommends limiting the extractions
to a maximum of two or three pieces and not stopping the anticoagulant treatment. It is recommended to perform the intervention about 12 hours after the last dose and not to take the next dose of DOAC until a good hemostasis is achieved, around 6 hours later [66].

4.7 Nonagenarian and centennial patients

There are no data available on the efficacy and safety of DOACs in nonagenarian and centennial patients [67]. As age increases, the risk of atrial fibrillation and embolism increases but also of bleeding [68]. Apixaban is the DOAC that has less renal elimination, and, compared to the VKA, apixaban and edoxaban at low doses (30 mg) are those that had lower rates of major hemorrhages in this age group, although the latter was less effective in the prevention of ischemic stroke. A subanalysis of the ARISTOTLE study concludes that patients with atrial fibrillation and a single associated factor (advanced age, low body weight, or renal dysfunction) have an increased risk of stroke or systemic embolism and major bleeding but show consistent benefits with the dose of 5 mg twice daily of apixaban vs. warfarin compared to patients without these characteristics. The dose of apixaban 5 mg twice daily is safe, effective, and appropriate for patients with only one dose-reduction criterion [69]. There is a study that indicates that there is an increased risk of ischemic stroke or systemic embolic event, in patients with a dose of apixaban 2.5 versus warfarin [70].

4.8 Elderly patient with poor therapeutic compliance or social isolation

The lack of adherence to chronic treatment with oral anticoagulants increases the risk of thromboembolic and hemorrhagic complications [71]. Multiple reasons have been described associated with the lack of adherence to anticoagulant treatment in the elderly, such as neuropsychiatric pathology, social situation, or lack of understanding of the disease [72]. DOACs present the advantages of the fixed dosage and do not need monitoring, which could improve the adherence and persistence of the treatment [71, 73, 74].

However, the transition from VKA to DOAC has not always been shown to ensure therapeutic compliance, which is even more important since this pharmacological group has a shorter half-life than VKA [22]. Therefore, an analysis of the reasons for nonadherence should always be performed before taking the anticoagulation decision and choosing the type of anticoagulant [1–31, 33–39, 43–69, 75–77] as well as, if indicated, carrying out strategies to ensure compliance with long-term treatment, regardless of the type of anticoagulant [78].

It is known that therapeutic regimens of a single dose per day can improve adherence [79], although this aspect is questioned given the variability of drug concentration and the risk of events when a dose is forgotten [80].

5. Comprehensive geriatric assessment before making a decision about OAC

As a result of what was previously exposed, it has been proposed to carry out a complete comprehensive geriatric assessment before to initiate anticoagulation treatment in people over 75 years with NVAF. The first step would be to assess a Barthel Index and Reisberg’s GDS scale as represented in Figure 2 [75]. Apart from the presence of Barthel Index ≥85 or GDS scale ≤5, it is also recommended to assess the short physical performance battery (SPPB) to identify frailty [35]. If frailty condition
was detected, Barthel Index is between 25 and 80, or if GDS scale is 6, it is necessary to include a comprehensive geriatric assessment with a Mini Nutritional Assessment Short Form (MNA-SF®) [43] for nutritional status, CIRS-G scale [76] to evaluate comorbidity, and STOPP/START criteria [77] to assess falling risk and polypharmacy and to identify potentially inappropriate medicines. Personalized anticoagulation use is the most important approach (Table 1).

6. Summary box

- The selection of the anticoagulant drug and its dose should be carried out individually and carefully, taking into account clinical, geriatric criteria, and the preferences of the patient.

- It seems reasonable that patients who do not receive such treatment should be limited to those with an obvious contraindication and those who are considered in short value because they are in the last days of their lives with very high competitive risks.

- In patients >75 years old, DOACs as a class were superior to warfarin with respect to both efficacy and safety, showing similar efficacy in the prevention of stroke and systemic embolization between them but with lowest risk of major bleeding for apixaban and lower rates of intracranial hemorrhage for apixaban, edoxaban, and dabigatran (than rivaroxaban or warfarin).
Conflict of interest

Alba María Costa Grille and Irene Criado Martín declare no conflict of interest. Roberto Petidier Torregrossa is a consultant for Bristol-Myers Squibb Company/Pfizer Inc. and Daiichi Sankyo.

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