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ORIGINAL ARTICLE

Appropriateness of oral anticoagulant therapy prescription and its associated factors in hospitalized older people with atrial fibrillation

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Keywords appropriateness of prescription, atrial fibrillation, internal medicine and geriatric wards, older patients, oral anticoagulant

AIMS

Although oral anticoagulants (OACs) are effective in preventing stroke in older people with atrial fibrillation (AF), they are often underused in this particularly high-risk population. The aim of the present study was to assess the appropriateness of OAC prescription and its associated factors in hospitalized patients aged 65 years or older.

METHODS

Data were obtained from the retrospective phase of Simulation-based Technologies to Improve the Appropriate Use of Oral Anticoagulants in Hospitalized Elderly Patients With Atrial Fibrillation (SIM-AF) study, held in 32 Italian internal medicine and geriatric wards. The appropriateness of OAC prescription was assessed, grouping patients in those who were and were not prescribed OACs at hospital discharge. Multivariable logistic regression was used to establish factors independently associated with the appropriateness of OAC prescription.

RESULTS

A total of 328 patients were included in the retrospective phase of the study. Of these, almost 44% ($N = 143$) were inappropriately prescribed OACs, being mainly underprescribed or prescribed an inappropriate antithrombotic drug ($N = 88$). Among the patients prescribed OACs ($N = 221$), errors in the prescribed doses were the most frequent cause of inappropriate use ($N = 55$). Factors associated with a higher degree of patient frailty were inversely associated with the appropriateness of OAC prescription.

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CONCLUSIONS

In hospitalized older patients with AF, there is still a high prevalence of inappropriate OAC prescribing. Characteristics usually related to frailty are associated with the inappropriate prescribing. These findings point to the need for targeted interventions designed for internists and geriatricians, aimed at improving the appropriate prescribing of OACs in this complex and high-risk population.

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Oral anticoagulants are the recommended choice for preventing stroke in patients with atrial fibrillation, including in older people.
- The available data on oral anticoagulant prescriptions are mainly provided within the framework of cardiology settings.

WHAT THIS STUDY ADDS

- In older patients with atrial fibrillation who are hospitalized in internal medicine and geriatric wards, there is still a high prevalence of inappropriate oral anticoagulant prescription.
- Inappropriate oral anticoagulant prescribing in older people is mainly related to their underuse or to errors in the doses prescribed.
- Characteristics usually related to frailty are associated with their inappropriate prescribing.
- Targeted interventions aimed at improving the appropriate prescribing of oral anticoagulants in this complex and high-risk population are needed.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, the prevalence of which increases with age [1]. Vitamin K antagonists (VKAs) have long been the only available oral anticoagulants (OACs) in patients with nonvalvular AF for the prevention of stroke [2]. The narrow therapeutic index, drug–drug interactions and the need for close monitoring were the main disadvantages of VKAs. In order to overcome these problems, the nonvitamin K antagonist oral anticoagulants (NOACs) have been introduced onto the market, with the advantages of allowing a fixed-dose regimen and no need of regular anticoagulation monitoring. NOACs, including the direct thrombin inhibitor, **dabigatran**, and the factor Xa inhibitors, **apixaban**, **edoxaban** and **rivaroxaban**, have been demonstrated to be effective in reducing the incidence of stroke or systemic embolic events, and are safer than the most-used VKA, **warfarin** [3]. Thus, they represent the currently recommended choice of agent for preventing stroke in patients with AF, including in older people [4]. Notwithstanding these recommendations, various studies have highlighted the frequent underuse of OACs in up to 40–60% of older people with AF [5, 6], even though the benefit has been widely demonstrated in these patients [7, 8]. In older patients, OAC underuse has been associated with the prescription of antiplatelet drugs [6, 9]. However, antiplatelet agents alone have a limited role in reducing the thromboembolic risk in AF, and also are no safer than OACs in terms of the risk of bleeding, especially in the elderly [10]. Furthermore, to date, most of the available data on OAC prescriptions have been provided within the framework of cardiology settings, and in younger patients. The only data on OAC prescriptions in older people with AF who are hospitalized in internal medicine and geriatric wards comes from the REgistro POliterapie-SIMI (REPOSI) register, which confirmed that the majority of them had been undertreated or inappropriately treated with antiplatelet drugs, both before [11] and after [12] the introduction of NOACs onto the market.

With this background, the objectives of the present study were: (i) to assess the appropriateness of OAC therapy at hospital discharge, according to criteria set up by means of a revision of the published literature; and (ii) to identify the factors associated with the appropriate prescription of OACs by 32 Italian internal medicine and geriatric wards in a cohort of older patients retrospectively included in the Simulation-based Technologies to Improve the Appropriate Use of Oral Anticoagulants in Hospitalized Elderly Patients With Atrial Fibrillation (SIM-AF) study.

Methods

Setting and data collection

The study was conducted in 32 Italian internal medicine and geriatric wards participating in the SIM-AF study (ClinicalTrials.gov #NCT03188211), a cluster randomized controlled trial aimed at assessing the effectiveness of simulation-based technologies, in order to improve the appropriate use of OACs in hospitalized older patients with nonvalvular AF. The wards participating in the SIM-AF study were recruited on a voluntary basis among the Italian internal medicine and geriatric wards belonging to the REPOSI register network [13]. A detailed description of the study protocol has been published previously [14]. Briefly, the SIM-AF study was divided in a retrospective pre-intervention phase, which preceded the randomization of wards to the intervention (educational programme with simulation

technologies) or control (current clinical practice), and an in-hospital post-intervention prospective phase. In the pre-intervention observational phase, every ward retrospectively analysed the medical records of at least 10 AF patients aged 65 years or older, consecutively admitted over the previous 8 months in their hospital wards (from October 2016 up to May 2017). The principal data collected included sociodemographic characteristics, laboratory parameters [such as serum creatinine, alanine aminotransferase (ALT) and aspartate aminotransferase (AST)], pharmacological therapies and previous diseases (such as stroke, major bleeding or coronary artery bypass graft) at hospital discharge.

For the purpose of the present study, patients included in the observational retrospective phase of SIM-AF were considered for analysis. To assess the prescription of OACs, we used the following Anatomical Therapeutic Chemical classification system (ATC) codes: B01AA03 (warfarin), B01AA07 (**acenocoumarol**), B01AF01 (rivaroxaban), B01AF02 (apixaban), B01AF03 (edoxaban), B01AE07 (dabigatran). The SIM-AF project was approved by the ethics committee of the Ca' Granda Maggiore Policlinico Hospital Foundation and then by the local ethical committees of the participating centres. The study was conducted according to Good Clinical Practice and the Declaration of Helsinki.

Criteria for prescription appropriateness

By means of a revision of the published literature, we considered the European Society of Cardiology (ESC) guidelines [4], the Beers criteria [15] and the European Public Assessment Report (EPAR) – summary of products characteristics [16] in order to define whether or not the prescribed drug was appropriate. Table S1 presents the criteria we employed in the study. OAC appropriateness was first defined by looking at the type and then at the dose of the drug chosen. To assess OAC therapy appropriateness, patients were grouped into those who were and were not prescribed OACs at the time of hospital discharge. When a patient was labelled as 'not appropriate' for one criterion, his/her assessment on prescription appropriateness was stopped and thus he/she was included in the inappropriately prescribed group.

The ESC guidelines recommend that the stroke risk in AF patients is estimated through the CHA_2DS_2-VASc score [4]. In general, men with a CHA_2DS_2-VASc score of 1 or more, and women with a score of 2 or more were considered to be at moderate or high risk, and likely to benefit from OAC therapy. Thus, they were considered as 'appropriate' for nonprescription only if they reported a contraindication to OAC treatment, such as a previous adverse drug reaction or bleed, risk of poor drug adherence or potential drug–drug interaction. As we included people aged 65 years or more, no low-risk patients (CHA_2DS_2-VASc score of 0) were represented in this cohort. Men with a CHA_2DS_2-VASc score $\geq$1, and women with a score $\geq$2 who had been prescribed an antithrombotic agent other than an OAC (such as an antiplatelet drug or heparin) were considered as 'not appropriate', owing to the wrong choice of drug prescribed. A combination of an OAC with an antiplatelet agent (**aspirin** or **clopidogrel**) were considered as 'appropriate' only if prescribed within the period of 1–12 months after an elective coronary stenting [4].

With reference to the dose of OACs, the recommended dose for dabigatran is 150 mg twice daily, rivaroxaban 20 mg once daily, apixaban 5 mg twice daily and edoxaban 60 mg once daily; for warfarin, this depends on the international normalized ratio (INR) and the time in the therapeutic range (TTR). Given that the INR and TTR were assessed only at discharge, we assumed that all of the warfarin and acenocoumarol prescriptions were 'appropriate'. As presented in Table S1, the recommended and thus appropriate adjustments for NOAC doses based on the presence of chronic kidney disease [as assessed by high values of serum creatinine or creatinine clearance (CrCl)], older age, specific drug–drug interactions, high risk of gastrointestinal bleeding [as assessed by means of a HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score $\geq$3 [4] and/or the presence of previous gastrointestinal bleeding] and severe hepatic impairment (as assessed by the presence of liver failure and/or values of ALT $\geq$41 U/l^{-1} and AST $\geq$33 U l^{-1} [17]). Patients with missing values of serum creatinine, CrCl or AST plus ALT were considered 'not assessable'. Finally, contraindicated and major drug–drug interactions were assessed for NOACs according to the INTERCheck® software database, routinely updated by the IRCCS – Istituto di Ricerche Farmacologiche "Mario Negri" and validated in the hospital setting [18].

Statistical analysis

Continuous variables were expressed as median and interquartile range (IQR). Comparisons between groups were performed using the Mann–Whitney U test. Categorical variables were expressed as counts and percentages and compared with the nonprescription chi-square test. To establish factors independently associated with appropriateness of OAC prescription or nonprescription, a logistic regression analysis was performed. All variables with a $P < 0.20$ at baseline for comparison between appropriate and inappropriate patients underwent univariate analysis. All variables with a $P < 0.10$ at univariate analysis were entered into the multivariable models. Two multivariable models were set up in order to consider the body mass index (BMI) both as a continuous variable (first model) or as classes according to World Health Organization definition (second model). A two-sided P-value <0.05 was considered to be statistically significant. All analyses were performed using SPSS v. 24.0 (IBM, New York, NY, USA).

Nomenclature of targets and ligands

Key ligands in this article are hyperlinked to corresponding entries in http://www.guidetopharmacology.org, the common portal for data from the IUPHAR/BPS Guide to PHARMACOLOGY [19].

Results

Overall, 328 older patients were included in the study by 32 internal medicine and geriatric wards at hospital discharge. Among them, 221 (67.4%) were prescribed with OACs at hospital discharge. Our previous work reported the main

characteristics of prescribed and nonprescribed patients in this cohort [14]. Briefly, most of the patients prescribed OACs (52%) were men, with a mean age of 83 years. The most prescribed NOAC was apixaban (46.5%) [14].

In the present analysis, out of the 328 patients, 172 (52.4%) were considered as appropriately prescribed OACs, whereas 143 (43.6%) were not appropriately prescribed. Table 1 shows the profiles of the appropriateness of OAC prescription in prescribed and non prescribed patients at hospital discharge. Of those prescribed OACs, in 153 cases (69.2%) this was appropriate, in 55 cases (24.9%) it was not appropriate and in 13 cases (5.9%) this was not assessable. Among those that were not appropriate, most (43/55, 78.2%) presented errors in the dose prescribed (i.e. full dose when there was an indication for a reduction, or a reduced dose when there was no indication for a reduction), the majority being in the reduced dose group (32/43 patients, 74.4%). Among patients with no OAC prescription, this was appropriate in only 19 cases (18%) as, even though they were at high risk of thromboembolic events, they had a contraindication for the OAC treatment (Table S1). However, most patients (82%) were not prescribed an OAC but with another, inappropriate antithrombotic drug (i.e. the wrong choice of drug). Only two patients presented a risk for a drug–drug interaction, both being prescribed apixaban together with clarithromycin or **ritonavir**, respectively.

Table 1

Profiles of the appropriateness of prescription of oral anticoagulants (OACs) in 328 prescribed and nonprescribed patients at hospital discharge

	Patients with OAC *N* (%)	**Patients without OAC *N* (%)**
Overall	221	107
APPROPRIATE	153 (69.2)	19 (18)
a) CHA_2DS_2-VASc ≥1 (men) and ≥2 (women) but with contraindication for OAC	–	19
b) Dose	153	–
Dabigatran	11	–
Rivaroxaban	13	–
Apixaban	22	–
Edoxaban	8	–
Warfarin	93	–
Acenocoumarol	6	–
NOT APPROPRIATE	55 (24.9)	88 (82)
a) CHA_2DS_2-VASc ≥1 (men) and ≥2 (women) and no contraindication for OAC	–	–
b) CHA2DS2-VASc ≥1 (men) and ≥2 (women) with other antithrombotic monotherapy (underprescription or wrong choice of drug)	–	88
c) Dual/triple therapy without elective coronary stenting	12	–
d) Dose	43	–
Dabigatran	5	–
Rivaroxaban	14	–
Apixaban	21	–
Edoxaban	3	–
Warfarin	–	–
Acenocoumarol	–	–
NOT ASSESSABLE	13 (5.9)	–
Dabigatran	1	–
Rivaroxaban	3	–
Apixaban	9	–
Edoxaban	–	–
Warfarin	–	–
Acenocoumarol	–	–

Table 2 reports the main characteristics of patients according to the appropriateness of OAC therapy at hospital discharge. Compared with patients for whom this was not appropriate, those appropriate for OAC prescription were younger, had a higher BMI and were more likely to have a history of acute coronary syndrome but were less likely to have a history of falls, hepatic or vascular disease (defined as a previous history of acute coronary syndrome or peripheral artery disease), or a risk of bleeding. Table 3 shows the results of univariate and multivariable logistic regression analyses. In the multivariable analysis, overweight ($P = 0.04$) and having undergone a coronary artery bypass graft ($P = 0.01$) were independently associated with the appropriate prescription of OACs, whereas a history of falls ($P < 0.05$), vascular disease ($P = 0.002$) and liver disease ($P = 0.02$) were inversely associated.

Discussion

The present study evaluated the appropriateness of OAC therapy in older patients with AF who have been hospitalized in internal medicine and geriatric wards and enrolled in the

Table 2

Characteristics of patients at hospital discharge according to the appropriateness of oral anticoagulant prescription

	Appropriateness No *N* = 143	Yes *N* = 172	*P*-value
Age, years [median (IQR)]	84 [79–88]	82 [77–87]	0.033
Age classes, *n* (%)			0.108
65–74 years	18 (12.6)	29 (16.9)	
75–84 years	56 (39.2)	80 (46.5)	
≥85 years	69 (48.3)	63 (36.6)	
Female gender, *n* (%)	76 (53.1)	84 (48.8)	0.446
Living status, *n* (%)			0.312
Alone	9 (6.4)	9 (5.2)	
Family	106 (75.2)	119 (69.2)	
Institutionalized	26 (18.4)	44 (25.6)	
Marital status, *n* (%)			0.488
Alone	14 (10.0)	12 (7.0)	
Married	65 (46.4)	89 (52.0)	
Divorced/widowed	61 (43.6)	70 (40.9)	
Education status, *n* (%)			0.351
None/primary	64 (45.1)	77 (45.0)	
Secondary	68 (47.9)	88 (51.5)	
Higher degree	10 (7.0)	6 (3.5)	
History of falls, *n* (%)	35 (24.5)	24 (14.0)	0.017
Current smoking, *n* (%)	33 (23.1)	31 (18.0)	0.267
Alcohol use, n (%)	22 (15.4)	19 (11.0)	0.255
ALT, UI l^{-1} [median (IQR)] *277*	18 [13–30]	19 [14–25]	0.875
AST, UI l^{-1} [median (IQR)] *253*	22 [15–31]	20 [15–29]	0.422
CrCl, ml/min^{-1} (median [IQR]) *295*	44.4 [30.1–65.1]	44.7 [31.8–62.3]	0.944
CrCl categories, *n* (%) *295*			0.412
≥60 ml min^{-1}	39 (29.5)	45 (27.6)	
30–59 ml min^{-1}	61 (46.2)	87 (53.4)	
<30 ml min^{-1}	32 (24.2)	31 (19.0)	
BMI, kg m^{-2} (median [IQR]) *297*	24.2 [22.2–27.3]	25.7 [22.7–28.9]	0.038

(continues)

Table 2

(Continued)

	Appropriateness No *N* = 143	Yes *N* = 172	*P*-value
BMI categories, *n* (%)			0.027
Underweight	7 (5.3)	2 (1.2)	
Normal weight	69 (51.9)	67 (40.9)	
Overweight	42 (31.6)	69 (42.1)	
Obesity	15 (11.3)	26 (15.9)	
SBP, mmHg [median (IQR)] *312*	120 [110–130]	120 [110–130]	0.688
DBP, mmHg [median (IQR)] *312*	70 [60–80]	70 [60–80]	0.947
Type of AF, *n* (%)			0.083
Paroxysmal	36 (25.2)	50 (29.1)	
Persistent	77 (53.8)	97 (56.4)	
Permanent	16 (11.2)	20 (11.6)	
Unknown	14 (9.8)	5 (2.9)	
Stroke/TIA, *n* (%)	34 (23.8)	30 (17.4)	0.164
Hypertension, *n* (%)	105 (73.4)	139 (80.8)	0.118
Diabetes mellitus, *n* (%)	35 (24.5)	52 (30.2)	0.255
CKD, *n* (%)	61 (43.0)	85 (49.7)	0.233
Neoplasm, *n* (%)	31 (21.7)	27 (15.7)	0.173
Pulmonary disease, *n* (%)	38 (26.6)	56 (32.6)	0.248
Heart failure, *n* (%)	80 (55.9)	103 (59.9)	0.480
Vascular disease, *n* (%)	63 (44.1)	55 (32.0)	0.027
PTCA/CABG, *n* (%)	15 (10.5)	30 (17.4)	0.079
Liver disease, *n* (%)	18 (12.6)	11 (6.4)	0.058
Previous major bleeding, *n* (%)	19 (13.3)	16 (9.3)	0.263
Dementia, *n* (%)	37 (25.9)	30 (17.4)	0.069
Depression, *n* (%)	21 (14.7)	24 (14.0)	0.853
Polypharmacy, *n* (%)	107 (74.8)	139 (80.8)	0.201
HAS-BLED [median (IQR)]	3 [2–4]	2 [2–3]	0.015
CHA_2DS_2-VASc [median (IQR)]	5 [4–6]	5 [4–6]	0.271

AF, atrial fibrillation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CABG, coronary artery bypass graft; CKD, chronic kidney disease; CrClm creatinine clearance; DBP, diastolic blood pressure; HAS-BLED, Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly; IQR, interquartile range; PTCA, percutaneous transluminal coronary angioplasty; SBP, systolic blood pressure; TIA, transient ischaemic attack

SIM-AF study. Almost 44% of patients were inappropriately prescribed OACs, being mainly underprescribed or prescribed a wrong antithrombotic drug. Among patients prescribed OACs, dosage errors were the most frequent cause of inappropriate prescription. Factors associated with a higher perceived frailty such as older age, a history of falls, liver disease and vascular disease were inversely associated with the appropriateness of OAC prescription.

Many studies have shown that OACs are underprescribed in older people with AF, and the use of antiplatelet agents is linked to a high likelihood of OAC underuse [5, 6, 11, 12]. Our study confirmed the underprescription of OACs in favour of other antithrombotic therapy among hospitalized older patients with AF. The under- or nonprescription of OACs in older patients with AF represents a clinical paradox: the subjects who might benefit the most from such a therapy are those who are either undertreated or prescribed inappropriate antiplatelet agents. Indeed, older patients present peculiarities and clinical characteristics that make the therapeutic decision-making process highly challenging for clinicians, in that they are frailer, affected by multiple comorbidities, take several medications [20, 21] and are *per se* at a

Table 3

Results from univariate and multivariable logistic regression analyses for the appropriateness of oral anticoagulant prescribing

	OR	95% CI	*P*-value
Univariate analysis			
Age (year)	0.97	0.94–1.00	0.030
History of falls	0.50	0.28–0.89	0.018
BMI (kg m^{-2})	1.07	1.01–1.12	0.020
BMI categories			
Underweight	0.29	0.06–1.47	0.136
Normal weight (ref.)	–	–	–
Overweight	1.69	1.02–2.82	0.043
Obesity	1.79	0.87–3.66	0.114
Type of AF			
Paroxysmal (ref.)	–	–	–
Persistent	0.91	0.54–1.53	0.714
Permanent	0.90	0.41–1.97	0.792
Unknown	0.26	0.09–0.78	0.016
Stroke/TIA	0.68	0.39–1.18	0.166
Hypertension	1.52	0.90–2.59	0.120
Neoplasm	0.67	0.38–1.19	0.174
PTCA/CABG	1.80	0.93–3.50	0.082
Vascular disease	0.60	0.38–0.95	0.028
Liver disease	0.47	0.22–1.04	0.063
Dementia	0.61	0.35–1.04	0.070
Multivariable analysis: Model 1			
History of falls	0.53	0.29–0.97	0.038
BMI (per kg m^{-2})	1.08	1.02–1.14	0.010
PTCA/CABG	2.67	1.25–5.70	0.011
Vascular disease	0.42	0.25–0.72	0.002
Liver disease	0.36	0.16–0.83	0.016
Multivariable analysis: Model 2			
History of falls	0.55	0.30–1.01	0.056
BMI categories			
Underweight	0.31	0.60–1.59	0.161
Normal weight (ref.)	–	–	–
Overweight	1.76	1.04–3.00	0.037
Obesity	2.72	0.97–4.40	0.060
PTCA/CABG	2.72	1.27–5.85	0.010
Vascular disease	0.42	0.25–0.72	0.002
Liver disease	0.37	0.16–0.84	0.018

AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass graft; CI, confidence interval; OR, odds ratio; PTCA, percutaneous transluminal coronary angioplasty; ref., reference; TIA, transient ischaemic attack

high risk of bleeding [22]. Moreover, in a noncardiological setting, poor knowledge of the guidelines could have a negative impact on OAC prescription in this at-risk population. A recent study confirmed that, even if the use of anticoagulant drugs increased over time in older AF patients, the non-use of anticoagulants was due to a high bleeding risk in these patients [23], even though an overall positive assessment of the risk/benefit ratio for these drugs has been established in this population [24].

Among patients prescribed OACs, errors in the doses used were the most frequent cause of inappropriate prescription. Even if the NOACs are marketed as having simplified dosing as compared with that for warfarin, the appropriate dose of these agents is dependent on several patient-specific factors, such as age, weight, baseline renal and hepatic impairment and concomitant drug use [16]. As shown in a previous study, in which the majority of patients on an inappropriate dose of OAC were found to be on a lower dose than recommended [25], we also found that most errors were due to unnecessarily reduced doses. This is probably due to the fact that it has been shown that lower doses are associated with a reduction in the risk of major bleeding [26]. Moreover, given that an antidote for NOACs is available only for dabigatran, prescribing lower doses makes clinicians more confident about the safety of the prescription. Given the complexity of dose adjustments and the potential adverse events that may derive from inappropriate dosing, it is highly recommended that clinicians take into account patients' baseline clinical characteristics and the drugs they are taking before starting on a NOAC. This also means that, before prescribing a NOAC, it is essential to consider conducting some liver function tests, such as ALT and AST levels, which are often omitted or not routinely collected in internal medicine and geriatric wards, by contrast with other tests, such as the measurement of haemoglobin or serum creatinine levels.

Finally, our evaluation of factors associated with the appropriateness of OAC prescription highlighted that frailer patients are usually inappropriately prescribed OACs. These findings are in line with our previous results [14] and those coming from a sub-analysis from the Prevention of thromboembolic events – European Registry in Atrial Fibrillation (PREFER-AF) study [27]. A history of falls was inversely associated with the appropriate use of OACs. Among the 35 patients with a history of falls who were inappropriately prescribed, approximately one-third were prescribed no antithrombotic agent (data not shown). This was probably due to the fear of treating older patients who had already undergone a traumatic event leading to bleeding. By contrast, a third of those who were not prescribed OAC were inappropriately prescribed an antiplatelet drug (data not shown). It is known that anticoagulation is often avoided in patients with AF who are at an increased risk of falling, but a recent study showed that, even in these patients, the NOAC edoxaban resulted in a greater absolute reduction in the risk of severe bleeding events and all-cause mortality compared with warfarin [28]. In this study, the concomitant presence of vascular disease or peripheral artery disease was associated with inappropriate prescription of OACs. This is an important issue, as recent ESC guidelines for peripheral arterial diseases recommended that only OACs should be prescribed in AF patients with these diseases [29].

Limitations and strengths

The present study had some limitations. The main limitation was the overall small number of subjects involved, which would have affected the multivariable analysis results for some variables (i.e. age). Moreover, some laboratory values, such as AST and ALT levels, were missing. Furthermore, we did not collect repeated measures of INR and TTR. Finally, we were not able to follow up these patients after hospital discharge. Despite all these limitations, our data provided a reliable view on current clinical practice and on the appropriateness of OAC prescribing in older AF patients hospitalized in a large sample of Italian internal medicine and geriatric wards.

Conclusions

The study emphasizes that there is still a high prevalence of inappropriate prescribing of OACs in hospitalized older patients with AF, and that characteristics linked to frailty are associated with the inappropriate prescribing of this class of drugs. These findings call for targeted interventions by clinicians, aimed at both obtaining a deeper knowledge of the benefits and risks of OACs, and also improving the appropriate prescribing of these drugs in the older population with AF, thus increasing their use and decreasing errors in the doses prescribed. For this purpose, we hope that the SIM-AF trial will demonstrate that an educational simulation-based intervention will be effective at improving the appropriateness of OAC prescription in older patients with AF who are admitted to internal medicine and geriatric hospital wards and thus perhaps reduce the risk of thromboembolic complications in this high-risk population.

Competing Interests

There are no competing interests to declare.

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Contributors

C.F. and S.A. conceived the study and the study design, and contributed to the acquisition and assessment of the data. C.F. wrote the manuscript. M.P. performed the statistical analysis. All authors participated in discussing and interpreting the results, revised the manuscript critically for important intellectual content and approved the final draft.

Appendix

Collaborators of the Simulation-based Technologies to Improve the Appropriate Use of Oral Anticoagulants in Hospitalized Elderly Patients With Atrial Fibrillation (SIM-AF) study

Steering committee

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Table S1 Criteria for the appropriateness of oral anticoagulant (OAC) therapy in patients with atrial fibrillation