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ORIGINAL ARTICLE

Appropriateness of prescription of oral anticoagulant therapy in acutely hospitalized older people with atrial fibrillation. Secondary analysis of the SIM-AF cluster randomized clinical trial

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Aims: To assess the appropriateness of oral anticoagulant (OAC) prescription and its associated factors in acutely hospitalized elderly patients.

Methods: Data were obtained from the prospective phase of SIM-AF (SIMulation-based technologies to improve the appropriate use of oral anticoagulants in hospitalized elderly patients with Atrial Fibrillation) randomized controlled trial, aimed to test whether an educational intervention improved OAC prescription, compared to current clinical practice, in internal medicine wards. In this secondary analysis, appropriateness of OAC prescription was assessed at hospital admission and discharge.

Results: For 246 patients, no significant differences were found between arms (odds ratio 1.38, 95% confidence interval [CI] 0.84–2.28) in terms of appropriateness of OAC prescription. Globally, 92 patients (37.4%, 95% CI = 31.6–43.6%) were inappropriately prescribed or not prescribed at hospital discharge. Among 51 patients inappropriately prescribed, 82% showed errors on dosage, being mainly underdosed (n = 29, 56.9%), and among 41 inappropriately not prescribed, 98% were taking an antiplatelet drug. Factors independently associated with a lower probability of appropriateness at discharge were those related to a higher risk of bleeding (older age, higher levels of aspartate aminotransferase, history of falls, alcohol consumption) and antiplatelet prescription at admission. The prescription of OACs at admission was the strongest predictor of appropriateness at discharge (odds ratio = 7.43, 95% CI = 4.04–13.73).

Conclusions: A high proportion of hospitalized older patients with AF remains inappropriately prescribed or nonprescribed with OACs. The management of these patients at hospital admission is the strongest predictor of prescription appropriateness at discharge.

The collaborators of the SIM-AF (SIMulation-based technologies to improve the appropriate use of oral anticoagulants in hospitalized elderly patients with Atrial Fibrillation) Study are listed in the Online Appendix.

Trial Registration: ClinicalTrials.gov identifier: NCT03188211.

PI statement: The authors confirm that the PI for this paper is Carlotta Franchi.

KEYWORDS

appropriateness of prescription, clinical pharmacology, clinical trials, drug utilization, medication errors, prescribing

1 | INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia with an increasing prevalence with aging up to >10% in people older than 80 years.[1] Vitamin K antagonists (i.e. **warfarin**) have mainly been used for >20 years as oral anticoagulants (OACs) in the management of patients with AF. In more recent years, the wider therapeutic index, fewer potential drug–drug interactions, the less frequent need of patient monitoring and even a higher safety with a similar effectiveness, promoted a wider use of direct OACs (DOACs), such as **rivaroxaban**, **dabigatran**, **apixaban** and **edoxaban**.[2-4] Recent observational studies highlighted a high prevalence of inappropriateness in the prescription of DOACs, mainly due to errors in the chosen dosages.[5,6] These findings were also confirmed in a recent cluster randomized trial, the SIM-AF study (SIMulation-based technologies to improve the appropriate use of OACs in hospitalized elderly patients with Atrial Fibrillation). In the retrospective phase of the SIM-AF study 44% of patients were inappropriately prescribed at hospital discharge, mainly for underprescription or wrong choice of the antithrombotic drug.[7,8] By the end of September 2018 also the prospective phase of the SIM-AF study was concluded and complete data of older patients with AF admitted to internal medicine and geriatric wards became available.[7,8] The main results showed that the prevalence of patients prescribed with OACs increased in the intervention arm from the retrospective to the prospective phase. In the present work, we present a secondary analysis on data obtained from the prospective phase of the study, in order to assess: (i) whether or not the educational intervention improved the appropriateness of OAC prescription at hospital discharge; (ii) any change in the prevalence of appropriate prescription between hospital admission and discharge; (iii) the factors independently associated with appropriateness of OAC prescription; and (iv) the related clinical outcomes.

What is already known about this subject

- Oral anticoagulants are the drug of choice to prevent stroke in patients with atrial fibrillation (AF), also in older people.
- In older patients with AF acutely hospitalized in internal medicine and geriatric wards there is a high prevalence of inappropriate prescription of oral anticoagulants.

What this study adds

- This study confirmed that there is a high prevalence of inappropriate oral anticoagulant prescribing in older people, mainly related to errors on the prescribed doses or to the alternative prescription of antiplatelets.
- Even though the prevalence of patients appropriately prescribed increased from hospital admission to discharge, a high proportion of those appropriately prescribed at admission became inappropriate at the time of discharge.
- The management of older AF patients at hospital admission is the strongest predictor of oral anticoagulant prescription appropriateness at the time of discharge, suggesting that physicians hardly perform a critical review of antithrombotic therapies.

2 | METHODS

2.1 | Setting and data collection

This study was conducted in 32 Italian internal medicine and geriatric wards participating to the SIM-AF study (ClinicalTrials.gov #NCT03188211), a cluster randomized controlled trial aimed to assess the effectiveness of a simulation-based educational course in order to increase the use of OACs in hospitalized older patients with AF. A detailed description of the trial design was published elsewhere.[7-9] Briefly, the SIM-AF study comprised a retrospective preintervention phase, which preceded the cluster randomization of the wards to intervention (educational programme with computer-based simulation technique) or control (current clinical practice) plus in an in-hospital postintervention prospective phase followed by a 6-month postdischarge follow-up. During the retrospective preintervention phase (April to May 2017), the physicians of each hospital ward had to scrutinize the medical records of at least 10 AF patients aged 65 years or older and acutely hospitalized within the previous 6 months.[7,8] In the postintervention prospective phase, every ward consecutively scrutinized and enrolled AF patients aged 65 years or older, and acutely admitted to their hospital wards from September 2017 up to January 2018. All in all, patients aged 65 years or older with known or newly diagnosed atrial fibrillation, regardless whether or not they were prescribed with OACs and acutely admitted to the participating wards were eligible for inclusion in the study. Exclusion criteria were: absolute contraindication to OAC, re-hospitalization if a patient was already included in the study and life expectancy <6 months, consent refusal. The inclusion/exclusion criteria adopted in the pre- and postintervention phases were the same (except for the consent refusal pertaining to the prospective phase only).

The intervention had the goal of making physicians more confident in prescribing OACs to hospitalized elderly patients with AF and multiple chronic diseases, often exposed to polypharmacy. It was based on a simulation technique employing an e-learning platform called Dr Sim (http://drsim.accuratesolutions.it), which provided a highly interactive learning environment through the development of a 10 simulated clinical scenario, in which the learner is asked to manage virtual patients in the internal medicine setting. Each case dealt with specific aspects related to OAC prescription. The course was jointly developed by physicians (with expertise in thrombosis and geriatrics) and clinical pharmacologists.

The principal data collected included sociodemographic characteristics, a few laboratory parameters (such as serum creatinine, alanine aminotransferase [ALT], aspartate aminotransferase [AST]), drug therapies and previous diseases (such as stroke, major bleeding, coronary artery by-pass graft) as recorded both at hospital admission and discharge.

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 the Good Clinical Practice and the Declaration of Helsinki.

For the purpose of this study, only patients included in the prospective phase of SIM-AF were considered for analysis. To assess the prescription of OACs, we used the following Anatomical Therapeutic Chemical classification system codes: B01AA03 (warfarin), B01AA07 (**acenocoumarol**), B01AF01 (rivaroxaban), B01AF02 (apixaban), B01AF03 (edoxaban), B01AE07 (dabigatran).

2.2 | Criteria for prescription or nonprescription appropriateness

We have previously described[7] the criteria employed to define whether or not drugs were appropriately prescribed (Table S1), summing-up the European Society of Cardiology guidelines,[10] the Beers criteria[11] and the European public assessment report—summary of products characteristics.[12] OAC appropriateness was first defined looking at the type and then at the dose of the drug chosen. To assess appropriateness, patients were grouped in those prescribed or not with OACs at the time of hospital admission and discharge. When a patient was labelled as *not appropriate* for 1 criterion, their assessment was stopped.

The European Society of Cardiology guidelines recommend to estimate the 10-year risk of stroke in AF patients through the CHA_2DS_2-VASc score,[10] men with CHA_2DS_2-VASc score of 1 or more and women with 2 or more being considered at moderate or high risk and at benefit from OAC therapy. Because we only included people aged 65 years or more, all patients were eligible for OAC therapy. Thus, patients with those scores or higher were considered *appropriate* for nonprescription only if they had an absolute contraindication to OAC treatment, such as previous adverse drug reaction or bleeding, risk of poor drug adherence or potential drug–drug interaction. Patients not prescribed with OAC but prescribed with any other antithrombotic agent (such as antiplatelets or heparins) were considered *not appropriate* due to the wrong choice of drug prescribed. In particular, heparin was considered appropriately prescribed only if there was a high risk of gastrointestinal bleeding, refusal by patient of OAC therapy, before bridging to OAC therapy and when the indication was for orthopaedic surgery.

Combinations of OAC with antiplatelets (**aspirin** or **clopidogrel**) were considered *appropriate* only if prescribed within the period of 1 up to 12 months after an elective coronary stenting.[10]

Concerning the dosage of OACs in patients with AF, the recommended doses for dabigatran were 150 mg twice daily, rivaroxaban 20 mg once daily, apixaban 5 mg twice daily, edoxaban 60 mg once daily and warfarin dosages on the basis of the values of the International Normalized Ratio (INR) and the Time in Therapeutic Range (TTR). Because in this study the INR and TTR were assessed only at discharge, we assumed that all the warfarin and acenocoumarol prescriptions were *appropriate*. The recommended and thus appropriate adjustments for DOACs doses were based upon the presence of chronic kidney disease (as assessed by high serum values of creatinine or creatinine clearance), older age, lower weight, specific drug–drug interactions, a high risk of gastrointestinal bleeding (as assessed by means of a HAS-BLED score ≥ 3[10] 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 and AST $\geq$ 33 U/L[13]). Patients with missing values of serum creatinine, creatinine clearance or AST plus ALT were considered *not assessable* and then excluded from the analysis. Changes on prescription or nonprescription appropriateness from hospital admission to discharge were also evaluated.

2.3 | Statistical analysis

Demographic and clinical characteristics of the enrolled patients were summarized as proportions or medians and interquartile ranges (IQR) according to OAC appropriateness prescription. To assess patients' characteristics and prognostic factors independently associated to appropriate prescription or not prescription, the generalized estimating equation (GEE) extension of the logistic regression model was used to take into account correlations among patients within clusters. All variables with $P < .10$ at univariate analysis were then entered in the multivariable models. Three multivariable models were set up in order to consider separately adjustments for appropriateness (model I), antiplatelet use (model II) or OAC use (model III) at hospital admission. The clinical outcomes (major thromboembolic events such as stroke, transient ischaemic attack, acute coronary syndrome, other major arterial or venous thromboembolism; bleeding events; rehospitalizations for any reason and mortality) were assessed at 6 months of postdischarge follow up. The impact on these events of being appropriately or not prescribed with OACs was assessed as above. A 2-sided *P*-value <.05 was considered statistically significant. All analyses were performed using SAS v. 9.4 (SAS Institute Inc., Cary, NC, USA).

2.4 | 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.[14]

3 | RESULTS

Overall, 247 patients were included in the SIM-AF study by 32 internal medicine and geriatric wards (126 in the intervention arm and 121 in the control arm). Patients characteristics according to the intervention and control arms are reported elsewhere.[9] Of the 247 patients, 1 was not assessable for missing data and then excluded, so that 154 patients (62.3%, 95% confidence interval [CI] = 56.4–68.4%) were appropriately prescribed or not with OACs at the time of hospital discharge: 83/125 (66.4%, 95% CI = 57.7–68.4%) in the intervention arm *vs* 71/121 (58.7%, 95% CI = 49.8–67.1%) in the control arm. No statistically significant differences were found between arms (odds ratio [OR] 1.38, 95%CI 0.84–2.28). Table 1 reports the main characteristics of appropriate and not appropriate patients at hospital discharge. Briefly, compared to those not appropriately prescribed, patients appropriately prescribed with OACs were younger, more frequently males, with a less frequent history of falls, less alcohol drinking and already appropriately prescribed at the time of hospital admission. All in all, 60 patients (24.3%) were prescribed with a vitamin K antagonist. The most prescribed DOAC was apixaban (*n* = 54, 46.2%), followed by rivaroxaban (*n* = 25, 21.4%), edoxaban (*n* = 21, 17.9%), and dabigatran (*n* = 17, 14.5%). Table 2 shows the profiles of OAC therapy appropriateness according to OAC prescription at discharge. Most appropriate patients were prescribed with OACs (87.0%). Among those prescribed but not appropriately, the majority showed errors on dosage (42/51 = 82.4%), being most frequently prescribed with a reduced dose (29/42 = 69.0%). Among patients without OAC prescription (41/92 = 44.6%), 97.6% (40/41) were prescribed with an inappropriate anthitrombotic drug such as antiplatelet without any indication.

3.1 | Changes on appropriateness of OAC therapy from hospital admission to discharge

Changes in the profile of appropriateness from hospital admission to discharge are summarized in Table 3. From hospital admission to discharge there was an overall increasing proportion of patients appropriately prescribed or not (Δ = 7.6, 95%CI = 0.9–14.3). Out of 136 appropriate patients at admission, 108 (79.4%) were still appropriately prescribed at discharge but 27 (19.9%) became inappropriate. Among those not appropriate at admission (*n* = 111), 65 (58.6%) were still inappropriate at discharge, but 46 (41.4%) became appropriate.

3.2 | Factors associated to appropriateness of prescription or nonprescription of OACs

Table 4 shows the results of the multivariable logistic regression analyses. Being prescribed (OR 2.75; 95%CI 1.56–4.84) as well as being appropriately prescribed at admission (OR 2.75; 95%CI 1.56–4.84) were associated with the appropriateness of OAC prescription at hospital discharge. By contrast, older age, higher levels of AST, history of falls, alcohol consumption, being prescribed with an antiplatelet drug at hospital admission (OR 0.48; 95%CI 0.25–0.94) were associated with a lower probability of being appropriately prescribed at discharge.

3.3 | Clinical outcomes in appropriate and not appropriate patients

A total of 213 patients were assessable for follow-up: 131 among those appropriately prescribed/not prescribed and 82 among those not appropriately prescribed/not prescribed. Table S2 reports the number of clinical events according to the appropriateness profiles. No statistically significant differences were found in appropriately and not appropriately prescribed patients at hospital discharge for major thromboembolic events (OR = 0.65; 95%CI = 0.23–1.83) nor for rehospitalization (OR = 0.96; 95%CI = 0.52–1.75). Vital status was ascertained for 226 patients and 48 patients died: 17 patients among those appropriately prescribed and 31 among those not. No evidence of association between not appropriateness and death was found (OR = 1.17; 95%CI = 0.64–2.17).

4 | DISCUSSION

This study assessed the appropriateness of OAC therapy in older patients with AF acutely hospitalized in internal medicine and geriatric wards and included in the prospective phase of the SIM-AF clinical trial. Nearly 38% of these patients were still inappropriately prescribed or not prescribed with any OAC at hospital discharge: among those inappropriately prescribed, the most prevalent errors were on DOAC dosage, while, among those inappropriately not prescribed with any OAC, almost all were actually prescribed with an antiplatelet drug. Prevalence of patients appropriately prescribed slightly increased from hospital admission (55.3%) to discharge (62.6%). However, even though 41% of patients became appropriately prescribed at discharge, 20% of those appropriately prescribed at admission became inappropriate. Factors related to a higher risk of bleeding (older age, higher levels of AST, history of falls, alcohol consumption) were associated with a lower likelihood of being appropriately prescribed at discharge. The appropriateness of prescription at the time of hospital admission was the strongest predictor of appropriateness at discharge. Many studies have shown that OACs are still under prescribed in older people with AF and the alternative use of antiplatelets is associated to a high likelihood of this underuse.[9,17,18] Our study confirms the under prescription of OACs in favour of the inappropriate antithrombotic therapy among hospitalized older patients with

TABLE 1 Characteristics at hospital discharge of patients with atrial fibrillation according to the appropriateness of prescription or nonprescription of oral anticoagulants

	Appropriateness		
	Yes *n* = 154	No *n* = 92	*P*-value
Age, y (median [IQR])	81 [77–85]	84 [79–87]	.006
Age classes, *n* (%)			
65–74 y	28 (18.2)	10 (10.9)	
75–84 y	82 (53.2)	39 (42.4)	
≥85 y	44 (28.6)	43 (46.7)	
Male sex, *n* (%)	72 (46.8)	40 (43.5)	.60
Living status, *n* (%)			.18
Alone	35 (22.7)	28 (30.4)	
Family	116 (75.3)	59 (64.1)	
Institutionalized	3 (2)	5 (5.4)	
Marital status, *n* (%)			.29
Single	8 (5.2)	9 (9.8)	
Married	89 (57.8)	42 (45.6)	
Divorced/widowed	57 (37.0)	41 (44.6)	
Scholar status, *n* (%)			.14
None/primary	84 (54.5)	34 (37.0)	
Secondary	64 (41.6)	53 (57.6)	
High degree	6 (3.9)	5 (5.4)	
History of falls, *n* (%)	27 (17.5)	24 (26.1)	.03
Current smoking, *n* (%)	20 (13.0)	15 (16.3)	.46
Alcohol use, *n* (%)	15 (9.7)	19 (20.6)	.003
ALT, UI/L (median [IQR])	18 [14–27]	21 [14–32]	.03
AST, UI/L (median [IQR])	20 [16–27]	22 [16–32]	.002
CrCl, mL/min (median [IQR])	48 [34.1–67.2]	47.3 [32.7–67.5]	.32
CrCl classes, *n* (%)[4]			
>90 mL/min	14 (9.3)	5 (5.5)	
>60 mL/min	34 (22.5)	23 (25.3)	
>30 mL/min	75 (49.7)	47 (51.6)	
>15 mL/min	24 (15.9)	14 (15.4)	
0–15 mL/min	4 (2.6)	2 (2.2)	
BMI, kg/m^2 (median [IQR])	26.1 [23.4–28.7]	25.0 [22.8–28.4]	.06
SBP, mmHg (median [IQR])	130 [115–140]	130 [110–140]	.40
DBP, mmHg (median [IQR])	70 [65–80]	70 [60–80]	.32
Type of AF, *n* (%)			.93
Paroxysmal	47 (30.5)	28 (30.4)	
Persistent	23 (14.9)	12 (13.0)	
Permanent	74 (48.0)	47 (51.1)	
Unknown	10 (6.5)	5 (5.4)	
Barthel index [15]			.89
Total	19 (13.2)	9 (10.6)	
Severe	21 (14.6)	12 (14.1)	

(Continues)

TABLE 1 (Continued)

	Appropriateness		
	Yes *n* = 154	No *n* = 92	*P*-value
Moderate	28 (19.4)	20 (23.5)	
Mild	28 (19.4)	17 (20.0)	
No dependent	48 (33.3)	27 (31.8)	
Short blessed test[16]			.86
Normal	42 (29.2)	23 (27.4)	
Possible	30 (20.8)	18 (21.4)	
Moderate	45 (31.2)	30 (35.7)	
Severe	27 (18.8)	13 (15.5)	
Stroke/TIA, *n* (%)	25 (16.2)	13 (14.1)	.69
Hypertension, *n* (%)	132 (85.7)	71 (77.2)	.16
Diabetes mellitus, *n* (%)[1]	46 (29.9)	35 (38.5)	.25
CKD, *n* (%)	69 (44.8)	36 (39.1)	.40
Cancer, *n* (%)	27 (17.5)	20 (21.7)	.37
Pulmonary disease, *n* (%)	51 (33.1)	33 (35.9)	.62
Heart failure, *n* (%)	98 (63.6)	49 (53.3)	.14
PVD, *n* (%)	59 (38.3)	28 (30.4)	.26
PTCA/CABG, *n* (%)	28 (18.2)	12 (13.0)	.29
Liver disease, *n* (%)	9 (5.8)	4 (4.4)	.62
Previous major bleeding, *n* (%)	13 (8.4)	8 (8.7)	.91
Dementia, *n* (%)	29 (18.8)	15 (16.3)	.57
Depression, *n* (%)	30 (19.5)	15 (16.3)	.48
Polypharmacy, *n* (%)	129 (83.8)	72 (78.3)	.23
HAS-BLED (median [IQR])	2 [1–3]	2 [2–3]	.29
CHA_2DS_2-VASc (median [IQR])	5[4–6]	5 [4–5]	.78
Appropriateness at admission, n(%)	108 (70.1)	27 (29.3)	<.0001
OAC use at admission, n(%)	113 (73.4)	48 (52.2)	<.0001

AF = atrial fibrillation; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; CABG = coronary artery by-pass graft; CKD = chronic kidney disease; CrCl = creatinine clearance; DBP = diastolic blood pressure; IQR = interquartile range; PTCA = percutaneous transluminal coronary angioplasty; PVD = peripheral vascular disease; OAC = oral anticoagulant; SBP = systolic blood pressure; TIA = transient ischaemic attack. Polypharmacy did not include the anthithrombotic drugs.

AF.[7] Accordingly, subjects who may most benefit from such a therapy are instead those undertreated or inappropriately prescribed with antiplatelet agents. Even if the older patients present clinical characteristics that make the therapeutic decision process challenging for physicians (i.e. they are frail, affected by multimorbidity, take several medications[15,16,19-21] and are *per se* at a high risk of bleeding[22]), the overall positive risk/benefit ratio for these drugs has been previously established also in this population.[23] A recent study confirmed that, even if the use of OACs increased over time in older AF patients,[8,15,16] their nonuse was due to a high bleeding risk in these patients.[24]

Even if the DOACs were introduced with simplified dosing in comparison with vitamin K antagonists, their appropriate dosage depends upon several patient-specific factors such as age, weight, baseline renal and hepatic impairments and concomitant drug use.[25] Among patients inappropriately prescribed with DOACs, errors on the used dosages were the most frequent cause of inappropriate prescription, almost always related to unnecessarily reduced dosages. The attitude of physicians to reduce DOAC dosages is perhaps due to 2 reasons: (i) lower doses have been associated with a reduction of the risk of major bleeding[26]; (ii) to date, only dabigatran has an antidote able to reverse bleeding. The fact that internists and geriatricians are hardly confident in the management of anticoagulation in these at high risk population can explain why we found that the factors associated to a higher risk of bleeding (i.e. older age, higher levels of AST, history of falls, alcohol consumption) were those associated to a lower likelihood of prescription appropriateness at hospital discharge. We also found that prescription at hospital admission, which represents the drugs prescribed outside the hospital wards, was strongly related to prescription appropriateness at hospital discharge, suggesting that

TABLE 2 Profiles of appropriateness of oral anticoagulant (OAC) therapy in 246 prescribed and nonprescribed patients at hospital discharge

	Appropriate *n* (%)	Not appropriate *n* (%)
Overall	***154***	***92***
Patients prescribed with OACs	***134 (87.0)***	***51 (55.4)***
a) Dual/triple therapy with elective coronary stenting	10 (0.7)	-
b) Dual/triple therapy without elective coronary stenting	-	9 (17.6)
c) Heparin	1 (0.7)	
d) Dose	63 (47.0)	**42 (82.4)**
Dabigatran	11	6
Rivaroxaban	13	8
Apixaban	25	24
Edoxaban	14	4
e) Warfarin/acenocoumarol	60 (45.0)	-
Patients not prescribed with OACs	***20 (13.0)***	***41 (44.6)***
a) CHA_2DS_2-VASc $\geq$ 1 (men) and $\geq$ 2 (women) with contraindication for OAC	4 (20.0)	
b) CHA_2DS_2-VASc $\geq$ 1 (men) and $\geq$ 2 (women) without contraindication for OAC		1 (2.4)
c) Heparin	16 (80.0)	
d) CHA2DS2-VASc $\geq$ 1 (men) and $\geq$ 2 (women)with other antithrombotic monotherapy (underprescription/wrong choice of drug)		**40 (97.6)**

One patient prescribed with apixaban was not assessable for the appropriate dose because of missing value on creatinine clearance; the patient prescribed with OAC and heparin had undergone a bridging therapy for an orthopaedic surgery.

TABLE 4 Results from multivariable logistic regression analyses for OAC appropriateness of prescription or nonprescription at hospital discharge

	OR	95% CI	*P*-value
Model 1			
Age (1 y)	0.93	0.88–0.98	.01
Sex (male *vs* female)	0.93	0.52–1.65	.80
History of falls (yes *vs* no)	0.39	0.20–0.74	.004
BMI	1.01	0.97–1.06	.63
AST	0.97	0.96–0.99	.001
Alcohol consumption (yes *vs* no)	0.29	0.15–0.54	.001
Appropriateness at admission (yes *vs* no)	7.43	4.02–13.73	.0001
Model 2			
Age (1 y)	0.94	0.90–0.99	.02
Sex (male *vs* female)	1.08	0.62–1.91	.77
History of falls (yes *vs* no)	0.58	0.34–0.99	.04
BMI	1.02	0.98–1.07	.29
AST	0.97	0.96–0.99	.0009
Alcohol consumption (yes *vs* no)	0.32	0.18–0.57	.0001
Antiplatelet use at admission (yes *vs* no)	0.46	0.25–0.85	.03
Model 3			
Age (1 y)	0.95	0.90–0.99	.03
Sex (male *vs* female)	1.08	0.62–1.90	.78
History of falls (yes *vs* no)	0.49	0.29–0.84	.009
BMI	1.03	0.98–1.07	.25
AST	0.97	0.96–0.99	.001
Alcohol consumption (yes *vs* no)	0.28	0.15–0.52	.001
OAC use at admission (yes *vs* no)	2.75	1.57–4.84	.0004

AST = aspartate aminotransferase; BMI = body mass index; OAC = oral anticoagulant; OR = odd ratio.

internists and geriatricians hardly perform a critical review of patient antithrombotic therapies, preferring to maintain the same drugs previously taken by patients. At the same time, 40% of patients inappropriately prescribed at admission became appropriately prescribed at discharge, but 20% of those appropriate at admission changed to inappropriate. By contrast, in the 1-year from the retrospective[7] to the prospective phase of the SIM-AF trial, we found an overall modest improvement in OAC prescription, from 56 to 62%. We did not find that being appropriately prescribed with OACs at hospital discharge resulted in a better clinical outcome at 6-month follow up. This is certainly due to the small number of clinical events which occurred in this short-term follow-up period. In the frame of the ORBIT-AF II registry,

TABLE 3 Changes in appropriateness from hospital admission to discharge

Discharge admission	Appropriate	Not appropriate (choice of drugs)	Not appropriate (dose)	Not assessable	Total
Appropriate	108 (79.4)	14 (10.3)	13 (9.6)	1 (0.7)	136
Not appropriate (wrong choice of drugs)	42 (50.0)	32 (38.1)	10 (11.9)		84
Not appropriate (dose)	4 (14.8)	4 (14.8)	19 (70.4)		27
Total	154	50	42	1	247

including more than 6900 outpatients with AF, those inappropriately prescribed with reduced doses of DOACs had a higher risk of thromboembolic events and death.[27] There is, however, a paucity of studies assessing the impact of appropriateness of OAC prescription on patient clinical outcomes, so that more studies are requested to drive stronger conclusions on this key clinical topic.

4.1 | Limitations

We found no statistically significant difference between intervention and control arms in terms of OAC prescription and appropriateness. This is probably explained by lack of compliance of physicians to the educational intervention,[7] which was specifically designed to increase the rate of OAC prescription, being the under prescription the main appropriateness issue. Differences among physicians on the basic knowledge of OAC prescription may be another possible explanation, but due to the lack of data, we could not explore this hypothesis. Another limitation of this study was the lack of long-term follow up, which would enable us to establish an association with major clinical outcomes. Furthermore, we failed to collect repeated measures of INR and TTR to better determine the appropriateness of vitamin K antagonists. Despite these limitations, the study allows us to provide detailed information on the appropriateness of OAC prescription in a real-world hospital setting dealing with older AF patients acutely admitted to a large number of Italian internal medicine and geriatric wards.

5 | CONCLUSIONS

A significant proportion of AF older patients hospitalized in internal medicine and geriatric wards are still receiving inappropriate prescription of OACs, even though in the frame of the SIM-AF trial there was an overall improvement over time of OAC prescription appropriateness. The prescription at hospital admission is associated to the appropriateness or not of prescription at discharge. Factors related to a higher risk of bleeding are associated to a lower likelihood to be appropriately prescribed at discharge. More educational programmes, specifically addressed to improve the quality of OAC prescription, are needed in internal medicine and geriatric wards to better manage this at high risk population of older patients. As shown in previous studies,[28,29] hospitalization, which could represent an opportunity to review the pharmacological therapies in the multimorbid and frail elderly, have again missed the chance to improve the quality of drug prescriptions.

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COMPETING INTERESTS

There are no competing interests to declare.

CONTRIBUTORS

C.F. conceived the study idea, the study design, did the acquisition and assessment of the data, and wrote the manuscript. S.A. did the acquisition and assessment of the data. I.A. performed the statistical analysis and did the assessment of the data. All authors participated in the discussion and interpretation of the results, revised the manuscript critically for important intellectual content and approved the final draft.

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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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