JAMDA 25 (2024) 545–551

JAMDA

journal homepage: www.jamda.com

Original Study

Predictors and Outcomes of Oral Anticoagulant Deprescribing in Geriatric Inpatients With Atrial Fibrillation: A Retrospective Multicenter Cohort Study

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Keywords:
Oral anticoagulant therapy
deprescribing
older adults
atrial fibrillation
frailty
inpatients

A B S T R A C T

Objective: To investigate prevalence and predictors of oral anticoagulant therapy (OAT) deprescribing in older inpatients with atrial fibrillation (AF), and its association with 1-year incidence of major clinical outcomes.
Design: Multicenter retrospective cohort study.
Setting and Participants: Inpatients aged ≥75 years with known AF on OAT at admission discharged from 3 Italian acute geriatric wards between January 2014 and July 2018.
Methods: Data from a routine Comprehensive Geriatric Assessment (CGA), along with OAT status at discharge were recorded. One-year incidence of all-cause death, stroke or systemic embolism (SSE), and major and clinically relevant nonmajor bleeding (MB/CRNMB) were retrieved from administrative databases. Associations were explored through multilevel analysis.
Results: Among 1578 patients (median age 86 years, 56.3% female), OAT deprescription (341 patients, 21.6%) was associated with bleeding risk, functional dependence and cognitive impairment, and inversely, with previous SSE and chronic AF. Incidences of death, SSE, and MB/CRNMB were 56.6%, 1.5%, and 4.1%, respectively, in OAT-deprescribed patients, and 37.6%, 2.9%, and 4.9%, respectively, in OAT-continued patients, without significant differences between groups. OAT deprescription was associated with all-cause mortality [adjusted odds ratio (aOR) 1.41, 95% CI 1.68-1.85], along with older age, comorbidity burden, cognitive impairment, and functional dependence, but with neither SSE nor MB/CRNMB incidence, as opposed to being alive and free from SSE and MB/CNRMB, respectively (aOR 0.68, 95% CI 0.25-1.82, and aOR 0.95 95% CI 0.49-1.85, respectively). Conversely, OAT deprescription was associated with higher odds of being dead than alive both in patients free from SSE and in those free from MB/CRNMB.
Conclusions and Implications: CGA-based OAT deprescribing is common in acute geriatric wards and is not associated with increased SSE. The net clinical benefit of OAT in geriatric patients is strongly related with the competing risk of death, suggesting that functional and cognitive status, as well as residual life expectancy, should be considered in clinical decision making in this population.

Funding Sources: This research did not receive any funding from agencies in the public, commercial, or not-for-profit sectors.
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https://doi.org/10.1016/j.jamda.2024.01.011
1525-8610/

Oral anticoagulant therapy (OAT), with direct oral anticoagulants (DOACs) recommended over vitamin K antagonists (VKAs), is the standard of care for patients with atrial fibrillation (AF) at high risk of stroke.[1,2] However, OAT is still widely underused, especially in older subjects.[3-8] Although clinical inertia and malpractice may contribute to OAT underprescription, "intentional" OAT nonprescription could be a common practice, reflecting the persistent uncertainties about the risks of harm and futility in patients with limited life-expectancy and a high burden of comorbidities, frailty, and geriatric syndromes.[3-6,9-18] There is also evidence that a mix of variables within the Comprehensive Geriatric Assessment (CGA), including functional dependence, cognitive impairment, and comorbidity burden, are associated with reduced OAT use in older AF patients,[3-6,9,10,15-22] and can also predict mortality in these patients.[6,8,21] Accordingly, and with few exceptions,[8] recent studies and meta-analyses have demonstrated that increasing severity of "frailty," irrespective of setting and tools used to identify it, is associated with a trend toward reduced OAT use in older AF patients.[3,5,6,9,10,16,23-25] Moreover, in the Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail) consensus,[26] although panelists agreed that in most of such people anticoagulants should be stopped, this criterion was rejected because of concerns over the minority of patients in whom this would be potentially inappropriate. Notwithstanding, a not negligible proportion of older AF patients, mainly those in long-term care and some medical and geriatric inpatients, fulfill all STOPPFrail major criteria (ie, end-stage irreversible pathology, poor 1-year survival, severe functional and/or cognitive impairment, priority of symptom control) and might be considered for OAT deprescription.[26]

This area of uncertainty in clinical decision making has been acknowledged for the first time in the 2021 European Heart Rhythm Association (EHRA) practical guide on the use of DOACs, stating that "there may be no benefit to OAT in states of severe frailty or where life expectancy is likely to be limited,"[2] thereby including the option of not prescribing (or deprescribing) OAT in such patients. Also, in the 2020 Update to the 2016 American College of Cardiology/American Heart Association clinical performance and quality measures for adults with AF, the authors state that "in patients with AF, OAT should be individualized on the basis of shared decision-making after discussion of the absolute and relative risks of stroke and bleeding, as well as the patient's values and preferences."[27]

To our knowledge, no study so far has investigated the determinants and clinical implications of OAT deprescribing (ie, the intentional discontinuation of OAT) at hospital discharge in older patients with AF. We hypothesized that in this setting, OAT deprescribing would be mainly driven by poor health status and estimated short life-expectancy, would not impact on stroke or systemic embolism (SSE) incidence but might reduce major bleedings and clinically relevant nonmajor bleedings (MB/CRNMB). Therefore, in this multicenter retrospective cohort study, we aimed to (1) investigate variables associated with OAT deprescribing in older AF inpatients and (2) assess 1-year cumulative incidence and predictors of major clinical outcomes (death, SSE, and MB/CRNMB) in OAT-deprescribed and in OAT-continued patients.

Methods

Study Setting, Design, and Sample Derivation

We conducted a retrospective cohort study on patients aged ≥75 years consecutively discharged from January 2014 to July 2018 with a diagnosis of AF or atrial flutter (codes 427.31 and 427.32 of the *International Classification of Diseases, Ninth Revision Clinical Modification* [ICD-9-CM]) from 3 acute geriatric wards (AGWs) of Italian tertiary hospitals: A.O.U. Città della Salute e della Scienza di Torino (Turin), A.O.U. Pisana (Pisa), and A.O. Santa Croce e Carle (Cuneo).

In the present analysis, we focused on patients with known AF receiving OAT (ie, any VKA or DOAC) at admission. Patients with mechanical heart valves, those receiving heparin (but not OAT) at admission for any reason, and those who died during hospital stay were excluded. The study was approved by competent Ethics Committees and was conducted according to the principles of the Declaration of Helsinki. The results of the study are presented according to the STROBE statement.[28]

Baseline Clinical Variables

Baseline data were collected by geriatric medicine residents from electronic health records and discharge charts under the supervision of senior geriatricians. AF type was defined as paroxysmal or chronic (ie, persistent and permanent AF) according to current international recommendations. Individual stroke and bleeding risks were evaluated according to the CHA_2DS_2-VASc (congestive heart failure/left ventricular dysfunction, hypertension, age ≥75 years, diabetes mellitus, stroke/transient ischemic attack/systemic embolism, vascular disease, age 65-74 years, sex category)[29] and HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly)[30] scores, respectively. In the participating AGWs, a CGA is routinely performed at admission, including the Charlson Comorbidity Index,[31] scales of functional autonomy [basic activities of daily living (BADL) and instrumental activities of daily living (IADL)],[32,33] and of cognitive status (Short Portable Mental Status Questionnaire).[34] Supplementary Material 1 reports relevant cutoffs for CGA scales. For each patient, glomerular filtration rate at discharge was estimated according to the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula.[35]

Exposure

Prescription of OAT at admission and at discharge was recorded. Patients were considered OAT-deprescribed if they received no DOAC or VKA prescription at discharge, whereas they were considered OAT-continued if they received a DOAC or VKA prescription at discharge, irrespective of anticoagulant molecule switch.

Follow-up and Outcome Variables

Follow-up data extraction was conducted by experienced data analysts by assessing public health regional archives reporting vital status of residents receiving public healthcare in that region, and archives of hospital discharge records of the region, reporting patients' personal data, date and unit of hospital admission and discharge, main diagnoses at discharge, and main diagnostic and therapeutic procedures during hospital stay.

The primary outcome was overall mortality at 12 months from hospital discharge. Secondary outcomes included SSE and MB/CRNMB that required a hospital admission during the 12 months after discharge, identified on discharge records by means of ICD-9-CM codes. Site of MB/CRNMB was defined as intracranial, gastrointestinal, genitourinary, or other (Supplementary Table 1).

Statistical Analysis

Continuous data were reported as means and SDs or median and interquartile range (IQR, first to third quartile) as appropriate; categorical data were reported as number and percentage. For continuous variables, comparisons were performed using the unpaired Student *t* test or Wilcoxon-Mann-Whitney test depending on the type of distribution; for categorical variables, chi-square test or Fisher exact test were used, as appropriate. For survival analysis, the Kaplan-Meier

Table 1
Baseline and Outcome Variables in the Overall Sample and Stratified According to Oral Anticoagulant Therapy Continuation vs Deprescription

Variable	Overall Sample (n = 1578)	OAT Continued (n = 1237)	OAT Deprescribed (n = 341)	*P* Value
Age, y, median (IQR)	86 (82-89)	85 (81-89)	86 (83-90)	<.001
Female sex, n (%)	888 (56.3)	692 (55.9)	196 (57.5)	.61
Chronic AF, n (%)	1204 (76.3)	973 (78.7)	231 (67.7)	<.001
History of SSE, n (%)	361 (22.9)	269 (21.8)	92 (27.0)	.042
History of bleeding, n (%)	282 (17.9)	171 (13.8)	111 (32.6)	<.001
CHA_2DS_2-VASc score, mean ± SD	4.7 ± 1.4	4.7 ± 1.3	4.8 ± 1.4	.86
HAS-BLED score, mean ± SD*	1.9 ± 2.3	1.8 ± 0.8	2.3 ± 0.9	<.001
VKA at admission, n (%)	948 (60.1)	759 (61.4)	189 (55.4)	.048
Charlson Comorbidity Index, median (IQR)	3 (2-5)	3 (2-5)	4 (3-5)	<.001
BADL level of autonomy, n (%)				<.001
Complete autonomy (6 of 6)	479 (30.4)	409 (33.1)	70 (20.5)	
Partial dependence (4-5 of 6)	366 (23.2)	309 (25.0)	57 (16.7)	
Complete dependence (<4 of 6)	733 (46.4)	519 (41.9)	214 (62.8)	
IADL level of autonomy, n (%)				<.001
Complete autonomy (>4 of 8)	377 (23.9)	318 (25.7)	59 (17.3)	
Partial dependence (2-4 of 8)	494 (31.3)	398 (32.2)	96 (28.2)	
Complete dependence (<2 of 8)	707 (44.8)	521 (42.1)	186 (54.5)	
SPMSQ (number of errors), median (IQR)†	3 (1-6)	2 (1-5)	3 (1-8)	<.001
Cognitive impairment at SPMSQ†, n (%)				<.001
Absent (0-2 of 10)	765 (49.2)	629 (51.5)	136 (41.0)	
Mild (3-4 of 10)	294 (18.9)	238 (19.5)	56 (16.9)	
Moderate (5-7 of 10)	239 (15.4)	198 (16.2)	41 (12.3)	
Severe (≥8 of 10)	256 (16.5)	157 (12.8)	99 (29.8)	
eGFR, mL/min, mean ± SD‡	52.6 ± 21.6	53.5 ± 21.4	49.2 ± 22.1	.0014
Enrollment center				<.001
Cuneo	344 (21.8)	300 (24.3)	44 (12.9)	
Torino	464 (29.4)	404 (32.7)	60 (17.6)	
Pisa	770 (48.8)	533 (43.1)	237 (69.5)	
Outcomes at 12-month follow-up				
Death by any cause, n (%)	658 (41.7)	465 (37.6)	193 (56.6)	<.001
SSE, n (%)	41 (2.6)	36 (2.9)	5 (1.5)	.14
MB/CRNMB, n (%)	74 (4.7)	60 (4.9)	14 (4.1)	.57
MB/CRNMB site, n (% on no. of bleedings)§				
Intracranial	10 (13)	8 (13.3)	2 (14.3)	>.99
Gastrointestinal	31 (42)	24 (40.0)	7 (50.0)	.56
Genitourinary	24 (33)	19 (31.7)	5 (35.7)	.76
Other	9 (12)	9 (15)	0	.19
SSE or MB/CRNMB, n (%)	111 (7.0)	94 (7.6)	17 (5)	.10

eGFR, estimated glomerular filtration rate; SPMSQ, Short Portable Mental Status Questionnaire.
*Data unavailable for 5 of 1578 patients (1 of 1237 OAT-continued and 4 of 341 OAT-deprescribed).
†Data unavailable for 24 of 1578 patients (15 of 1237 OAT-continued and 9 of 341 OAT-deprescribed).
‡Data unavailable for 32 of 1578 patients (23 of 1237 OAT-continued and 9 of 341 OAT-deprescribed).
§Fisher exact test.

method to month 12 was applied, and the log-rank test was used to assess differences in survival curves. Cumulative incidences of SSE and MB/CRNMB were assessed considering death as a competing event using the Fine and Gray test.[36]

To identify predictive variables for OAT deprescribing and to evaluate possible risk factors for all-cause death at 12 months, we built 2-level hierarchical multivariable models with dichotomous outcome, considering the recruiting center a second-level variable (level 2) and patient's clinical characteristics as first-level variables (level 1) (Supplementary Table 2).[37,38]

In order to evaluate the main secondary outcomes, taking into account the competing risk of death, we created for each event a secondary multilevel (polytomic) outcome by dividing the sample into 3 categories: "SSE," "dead without previous SSE," and "alive and free from SSE"; and, similarly, "MB/CRNMB," "dead without previous MB/CRNMB," and "alive and free from MB/CRNMB." For both outcomes, we performed a multilevel model (Supplementary Table 2). Results were expressed calculating the crude and adjusted odds ratios (aORs) and their 95% CIs.[37-39] Univariate analyses were performed on available data, whereas in multivariable models, in order not to lose statistical power we have replaced missing data with statistical summaries for those variables.

A retrospective power analysis was performed based on sample size: estimating a proportion of OAT deprescription between 15.0% and 30.0%, a sample size of 1578 patients yields a 2-sided 95% CI with widths equal to 0.036 and 0.046, respectively.

All statistical tests were 2-sided and were conducted using SAS, version 9.4 (SAS Institute), and Stata, version 17.0 (StataCorp). *P* values ≤.05 were considered statistically significant.

Table 2
Variables Associated With Oral Anticoagulant Therapy Deprescribing, Multivariable Analysis

Variable	Odds Ratio (95% CI)	*P* Value
Age, y	1.019 (0.992-1.046)	.16
HAS-BLED score	1.927 (1.621-2.291)	<.001
eGFR, mL/min	0.998 (0.991-1.004)	.47
Charlson Comorbidity Index	1.057 (0.965-1.158)	.23
SPMSQ, number of errors	1.057 (1.010-1.106)	.017
Chronic AF	0.603 (0.450-0.807)	<.001
History of SSE	0.640 (0.459-0.892)	.009
BADL partial dependence (4-5 of 6) vs complete autonomy (6 of 6)	0.862 (0.573-1.298)	.48
BADL complete dependence (<4 of 6) vs complete autonomy (6 of 6)	1.535 (1.057-2.228)	.023

eGFR, estimated glomerular filtration rate; SPMSQ, Short Portable Mental Status Questionnaire.

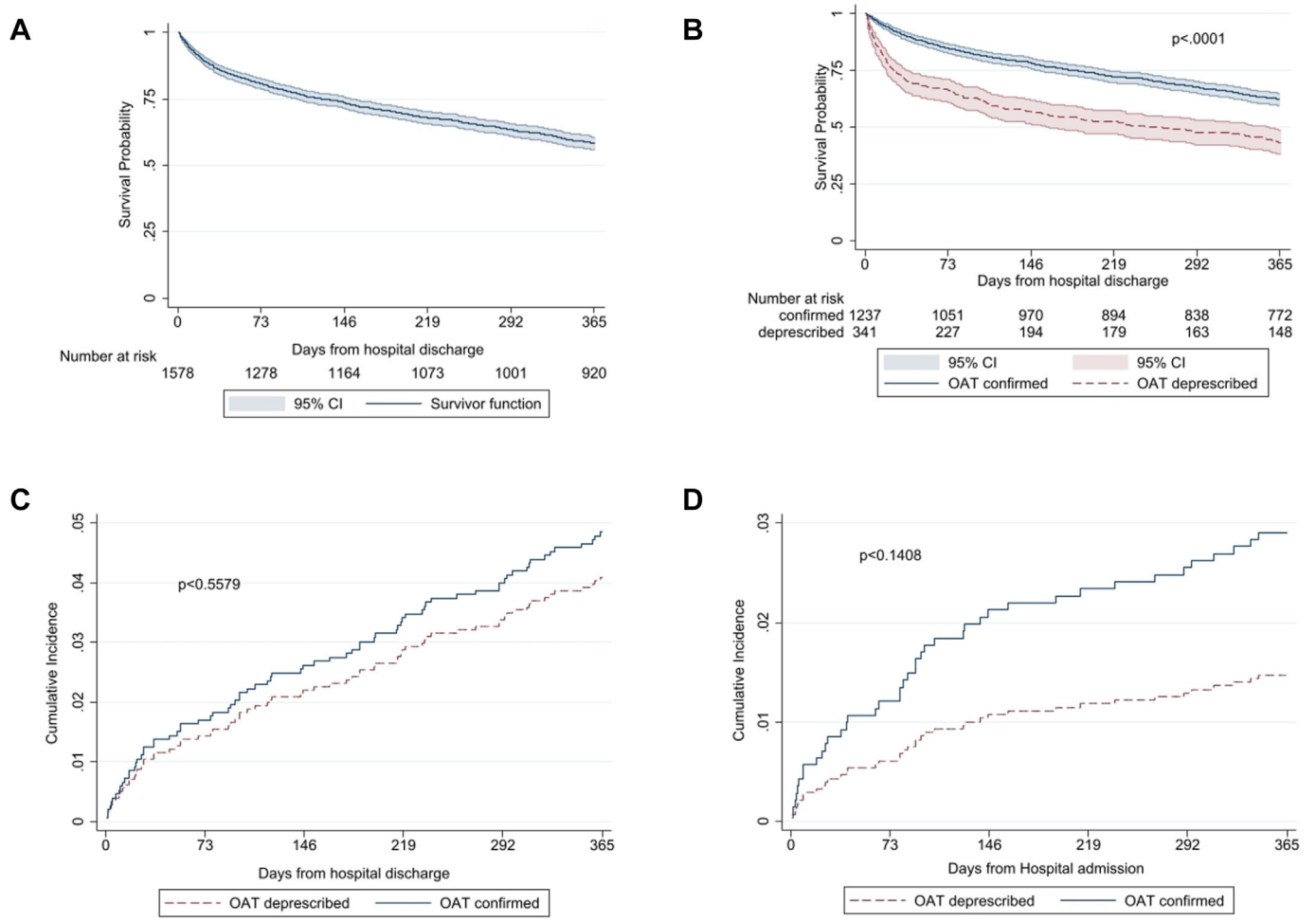

Fig. 1. Survival curves for (A) the overall sample and (B) stratified according to oral anticoagulant therapy status at discharge, and (C) cumulative incidence curves for stroke/systemic embolism and (D) major bleeding/clinically relevant nonmajor bleeding according to oral anticoagulant therapy status at discharge.

Results

The final sample included 1578 patients aged ≥75 years with an already known diagnosis of AF and on OAT at admission. Table 1 shows baseline and follow-up data of the overall sample and stratified according to OAT at discharge. Median patient age was 86 years (IQR 82-89), and 56.3% were female; AF was chronic in 76.3% of cases. A previous SSE had occurred in 22.9% of patients, whereas 17.9% had a bleeding history; cardioembolic risk scores were high (mean CHA_2DS_2-VASc 4.7 ± 1.4), whereas bleeding risk scores were relatively lower (mean HAS-BLED 1.9 ± 2.3). Sixty percent of patients received a VKA at admission. Geriatric syndromes were highly prevalent: 46.4% and 44.8% were completely dependent in BADL and IADL, respectively, whereas 31.9% showed moderate to severe cognitive impairment, and the median Charlson Comorbidity Index was 3.

At discharge, OAT was deprescribed in 341 patients (21.6%, 95% CI 19.6%-23.6%), whereas among OAT-continued patients 46.7% received warfarin, 18.2% apixaban, 17.2% dabigatran, 14.4% rivaroxaban, and 3.5% edoxaban. OAT deprescribing was independently associated with higher HAS-BLED scores, complete functional dependence in BADL, and more severe cognitive impairment at Short Portable Mental Status Questionnaire, whereas a history of SSE and of chronic AF were inversely associated with OAT deprescribing (Table 2).

At 1-year follow-up, death by any cause occurred in 658 (41.7%) patients, more frequently in OAT-deprescribed than in OAT-continued patients (56.6% vs 37.6%, respectively) (Supplementary Table 3). Median survival time for deceased patients at follow-up was 34 days (IQR 11-140) in OAT-deprescribed patients and 107 days (IQR 35-231) in OAT-confirmed patients. An SSE occurred in 41 (2.6%) patients, whereas at least an MB/CRNMB occurred in 74 (4.7%) patients, without significant differences among OAT-deprescribed and OAT-continued patients (1.5% vs 2.9% for SSE and 4.1% vs 4.9% for MB/CRNMB, respectively). The most frequent bleeding site was the gastrointestinal GI tract (31 patients), followed by the genitourinary tract (24 patients), whereas an intracranial hemorrhage occurred in 10 patients and other MB/CRNMB in 9 other patients. At least 1 SSE or MB/CRNMB occurred in 5% and 7.6% of OAT-deprescribed and OAT-continued patients, respectively. Figure 1 shows survival curves for the overall sample and stratified according to OAT at discharge, as well as cumulative incidence curves for SSE and MB/CRNMB.

Table 3 presents results from univariate and multivariable models on the association between OAT deprescribing and clinical outcomes at 12 months from discharge. OAT deprescribing was independently associated with mortality (aOR 1.41, 95% CI 1.68-1.85), along with older age and a higher burden of comorbidity, cognitive impairment, and dependence in BADL and IADL (Supplementary Table 4). Despite this finding, OAT deprescribing was associated neither with SSE nor with MB/CRNMB as opposed to being alive and free from the same event at 12 months from discharge (aOR 0.68, 95% CI 0.25-1.82, and aOR 0.95, 95% CI 0.49-1.85, respectively). The only variables

Table 3
Impact of Oral Anticoagulant Therapy Deprescription at Discharge on Clinical Outcomes at 12 Months From Discharge, Crude and Adjusted Odds Ratios

Clinical Outcome	OAT Continued (n = 1237)	OAT Deprescribed (n = 341)	OR (95% CI)	aOR (95% CI)*
Death at 12 mo from discharge, n (%)	465 (36.6)	193 (56.6)	2.165 (1.698-2.761)	1.406 (1.680-1.851)
Ischemic events at 12 mo from discharge, n (%)				
Alive and free from SSE	759 (61.4)	145 (45.5)	—	—
SSE	36 (2.9)	5 (1.47)	0.727 (0.281-1.884)	0.677 (0.252-1.818)
Dead without previous SSE	442 (35.7)	191 (56.0)	2.262 (1.769-2.892)	1.472 (1.115-1.943)
Bleeding events at 12 mo from discharge, n (%)				
Alive and free from MB/CRNMB	743 (60.1)	141 (41.4)	—	—
MB/CRNMB	60 (4.9)	14 (4.1)	1.231 (0.669-2.262)	0.953 (0.491-1.853)
Dead without previous MB/CRNMB	434 (35.1)	186 (54.6)	2.258 (1.761-2.896)	1.485 (1.120-1.967)

SPMSQ, Short Portable Mental Status Questionnaire.
*Adjusted for as follows: Level 1: patient's age, OAT deprescribing, history of SSE, history of bleeding, HAS-BLED score, CHA2DS2-VASc score, glomerular filtration rate, Charlson Comorbidity Index, SPMSQ score, BADL dependence level, and IADL dependence level; Level 2: Recruitment site.

independently associated with SSE were partial or complete dependence in BADL (aOR 2.80, 95% CI 1.02-7.67, and aOR 3.59, 95% CI 1.11-11.56, respectively), whereas a higher comorbidity burden was associated with MB/CRNMB (aOR 1.22, 95% CI 1.05-1.41) (Supplementary Table 5). On the other hand, OAT deprescribing was associated with higher adjusted odds of being dead than alive both in patients free from SSE and in those free from MB/CRNMB, alongside, among others, older age, higher comorbidity burden, and complete dependence in BADL and IADL (Supplementary Table 5).

Discussion

The main findings of this study may be summarized as follows: (1) in a national cohort of AF geriatric inpatients, OAT deprescribing at discharge occurred in 21.6% of patients and was mainly driven by cognitive and functional impairment and a history or high risk of bleeding; (2) 1-year all-cause mortality was 41.7%, a figure several folds higher than SSE occurrence, and significantly higher in OAT-deprescribed than in OAT-confirmed patients; (3) cumulative 1-year incidence of SSE was 1.5% in OAT-deprescribed and 2.6% in OAT-continued patients, whereas that of MB/CRNMB was 4.1% in OAT-deprescribed and 4.9% in OAT-continued patients; (4) OAT deprescribing was associated neither with a higher adjusted odds of having an SSE nor with a lower adjusted odds of having an MB/CRNMB.

Notably, in this cohort of hospital-discharged patients, OAT prescription rates were higher than those reported in recent community-based observational studies,[3,4,7,8,16,21] thereby excluding clinical inertia or malpractice. Moreover, we observed a lower-than-expected incidence of SSE in a population usually considered at extremely high risk of stroke.[12,25]

As a whole, these findings confirm that in geriatric wards OAT deprescription is an intentional process, driven by a poor expected net clinical benefit in reason of a CGA-estimated short life-expectancy and a high risk of bleeding or rebleeding.[4-6,9,10,15-21,40] Moreover, the finding of a higher overall mortality without increased risk of SSE in OAT-deprescribed patients supports the notion that the net clinical benefit of OAT declines with advancing age and with the competing risk of death,[41,42] in accordance with the EHRA caveat that "there may be no benefit to OAT in states of severe frailty or where life expectancy is likely to be limited."[2] Therefore, the decision about OAT prescription in these patients should not simply rely on cardioembolic and bleeding risk scales, but should include a global evaluation of health, functional and cognitive status, and residual life expectancy.[6] Shared decision making, accounting for the individual's life expectancy when weighing the benefits and harms of OAT use, would therefore be advisable in this setting.[26,41-43]

We are strongly convinced that OAT, and particularly DOACs, is beneficial for most older AF patients, including those with mild to moderate deficit-accumulation frailty.[6,17,24,44,45] At the same time, we recognize that evidence on the benefit of OAT in older adults with severe cognitive and functional limitations and reduced life expectancy is sparse and might not reflect that observed in experimental and observational studies, which have systematically excluded these patients.[6,17,24,41,42,46] Moreover, most studies claiming a net clinical benefit of OAT in frail patients, and which informed a recent European consensus on the topic,[47] included scant proportions of severely frail patients,[15,24,48,49] as compared with real-world figures,[50] and few of these studies have investigated OAT effectiveness accounting for the competing risk of death, which may provide a more realistic estimate of OAT benefit in this population.[39,41,42,51]

In this scenario, our findings add on and reinforce evidence from a few previous cohort studies that showed an uncertain benefit of OAT for very old patients in different clinical settings.[11-14,20,52-54] However, to our knowledge, this is the first study that has investigated the clinical implications of intentional OAT deprescribing at hospital discharge, which was shown to be CGA guided. Unfortunately, despite consistent evidence that variables associated with OAT nonuse also predict mortality in these patients,[3,4,6-16,20,23-25] there is not a reliable tool to guide OAT decision making. The CGA-based Multidimensional Prognostic Index (MPI)[55] represents a validated tool to identify older patients with limited life expectancy and has been recommended to guide OAT decisions in older AF patients.[45,56] However, a significantly lower mortality across all MPI groups in OAT users than in non-users has been demonstrated, thereby suggesting that the individual clinical assessment might further refine decision making over validated prognostic tools.[57] In fact, it is plausible that other subjective variables might influence physician decision making. Some clinicians may consider the potential futility of OAT prescription for prevention of stroke-associated disability in patients who are already completely dependent in BADL, and others may be aware that there is a high rate of functional loss that is independent from stroke in older AF patients.[58] Eventually, in keeping with the guidelines,[2] clinical scenarios with an unmodifiable high risk of bleeding or rebleeding may suggest a *primum non nocere* strategy in these polymorbid patients, irrespective of CGA assessment and life expectancy. In fact, a recent survey has reported that prior bleeding and risk of bleeding are the most important barriers to OAT prescription or continuation.[40]

Some limitations of the present study should be addressed. First, this is a retrospective observational study; thus, we could not determine causal links but only associations between clinical variables, therapeutic choices, and clinical implications. However, because of the body of evidence in favor of OAT prescription and the scarcity of data on OAT effectiveness in extremely frail older adults, an experimental approach might not be feasible yet. Moreover, despite relying on standardized CGA data, we were unable to fully capture the spectrum

of variables that could impact the clinical decision making on OAT deprescribing, a factor that regrettably made the use of inverse probability of treatment weighting techniques unfeasible because of an insufficient correction of the selection bias. Therefore, we decided to use hierarchical multivariable models to avoid loss of statistical power in our analyses. To determine outcomes of interest, we relied on regional centralized archives, and despite the complete accuracy of mortality data (ie, all patients had follow-up data on vital status at 12 months from discharge), cause of death was unavailable and, thus, we cannot exclude some missed fatal ischemic or bleeding events occurring outside of the hospital, which however should be extremely rare. Moreover, it cannot be excluded that some SSE and MB/CRNMB leading to hospitalization could have happened outside the region of residence of the patient, and thus be missed, although this seems an unlikely event in a population of mainly vulnerable, dependent older subjects. Eventually, in keeping with most observational studies, also because hospital discharge records in Italy do not report prescribed therapy at discharge, we do not have data about adherence to therapy or subsequent OAT deprescribing in OAT-continued patients at discharge, possibly reducing differences in ischemic and hemorrhagic events among groups. On the other side, some strengths of this study should also be considered. First, the routine adoption of CGA in the AGWs of the study allowed to capture a real-world prescription image, free from possible distortions on the use of ad hoc CGA protocols for prospective studies. Moreover, the use of regional archives allowed to capture all clinical events that prompted a hospital admission within the region of residence, which was clinically meaningful. Although the study was conducted in 3 Italian AGWs, many patients admitted to medicine wards have similar age and clinical characteristics, thereby suggesting the potential generalizability of the present findings to acute medical ward inpatients. Lastly, even if we were not able to use a time-to-event approach because of a violation of the proportional hazards assumption, the use of a multilevel (polytomic) outcome approach allowed us to evaluate the risk of major ischemic and hemorrhagic events in OAT-deprescribed and OAT-continued patients free from the huge impact of a competing risk of death several folds higher, giving important insights for clinical decision making in this population. Indeed, geriatricians often consider competing risks when caring for older patients but, despite the clinical importance of this assessment, competing risks are less frequently regarded in disease outcomes research.

Conclusions and Implications

To our knowledge, this is the first study to have investigated the prevalence, clinical correlates, and impact of OAT deprescribing at discharge in AF geriatric inpatients. More than one-fifth of patients were OAT-deprescribed, more frequently those with a high burden of cognitive and functional impairment and a history or high risk of bleeding. At 1-year follow-up, the overall mortality was 41.7% and associated with the same CGA-based variables as OAT deprescribing. OAT-deprescribed patients, however, did not have a higher risk of SSE than OAT-continued patients, highlighting the potential futility of OAT in these vulnerable patients, in accordance with current guidelines on the topic.

Disclosure

The authors declare no conflicts of interest.

Acknowledgments

We would like to thank Drs Enrica Grisoglio, Marina Iacovino, and Federica Li Puma for their support in baseline data collection and Drs Daniela Di Cuonzo and Gianni Ciccone for their support in outcome assessment.

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Supplementary Material 1. Cutoffs for Scales Derived From the Comprehensive Geriatric Assessment

The following cutoffs were used to categorize scales derived from the Comprehensive Geriatric Assessment at admission: For Katz's Basic Activities of Daily Living (BADL), a scale that evaluates 6 functions, with higher scores indicating a higher level of autonomy: Complete autonomy: 6 of 6 functions preserved; Partial dependence: 4 of 5 of 6 functions preserved; Complete dependence: $<$4 of 6 functions preserved.

- For Lawton's Instrumental Activities of Daily Living (IADL), a scale that evaluates 8 functions, with higher scores indicating a higher level of autonomy: Complete autonomy: $>$4 of 8 functions preserved; Partial dependence: 2 to 4 of 8 functions preserved; Complete dependence: $<$2 of 8 functions preserved.
- For Short Portable Mental Status Questionnaire (SPMSQ), a questionnaire that evaluates cognitive impairment on the basis of number of errors given to 10 specific answers, with higher scores indicating a higher level of cognitive impairment: Absence of cognitive impairment: 0 to 2 errors to 10 questions; Mild cognitive impairment: 3 or 4 errors to 10 questions; Moderate cognitive impairment: 5 of 7 errors to 10 questions; Severe cognitive impairment: $\geq$8 errors to 10 questions.

Supplementary Table 1
International Classification of Diseases, Ninth Revision, Clinical Modification (*ICD-9-CM*) Codes Used to Identify Outcomes of Interest in Hospital Discharge Records

Stroke and systemic embolism (SSE)
433.01,433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 435.X, 436, 444.X
Major bleedings and clinically relevant nonmajor bleedings (MB/CRNMB)
Intracranial site
430, 431, 432.X, 800.2X, 800.3X, 800.7X, 800.8X, 801.2X, 801.3X, 801.7X, 801.8X, 803.2X, 803.3X, 803.7X, 803.8X, 804.2X, 804.3X, 804.7X, 804.8X, 852.XX, 853.XX
Gastrointestinal site
456.0, 456.20, 530.21, 530.7, 530.82, 531.0X, 531.2X, 531.4X, 531.6X, 532.0X, 532.2X, 532.4X, 532.6X, 533.0X, 533.2X, 533.4X, 533.6X, 534.0X, 534.2X, 534.4X, 534.6X, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.83, 537.84, 562.02, 562.03, 562.12, 562.13, 569.3, 569.85, 578.X
Genitourinary site
596.7, 599.7, 623.8, 626.9
Other sites
285.1, 360.43, 362.43, 362.81, 363.61, 363.62, 363.72, 364.41, 376.32, 379.23, 420.3, 459.0, 568.81, 719.10, 784.7, 786.3, 860.2

The X stands for any digit in the *ICD-9-CM* code.

Supplementary Table 2
Variables Introduced in Multivariable Models for Oral Anticoagulant Therapy Deprescribing and Main Clinical Outcomes in Statistical Analysis

Multivariable Model 1: Variables associated with oral anticoagulant therapy deprescribing
Level 1—Patient's clinical data: patient's age, atrial fibrillation type, history of SSE embolism, HAS-BLED score, glomerular filtration rate, Charlson Comorbidity Index, SPMSQ score, BADL dependence level [complete autonomy 6/6 (reference category), partial dependence 4-5/6, complete dependence <4/6].
Level 2: Recruitment site (Pisa, Torino, Cuneo).
Multivariable Model 2: Variables associated with death by any cause at 12 mo from discharge
Level 1—Patient's clinical data: patient's age, oral anticoagulant therapy deprescribing, history of SSE, history of bleeding, HAS-BLED score, CHA_2DS_2-VASc score, glomerular filtration rate, Charlson Comorbidity Index, SPMSQ score, BADL dependence level [complete autonomy 6/6 (reference category), partial dependence 4-5/6, complete dependence <4/6], IADL dependence level [complete autonomy >4/8 (reference category), partial dependence 2-4/8, complete dependence <2/8]
Level 2—Recruitment site (Pisa, Torino, Cuneo)
Multilevel multivariable models for polytomic outcomes: SSE vs alive and free from SSE at 12 mo from discharge; dead without previous SSE vs alive and free from SSE at 12 mo from discharge; MB/CRNMB vs alive and free from MB/CRNMB at 12 mo from discharge; dead without previous MB/CRNMB vs alive and free from MB/CRNMB at 12 mo from discharge
Level 1—Patient's clinical data: patient's age, oral anticoagulant therapy deprescribing, history of SSE, history of bleeding, HAS-BLED score, CHA_2DS_2-VASc score, glomerular filtration rate, Charlson Comorbidity Index, SPMSQ score, BADL dependence level [complete autonomy 6/6 (reference category), partial dependence 4-5/6, complete dependence <4/6], IADL dependence level [complete autonomy >4/8 (reference category), partial dependence 2-4/8, complete dependence <2/8]
Level 2—Recruitment site (Pisa, Torino, Cuneo)

BADL, basic activities of daily living; CHA2DS2-VASc, congestive heart failure/left ventricular dysfunction, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack/systemic embolism, vascular disease, aged 65-74 years, sex category; CRNMB, clinically relevant non-major bleeding; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly; IADL, instrumental activities of daily living; MB, major bleeding; SPMSQ, Short Portable Mental Status Questionnaire; SSE, stroke or systemic embolism.

Supplementary Table 3
Variables Associated With All-Cause Mortality at 12 Months From Discharge, Univariate Analysis

Variable	Alive at 12 mo From Discharge (n = 920)	Dead at 12 mo From Discharge (n = 658)	*P* Value
Age, y, median (IQR)	85 (81-88)	87 (83-90)	<.001
Female sex, n (%)	515 (56.0)	373 (56.7)	.78
Chronic AF, n (%)	704 (76.5)	500 (76.0)	.81
History of SSE, n (%)	189 (24.5)	172 (26.1)	.009
History of bleeding, n (%)	141 (15.3)	141 (21.4)	.002
CHA_2DS_2-VASc score, mean ± SD	4.7 ± 1.3	4.8 ± 1.5	.07
HAS-BLED score, mean ± SD*	1.8 ± 0.8	2.0 ± 0.9	<.001
VKA at admission, n (%)	564 (61.3)	384 (58.4)	.24
OAT-deprescribed at discharge, n (%)	148 (16.1)	193 (29.3)	<.001
Charlson Comorbidity Index, median (IQR)	3 (2-4)	4 (3-5)	<.001
BADL level of autonomy, n (%)			<.001
Complete autonomy (6/6)	363 (39.4)	116 (17.6)	
Partial dependence (4-5/6)	226 (24.6)	140 (21.3)	
Complete dependence (<4/6)	331 (36.0)	402 (61.1)	
IADL level of autonomy, n (%)			<.001
Complete autonomy (>4/8)	288 (31.3)	89 (13.5)	
Partial dependence (2-4/8)	312 (33.9)	182 (27.7)	
Complete dependence (<2/8)	320 (34.8)	387 (58.8)	
SPMSQ (no. of errors)†, median (IQR)	2 (0-4)	4 (1-8)	<.001
Cognitive impairment at SPMSQ†, n (%)			<.001
Absent (0-2 of 10)	515 (56.3)	250 (39.1)	
Mild (3-4 of 10)	180 (19.7)	114 (17.8)	
Moderate (5-7 of 10)	125 (13.7)	114 (17.8)	
Severe (≥8 of 10)	94 (10.3)	162 (25.3)	
eGFR, mL/min‡, mean ± SD	55.1 ± 21.1	49.1 ± 22.0	<.001
Outcomes at 12-mo follow-up			
SSE, n (%)	16 (1.7)	25 (3.8)	.011
Major bleeding/CRNMB, n (%)	36 (3.9)	38 (5.8)	.09
Bleeding site§, n (% on no. of bleedings)			.09
Intracranial	7 (19.4)	3 (7.9)	
Gastrointestinal	13 (36.2)	18 (47.3)	
Genitourinary	9 (25.0)	15 (39.5)	
Other	7 (19.4)	2 (5.3)	

AF, atrial fibrillation; BADL, basic activities of daily living; CHA_2DS_2-VASc, congestive heart failure/left ventricular dysfunction, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack/systemic embolism, vascular disease, aged 65-74 years, sex category; CRNMB, clinically relevant non-major bleeding; eGFR, estimated glomerular filtration rate; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly; IADL, instrumental activities of daily living; IQR, interquartile range; MB, major bleeding; OAT, oral anticoagulant therapy; SPMSQ, Short Portable Mental Status Questionnaire; SSE, stroke or systemic embolism; VKA, vitamin K antagonist.

*Data unavailable for 5 of 1578 patients (3 of 920 alive at follow-up and 2 of 658 dead at follow-up).

†Data unavailable for 24 of 1578 patients (6 of 920 alive at follow-up and 18 of 658 dead at follow-up).

‡Data unavailable for 32 of 1578 patients (22 of 920 alive at follow-up and 10 of 658 dead at follow-up).

§Fisher exact test.

Supplementary Table 4
Variables Associated With All-Cause Mortality at 12 Months From Discharge, Multivariable Analysis

Variable	Odds Ratio (95% CI)	*P* Value
Age, y	1.054 (1.031-1.079)	<.001
CHA_2DS_2-VASc score	0.966 (0.874-1.068)	.50
HAS-BLED score	1.117 (0.946-1.320)	.19
eGFR, mL/min	0.992 (0.986-0.997)	.003
Charlson Comorbidity Index	1.140 (1.058-1.228)	<.001
SPMSQ, no. of errors	1.056 (1.012-1.101)	.012
History of SSE	0.992 (0.719-1.370)	.19
History of bleeding	1.253 (0.916-1.715)	.96
BADL partial dependence (4-5 of 6) vs complete autonomy (6 of 6)	1.355 (0.961-1.910)	.08
BADL complete dependence (<4 of 6) vs complete autonomy (6 of 6)	1.764 (1.208-2.576)	.003
IADL partial dependence (2-4 of 8) vs complete autonomy (>4 of 8)	1.208 (0.851-1.715)	.29
IADL complete dependence (<2 of 8) vs complete autonomy (>4 of 8)	1.544 (1.012-2.355)	.003
OAT-deprescribed at discharge	1.406 (1.680-1.851)	.015

BADL, basic activities of daily living; CHA_2DS_2-VASc, congestive heart failure/left ventricular dysfunction, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack/systemic embolism, vascular disease, aged 65-74 years, sex category; eGFR, estimated glomerular filtration rate; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly; IADL, instrumental activities of daily living; OAT, oral anticoagulant therapy; OR, odds ratio; SPMSQ, Short Portable Mental Status Questionnaire; SSE, stroke or systemic embolism.

Supplementary Table 5
Variables associated with ischemic and bleeding events at 12 months from discharge with competitive risk of mortality.

Variable	SSE (n = 41) vs Alive and Free From SSE (n = 904)		Dead Without Previous SSE (n = 633) vs Alive and Free From SSE (n = 904)	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age, y	1.030 (0.963-1.101)	.39	1.053 (1.029-1.077)	<.001
CHA_2DS_2-VASc score	1.253 (0.942-1.665)	.12	0.945 (0.853-1.046)	.28
HAS-BLED score	1.007 (0.615-1.648)	.98	1.136 (0.959-1.345)	.14
eGFR, mL/min	0.995 (0.979-1.011)	.55	0.992 (0.987-0.998)	.005
Charlson Comorbidity Index	0.953 (0.774-1.173)	.65	1.146 (1.063-1.235)	<.001
SPMSQ, no. of errors	0.896 (0.782-1.026)	.11	1.053 (1.009-1.099)	.019
History of SSE	1.747 (0.745-4.097)	.20	0.993 (0.715-1.380)	.97
History of bleeding	0.767 (0.270-2.179)	.62	1.222 (0.890-1.678)	.22
BADL partial dependence (4-5 of 6) vs complete autonomy (6 of 6)	2.800 (1.022-7.671)	.045	1.397 (0.985-1.982)	.06
BADL complete dependence (<4 of 6) vs complete autonomy (6 of 6)	3.586 (1.112-11.561)	.033	1.786 (1.216-2.624)	.003
IADL partial dependence (2-4 of 8) vs complete autonomy (>4 of 8)	0.636 (0.240-1.686)	.36	1.228 (0.859-1.756)	.26
IADL complete dependence (<2 of 8) vs complete autonomy (>4 of 8)	0.845 (0.271-2.639)	.77	1.585 (1.030-2.439)	.04
OAT-deprescribed at discharge	0.677 (0.252-1.818)	.44	1.472 (1.115-1.943)	.006
Variable	MB/CRNMB (n = 74) vs Alive and Free From MB/CRNMB (n = 884)		Dead Without Previous MB/CRNMB (n = 620) vs Alive and Free From MB/CRNMB (n = 884)	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age, y	1.005 (0.955-1.058)	.85	1.054 (1.029-1.079)	<.001
CHA2DS2-VASc score	0.820 (0.653-1.029)	.09	0.958 (0.864-1.062)	.42
HAS-BLED score	1.151 (0.798-1.662)	.45	1.154 (0.972-1.370)	.101
eGFR, mL/min	0.988 (0.976-1.000)	.04	0.993 (0.987-0.998)	.012
Charlson Comorbidity Index	1.218 (1.051-1.410)	.009	1.169 (1.082-1.262)	<.001
SPMSQ, number of errors	1.049 (0.948-1.161)	.36	1.055 (1.010-1.101)	.016
History of stroke/SE	1.209 (0.575-2.543)	.62	0.959 (0.689-1.335)	.80
History of bleeding	1.728 (0.920-3.247)	.09	1.215 (0.879-1.679)	.24
BADL partial dependence (4-5 of 6) vs complete autonomy (6 of 6)	1.291 (0.650-2.563)	.47	1.227 (0.859-1.753)	.26
BADL complete dependence (<4 of 6) vs complete autonomy (6 of 6)	1.134 (0.504-2.552)	.76	1.599 (1.083-2.361)	.018
IADL partial dependence (2-4 of 8) vs complete autonomy (>4 of 8)	1.271 (0.638-2.532)	.50	1.316 (0.914-1.893)	.14
IADL complete dependence (<2 of 8) vs complete autonomy (>4 of 8)	0.718 (0.279-1.848)	.49	1.788 (1.157-2.764)	.009
OAT-deprescribed at discharge	0.953 (0.491-1.853)	.89	1.485 (1.120-1.967)	.006

BADL, basic activities of daily living; CHA_2DS_2-VASc, congestive heart failure/left ventricular dysfunction, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack/systemic embolism, vascular disease, aged 65-74 years, sex category; eGFR, estimated glomerular filtration rate; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly; IADL, instrumental activities of daily living; OAT, oral anticoagulant therapy; OR, odds ratio; SPMSQ, Short Portable Mental Status Questionnaire; SSE, stroke or systemic embolism.