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Health status, geriatric syndromes and prescription of oral anticoagulant therapy in elderly medical in-patients with atrial fibrillation: a prospective observational study

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Although oral anticoagulants (OAs) proved to be effective for the prevention of stroke in elderly with atrial fibrillation (AF) [1], [2] and [3], this therapy is widely underused particularly in the oldest patients who, because of their high risk of stroke, should derive the greatest benefit from anticoagulant therapy [4], [5], [6] and [7]. We hypothesized that poor health conditions and the presence of common geriatric syndromes might influence physicians' attitude to prescribe OAs. We investigated the prevalence of common geriatric syndromes and contraindications to OAs in real-world older medical in-patients with AF, and whether these variables are associated with under-prescription of OAs at discharge.

Patients aged ≥ 65 years with known or first detected AF (defined paroxysmal, persistent or permanent according to current international recommendations) admitted in the period January–April 2014 at the following clinical units: Geriatria e Malattie Metaboliche dell'OssO, Medicina Interna 1U, Medicina Interna 3U, Medicina Interna 4U, Medicina Interna 6, Medicina Interna DEA (Città della Salute e della Scienza-Molinette, Torino), Geriatria (A.O.U. S. Luigi Gonzaga, Orbassano), and Geriatria (A.S.O. S. Croce e Carle, Cuneo) underwent a standardized evaluation by resident doctors under the supervision of senior specialists in geriatrics, including stroke and bleeding risk according to CHA₂DS₂-VASC and HAS-BLED score, comorbidity (CHARLSON index), moderate or severe cognitive impairment (scores of 5–7 and ≥ 8 respectively, at the SPMSQ, Short Portable Mental Status Questionnaire), partial or total functional dependence (scores of 1–2 and ≥ 3 respectively, at the ADL, Activities of Daily Living, and ≤ 9 at the IADL, Instrumental Activities of Daily Living Scale), depression (score ≥ 7 at the GDS, Geriatric Depression Scale short form), frailty (score ≥ 4 at the Groningen Frailty indicator), malnutrition (score ≤ 11 at the MNA, Mini Nutritional Assessment), and risk of falls (score ≥ 2 at the Conley's scale). Glomerular filtration rate was estimated according to the Cockcroft–Gault formula. The following conditions were considered major contraindications to anticoagulation: recent (< 3 months) major cerebral or systemic bleeding (defined as fatal bleeding, and/or symptomatic bleeding in a critical area or organ, and/or bleeding causing a fall in hemoglobin level of 20 g/l, 1.24 mmol/l, or more, or leading to transfusion of two or more units of whole blood or red cells), and/or bleeding causing patient's hospitalization according to current international recommendations, recent surgery, severe thrombocytopenia, history of alcohol abuse, liver failure/cirrhosis, advanced malignancies, psychiatric disorders, and allergy to an oral anticoagulant. Antithrombotic therapy was recorded at admission and at discharge. Finally, a brief questionnaire was submitted to each discharging physician, requiring the indication of the main reason for denying OAs among these options: 1) not indicated; 2) no clear evidence of benefit in these real-world older patients; 3) fear of bleeding; 4) harm greater than benefit; 5) “futile” therapy; 6) difficult or impossible management of OA therapy; 7) advanced age; and 8) very short life expectancy.

Signed informed consent was obtained for all participants and the study was conducted according to the recommendations guiding physicians in biomedical research involving human subjects. Univariate associations were evaluated using ANOVA, Chi-square and Mann–Witney tests; independent associations between significant variables from univariate analysis and prescription of oral anticoagulants were evaluated using a logistic regression model (forward stepwise method).

Among 631 patients with AF, informed consent and complete data were available for 550 patients; 37 subjects died in the hospital leaving a sample of 513 patients. Table 1 shows the main demographic and clinical variables of the sample studied: mean age was 81.7 years and 55.6% were females; frailty and functional dependence were observed in roughly more than two thirds and half of the patients,

respectively; 40% of patients had moderate or severe cognitive impairment. Mean CHA₂DS₂-VASC and HAS-BLED scores were 4.7 ± 1.4 and 2.9 ± 1.1 , respectively. During hospital stay, ≥ 1 contraindications to OAs were documented in 83 patients. At discharge oral anticoagulant therapy was prescribed in 48.7% of the patients, and 27.7% of the patients received antiplatelet therapy only. Table 2 shows variables independently associated with the prescription of OAs in the overall sample and in patients without contraindications. Younger age, permanent AF, absence of contraindications, lower comorbidity, greater cardio-embolic risk and lower risk of bleeding were associated with the prescription of anticoagulant therapy in the overall sample, while among patients without contraindications, younger age, permanent AF, greater cardio-embolic risk, lower risk of bleeding, and functional independence were associated with prescription of anticoagulant therapy. Advanced age, very short life expectancy, difficult or impossible management of therapy, perceived fear of bleeding and harm greater than benefit were the most common reasons why physicians withhold OAs.

Table 1. Demographic and clinical variables in the total sample of patients.

Age, years, m \pm sd	81.7 \pm 6.8
Age \geq 75 years, n (%)	466 (84.7)
Female, n (%)	306 (55.6)
BMI, m \pm sd	25.5 \pm 5.3
AF known before admission, n (%)	483 (87.8)
Paroxysmal AF, n (%)	154 (28.0)
Permanent AF, n (%)	329 (59.8%)
CHARLSON, m \pm sd	3.4 \pm 2.2
ADL dependent, n (%)	251 (45.6)
IADL dependent, n (%)	356 (64.7)
Moderate–severe cognitive impairment, n (%)	221 (40.2)
Depression, n (%)	202 (36.7)
Frail, n (%)	426 (77.5)
At risk of malnutrition, n (%)	434 (78.9)
Dementia, n (%)	89 (16.2)
Depression, n (%)	71 (12.9)
eGFR < 60 ml/min, n (%)	157 (28.5)
Oral anticoagulant therapy at entry, n (%)	261 (47.4)
Oral anticoagulant therapy only at entry, n (%)	228 (41.4)
Antiplatelet therapy at entry, n (%)	183 (33.3)
Oral anticoagulant and antiplatelet therapy at entry, n (%)	33 (6.0)
Other	32 (5.8)
No antithrombotic therapy at entry, n (%)	74 (13.5)
CHA ₂ DS ₂ -VASC, m \pm sd	4.7 \pm 1.4
HAS-BLED, m \pm sd	2.9 \pm 1.1
Patients with ≥ 1 major contraindications to oral anticoagulant therapy, n (%)	83 (15)
Mean length of stay, days, m \pm sd	15.8 \pm 13.2
Oral anticoagulant therapy at discharge, n (%)	250 (48.7)
Oral anticoagulant therapy only, n (%)	222 (43.3)
Warfarin	214 (85.6)
Dabigatran	21 (8.4)
Rivaroxaban	6 (2.4)
Apixaban	9 (3.6)
Antiplatelet therapy only, n (%)	142 (27.7)
Oral anticoagulant and antiplatelet therapy, n (%)	28 (5.4)
Other	29 (5.6)
No antithrombotic therapy, n (%)	92 (18)

Table 2. Variables associated with prescription of oral anticoagulant therapy at discharge: multivariate analysis in the total sample of patients (A) and in those who did not have contraindications to oral anticoagulant therapy (B).

	A: total sample of patients			B: without contraindications to oral anticoagulant therapy		
	OR	95% IC	P value	OR	95% IC	P value
Age, years	0.706	0.594–0.840	< .0001	0.738	0.612–0.890	0.0014
Permanent AF	1.000			1.000		
Persistent AF	0.890	0.425–1.863	0.7569	0.759	0.332–1.739	0.5148
Paroxysmal AF	0.211	0.130–0.345	< .0001	0.204	0.121–0.345	0.0010
CHA ₂ DS ₂ -VASC	1.491	1.212–1.835	0.0002	1.470	1.168–1.850	0.0010
HAS-BLED	0.642	0.493–0.837	0.0010	0.626	0.470–0.834	0.0010
CHARLSON index	0.866	0.779–0.964	0.0084	0.859	0.764–0.965	0.0108
Contraindications	0.325	0.167–0.634	0.0010			
Dependent (ADL)	0.637	0.377–1.074	0.0909	0.640	0.365–1.125	0.1209
Cognitive impairment (SPMSQ)	0.789	0.466–1.335	0.3766	0.632	0.359–1.113	0.1120
Depression (GDS)	1.369	0.847–2.212	0.1993	1.561	0.933–2.610	0.0897
Frailty (Groningen)	0.792	0.425–1.476	0.4628	0.803	0.410–1.570	0.5205
No malnutrition (MNA)	1.500	0.815–2.759	0.1926	1.401	0.722–2.719	0.3188
Facility vs home discharge	0.670	0.393–1.144	0.1426	0.596	0.334–1.064	0.0801

We observed the high prevalence of poor health status and functional and cognitive impairment among older medical in-patients with AF, with roughly half of them receiving a prescription for OAs at discharge. Our findings suggest that at least 15% of the older medical in-patients could have clinical conditions temporarily or definitely contraindicating anticoagulation. Beyond the presence of contraindications, the underuse of OAs appears to be mainly accounted for by older age and the high prevalence of comorbidities, whereas no significant association was observed with other variables such as frailty, functional dependence and cognitive impairment. The prevalence and clinical implications of geriatric syndromes on OA prescription have never been systematically investigated, despite previous studies having clearly demonstrated the prognostic and clinical relevance of these syndromes in other heart diseases, such as heart failure [8] and [9] and aortic stenosis [10]. Although a clear trend to the underuse of anticoagulation was observed in patients presenting with such syndromes, our findings failed to demonstrate an independent association between geriatric syndromes and under-prescription of OAs, which in contemporary older medical in-patients still appears to be mainly accounted for by older age, despite the bulk of evidence supporting the net clinical benefit of this therapy particularly in the older subjects [2] and [3]. In conclusion, older AF medical in-patients have poor health and functional status, and approximately half of them receive anticoagulant therapy at discharge; under-prescription of OAs appears to be driven mainly by patients' age and comorbidity rather than by the presence of geriatric syndromes. Data on the efficacy of OAs in older medical in-patients with AF are urgently needed to support physicians in daily clinical practice.

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