The role of comprehensive geriatric assessment and functional status in evaluating the patterns of antithrombotic use among older people with atrial fibrillation

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Abstract

Aim of the study is to investigate the use of antithrombotic drugs in older patients with atrial fibrillation (AF) at the time of hospital discharge. We enrolled 399 ≥65 years old patients with AF consecutively admitted to our acute geriatric unit from September 2012 to February 2014. Utilization of antithrombotic drugs, comorbidities, functional, mental and nutritional status were evaluated through a comprehensive geriatric assessment (CGA). A Logistic regression model was used to assess variables associated with antithrombotic use. On admission, 198 patients (49.6%) used oral anticoagulants (OAC), 125 (21.3%) antiplatelets, 32 (8%) low weight molecular heparin (LMWH) and 44 (11%) none of them. At discharge the proportion of patients on OAC increased to 55.7%. Age > 90 years (OR = 2.57, CI = 1.28–5.16, p-value = 0.008), severe functional impairment (OR = 3.38, CI = 1.63–7.01, p-value = 0.001), polypharmacy (OR = 2.07, CI = 1.1–3.86, p-value = 0.023), HAS-BLED score (OR = 1.64, CI = 1.09–2.47, p-value = 0.019) and ≥1 OAC contraindication (OR = 5.01, CI = 2.68–9.34, p-value < 0.001) were all associated with OAC underuse.

In conclusion, OAC is underused in geriatric patients with AF, while antiplatelet, LMWH and no antithrombotic therapy are relatively overused. Factors associated with the decision to not prescribe OAC lie on a mix of clinical and geriatric variables, among which functional status is particularly relevant.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an overall prevalence ranging from 1 to 4.5% (Friberg & Bergfeldt, 2013; Go et al., 2001), up to >10% in people aged 75 years or more (Wilke et al., 2013). It is associated with increased mortality, especially after ischemic stroke and other thromboembolic events (Fang et al., 2008; Taggar, Marin, & Lip, 2008) and, in survivors, with residual functional impairment, increased risk of developing dementia and reduced quality of life (Dublin et al., 2011; Goren, Liu, Gupta, Simon, & Phatak, 2013). Based on various randomized controlled trials, international guidelines (Camm et al., 2012; January et al., 2014) strongly recommend the use of oral anticoagulants (OAC) − either vitamin K antagonists(VKA) (Investigators SPiAF, 1991; Friberg, Rosenqvist, & Lip, 2012; Petersen, Boysen, Godtfredsen, Andersen, & Andersen, 1989) or novel oral anticoagulants (NOAC) (Banerjee, Lane, Torp-Pedersen, & Lip, 2012) − to prevent thromboembolism due to AF. In fact, the use of OAC may determine a significant reduction of ischemic stroke, mortality, inpatient service use and total health care costs (Casciano, Dotiwala, Martin, & Kwong, 2013). These benefits have been demonstrated to be greatest among older community-dwelling subjects (Mant et al., 2007; Singer et al., 2009).

However, despite recommendations, OACs are still underused in clinical practice (Gamra et al., 2014; Ogilvie, Newton, Welner, Cowell, & Lip, 2010), with nearly the half of eligible patients who do not actually receive antithrombotic prophylaxis (Pugh, Pugh, & Mead, 2011) or receive drugs which are less effective than OAC, such as antiplatelets (APT) (Lip et al., 2014; Plichart et al., 2013). Although several conditions have been reported to be associated with under-prescription of OAC (Bahri et al., 2015; Wang et al., 2014), reasons of underuse are not completely known; it could be hypothesized that, beyond OAC eligibility, other variables, such as socio-demographic context, co-occurrence of chronic diseases and perception of patients' non-adherence to OAC may contribute to persistent under-use of OAC.

The Comprehensive Geriatric Assessment (CGA) is a "multidimensional interdisciplinary diagnostic process focusing on multiple health problems of an old person, in order to develop a coordinated and integrated plan for treatment and long term follow up" (Rubenstein, Stuck, Siu, & Wieland, 1991). Unlike standard medical evaluation, CGA also assesses nonmedical domains, including cognitive, functional, nutritional and socio-environmental status, and it is considered the best approach in geriatric medicine for identifying the factors concurring to determine the elder's global health status.

To date only few studies assessed the components of CGA as potentialdeterminants of antithrombotics use in elderly patients with AF. These studies focused only on particular groups of patients, such as those with Alzheimer disease (Tavassoli et al., 2013), or neglected relevant CGA domains, such as the nutritional (Perera, Bajorek, Matthews, & Hilmer, 2009; Tulner et al., 2010) and functional status (Sanchez-Barba, Navarrete-Reyes,

& Avila-Funes, 2013). Furthermore, until now no studies have assessed the rate of prescription of low molecular weight heparin (LMWH), an antithrombotic treatment that it's frequently used as a bridge therapy to replace coumarins before invasive procedures in patients with AF (Gallego, Apostolakis, & Lip, 2012).

Therefore, we undertook the current study to assess in a cohort of elderly patients with AF admitted to an acute geriatric unit (AGU) the use of antithrombotic prevention treatments on admission and at discharge and the clinical and CGA variables associated with OAC underuse at discharge.

2. Methods

This was a retrospective observational study on patients consecutively admitted between September 2012 and February 2014 to the AGU of the San Gerardo Hospital, Monza, Italy. The AGU is a 40-bed acute geriatric ward staffed with geriatricians and specialists in internal medicine. The admission is mainly from the hospital's Emergency Department. Inclusion criteria for this study were: age ≥65 years and documented evidence of an AF and/or either ECG or Holter performed in the 12 months prior to admission. AF clinical types were distinguished as: paroxysmal AF (episodes of the arrhythmia that terminate spontaneously); persistent AF (episodes that are sustained 7 days or more and are not self-terminating); permanent AF (ongoing long-term episodes) The only exclusion criterion was the presence of mechanical heart valve. For the analyses at discharge, we also excluded the patients who underwent surgery and those who have died during hospitalization. The study was approved by the hospital Ethics Committee.

The CGA was performed by trained staff physicians. The data collected on admission included socio-demographics (age, sex and living conditions), comorbidity, functional and nutritional status, cognitive status and drugs currently taken. We also collected data about C-reactive protein, albumin, ureaand creatinine serum levels. At discharge only the functional status and the drugs prescribed were assessed. Comorbidity was assessed using the Charlson Comorbidity Index (Charlson, Pompei, Ales, & MacKenzie, 1987), functional status using the Katz activities of daily living (ADL) (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963) and nutritional status using the Mini-Nutritional Assessment Short Form (MNA-SF) (Kaiser et al., 2009), through patient and surrogate interview referring to one month before the admission. Severe functional impairment was defined as a loss of all the six activities described in the Katz Index. History of falls was evaluated by asking both patients and caregivers if any fall occurred within the 3 months before admission and polypharmacy was defined as the co-occurring assumption of >5 drugs (Onder et al., 2012). The Mini Mental State Examination (MMSE) was used to assess cognitive status (Folstein, Folstein, & McHugh, 1975). It was administered only to patients without delirium, coma, aphasia, or severe hearing or visual impairment, generally 3 days after admission. If the conditions that prevented MMSE assessment on admission were

still present at discharge, the MMSE score was missed. Dementia was ascertained by AGU physicians on admission in accordance with the DSM-IV-TR criteria (American Psychiatric A, 2000); patient was deemed as having dementia if cognitive impairment was present for at least 6 months prior to hospitalization, based on clinical case notes and collateral history from family and/or carers. Severe dementia were defined by a score of ≤15/30 at the Mini Mental Score Examination and/or a score of ≥3/5 at the Clinical Dementia Rating, according to previous studies (Hughes, Berg, Danziger, Coben, & Martin, 1982; Vellas et al., 2005).

The HAS-BLED and CHA_2DS_2-VASc were calculated for each patients based on review of medical records and caregivers' reports. The attending physicians recorded all data using an electronic database. At the end of the study period, the electronic medical records and the hospital discharge letters were reviewed by two of us (AM and GB) in order to ensure accuracy of patients' details.

Patients were classified into OAC and no OAC users and subclassified into APT, LMWH or no-prophylactic drug users. OAC included warfarin, acenocoumarol and new direct oral anticoagulants; APT included aspirin, clopidogrel and dipyridamole while LMWH enoxaparin sodium and nadroparin calcium. At discharge, patients taking both OAC and APT (n = 10) and those taking both LMWH and OAC (n = 32) were recorded into OAC group, while those taking both APT and LMWH (n = 10) were recorded into LMWH (n = 5) or APT group (n = 5), depending on their clinical history.

Continuous variables were described using quartiles and the Wilcoxon Mann Whitney (Kruskal-Wallis test) was applied for comparing two (four) treatment groups. Categorical variables were presented as frequencies and percentages and the Fisher exact test or the chi-squared test were used for comparisons, where appropriate. A logistic regression model was developed for the assessment of various potential predictors on the odds of no OAC use and results were reported as odds ratios (OR) and 95% Confidence Intervals (CI). A multinomial model was also evaluated investigating specifically the use of APT, LWMH and no thromboprophylaxis vs OAC. All the candidate predictors of antithrombotic prescription were first screened through univariate analyses and were retained in the final model, based on backward selection procedure and a-priori knowledge. Comparisons between competitive models were based on the Akaike Information Criterion (AIC) (Harrell, 2001) and sensitivity analyses were conducted to show the robustness of our results using other automatic selection procedures (Vittinghoff, Glidden, Shiboski, & McCulloch, 2012). The analyses were carried-out using SAS 9.2 software (SAS Institute Inc., Cary, USA) and all the test were performed two-tailed, with a significance level of 5%.

3. Results

Of the 1619 subjects admitted to the AGU during the study period, 399 (median age of 85 years and 59.4% females) had a diagnosis of AF, yielding a prevalence of 24.6%. AF was paroxysmal in 63 (15.8%), persistent in 50 (12.5%) and permanent in 286 patients (71.7%).

One hundred ninety-eight (49.6%) patients took OAC on admission, 125 (31.3%) APT, 32 (8%) LMWH, and 44 (11%) none. Socio-demographic characteristics were different among groups: patients taking OAC had the lowest proportion of nonagenarians and were more frequently living at home without assistance, while those taking LMWH and those with any treatment were more frequently living in nursing home. Moreover, OAC users had more frequently a better functional and nutritional status than others, while LMWH and APT users were more frequently disabled, malnourished, comorbid and demented.

At discharge, 47 patients have died, 44 underwent non-elective surgery and 3 were assigned to mixed antithrombotic treatments; these patients were therefore excluded from further analyses, leaving a sample of 305 patients. The proportion of patients taking OAC increased from admission to discharge (55.7% vs 49.6%), as well as the proportion of those taking LMWH (13.4% vs 11%); on the contrary, the proportion of patients prescribed APT decreased (19% vs 31.3%) and the proportion of those with no antithrombotic prevention treatment remained substantially unchanged (11.8% vs 11%). Table 1 shows the main characteristics at discharge. As expected, old age (i.e., ≥ 90 years) was still associated with OAC underuse while better functional status was associated with OAC prescription. Malnutrition, severe dementia and comorbidity were more common among non-OAC patients, though with non-significant association.

Table 1. Characteristics at discharge of the 305 elderly patients with atrial fibrillation.

Characteristic[a]	OAC	No OAC	p-value[*]	APT	LWMH	No therapy	p-value[**]
	n = 170	n = 135		n = 58	n = 41	n = 36	
Age, median (IQR)	83 (80–88)	85 (81–90)	0.082	85.5 (81–90)	85 (80–88)	85 (83–90)	0.281
Age ≥ 90yrs, n (%)	26 (15.3)	34 (25.2)	0.031	16 (27.6)	8 (19.5)	10 (27.8)	0.119
Female sex, n (%)	105 (61.8)	78 (57.8)	0.48	38 (65.5)	27 (65.9)	13 (36.1)	0.018
Living status, n (%)			0.055				0.232
Home	42 (24.7)	19 (14.1)		10 (17.2)	4 (9.8)	5 (13.9)	
Home with assistance	119 (70)	105 (77.8)		44 (75.9)	32 (78.1)	29 (80.6)	
Nursing home	9 (5.3)	11 (8.1)		4 (6.9)	5 (12.2)	2 (5.56)	
History of falls, n (%)	29 (17.1)	21 (15.6)	0.725	8 (13.8)	8 (19.5)	5 (13.9)	0.85

Characteristic[a]	OAC	No OAC	p-value[*]	APT	LWMH	No therapy	p-value[**]
	n = 170	n = 135		n = 58	n = 41	n = 36	
MMSE, median (IQR)	21 (15–26)	20 (13–25)	0.147	17 (10.5–24)	19 (7–24)	23.5 (20–27)	0.006
Severe dementia, n (%)	48 (28.74)	54 (40.3)	0.035	27 (46.6)	20(50.0)	7 (19.4)	0.003
BADL at discharge, median (IQR)	2 (1–5)	1 (0–2)	<0.001	1 (0–3)	0 (0–1)	2 (1–4)	<0.001
Severe functional impairment, n (%)	27 (15.9)	48 (35.6)	<0.001	19 (32.8)	22 (53.7)	7 (19.4)	<0.001
MNA-SF, median (IQR)	9 (7–12)	8 (6–11)	0.026	8 (6–12)	7 (5–9)	10 (7–12)	0.018
Malnutrition, n (%)	49 (28.8)	53 (39.3)	0.055	22 (37.9)	22 (53.7)	9 (25.7)	0.001
Albumin, median (IQR)	3.4 (3.1–3.7)	3.3 (3.0–3.6)	0.215	3.4 (3.1–3.6)	3.2 (2.9–3.5)	3.4 (3.1–3.6)	0.203
Atrial fibrillation type, n (%)			0.061				0.115
Paroxysmal	18 (10.6)	23 (17.0)		8 (13.8)	7 (17.9)	8 (22.2)	
Persistent	16 (9.4)	20 (14.8)		11 (18.9)	3 (7.3)	6 (16.7)	
Permanent	136 (80.0)	92 (68.2)		39 (67.2)	31 (75.6)	22 (61.1)	
Charlson comorbidity index, median (IQR)	2 (1–4)	3 (2–4)	0.082	3 (2–5)	3 (2–4)	3 (1.5–5)	0.306
Myocardial infarction, n (%)	32 (18.8)	29 (21.5)	0.564	11 (19.0)	7 (17.1)	11 (30.6)	0.405
Congestive heart failure, n (%)	72 (42.4)	42 (31.1)	0.044	17 (29.3)	10 (24.4)	15 (41.7)	0.084
Peripheral vascular disease, n (%)	30 (17.6)	22 (16.3)	0.755	6 (10.3)	8 (19.5)	8 (22.2)	0.433
Cerebrovascular disease, n (%)	38 (22.4)	40/29.6)	0.148	19 (32.8)	13 (31.7)	8 (22.2)	0.318
COPD, n (%)	48 (28.2)	28 (20.7)	0.133	11 (19.0)	5 (12.2)	12 (33.3)	0.072
Connective tissue disease, n (%)	2 (1.2)	5 (3.7)	0.143	4 (6.9)	1 (2.4)	0	0.06
Peptic ulcer disease, n (%)	7 (4.1)	5 (3.7)	0.853	4 (6.9)	0	1 (2.8)	0.366
Diabetes, n (%)	32 (18.8)	20 (14.8)	0.355	8 (13.8)	5 (12.2)	7 (19.4)	0.65
Complicated diabetes, n (%)	15 (8.8)	18 (13.3)	0.208	12 (20.7)	4 (9.8)	2 (5.6)	0.054
Moderate/severe CKD, n (%)	39 (22.9)	22 (16.3)	0.150	12 (20.7)	4 (9.8)	5 (11.4)	0.275
Hemiplegia, n (%)	13 (7.7)	19 (14.1)	0.069	7 (12.1)	11 (26.8)	1 (2.8)	<0.001

Characteristic[a]	OAC	No OAC	p-value*	APT	LWMH	No therapy	p-value**
	n = 170	n = 135		n = 58	n = 41	n = 36	
Leukaemia or lymphoma, n (%)	7 (4.1)	6 (4.4)	0.888	2 (3.5)	1 (2.4)	3 (8.3)	0.594
Solid tumor, n (%)	16 (9.4)	14 (10.4)	0.780	7 (12.1)	3 (7.3)	4 (11.1)	0.869
Solid tumor with metastasis, n (%)	3 (2.0)	5 (3.7)	0.293	1 (1.7)	2 (4.9)	2 (5.6)	0.046
Mild liver disease, n (%)	3 (1.8)	7 (5.2)	0.096	5 (8.6)	1 (2.4)	1 (2.8)	0.003
Moderate to severe liver disease, n (%)	1 (0.6)	5 (3.7)	0.052	3 (5.2)	0	2 (5.6)	0.153
Number of drugs, median (IQR)	5 (4–6)	4 (3–5)	< 0.001	4 (3–6)	4.5 (3.5–6)	3 (2–4)	<0.001
Drugs at discharge, n (%)							
Beta-blockers	46 (27.1)	51 (62.2)	0.046	22 (37.9)	11 (26.8)	18 (50)	0.033
ACE-Inhibitors/ARBs	79 (46.5)	36 (26.7)	<0.001	15 (25.9)	9 (21.9)	12 (33.3)	0.003
Statins	20 (11.8)	15 (11.1)	0.859	9 (15.5)	3 (7.3)	3 (8.3)	0.574
Diuretics	84 (49.4)	60 (44.4)	0.388	25 (43.1)	17 (41.5)	18 (50)	0.710
Calcium channel blockers	19 (11.2)	12 (8.9)	0.511	8 (13.8)	3 (7.3)	1 (2.8)	0.315
Transdermal nitroglicerine	24 (14.1)	23 (44.3)	0.483	11 (18.9)	7 (17.1)	5 (13.9)	0.818
Polypharmacy (≥5), n (%)	42 (24.7)	42 (31.1)	0.214	21 (36.2)	9 (22.0)	12 (33.0)	0.249
CHA_2DS_2VASc, median (IQR)	4 (3–5)	4 (3–5)	0.619	4 (4–5)	4 (4–5)	3.5 (3–4.5)	0.092
HAS-BLED, median (IQR)	1 (1–2)	2 (1–2)	<0.001	2 (1–2)	2(1–2)	2(1–2)	0.001
Contraindication to OAC, n (%)	27 (16.3)	64 (49.2)	<0.001	23 (41.8)	19 (47.5)	22 (62.9)	<0.001
Discharge to Nursing Home, n (%)	14 (8.2)	22 (16.3)	0.030	8 (13.8)	9 (22.0)	5 (13.9)	0.09

Abbreviations: OAC, Oral Anti Coagulant; APT, Anti-Platelet Therapy; LMWH, Low Molecular Weight Heparin; MMSE, Mini Mental State Examination; BADL, Basic Activity of Daily Living; MNA-SF, Mini-Nutritional Assessment Short Form; COPD, Chronic Obstructive Pulmonary Disease; CKD, Chronic Kidney Disease; ARB, Angiotensin Receptor Blockers. Severe dementiawas defined as a MMSE score ≤ 15/30 or as a CDR score ≥ 3/5. Severe functional impairmentwas defined as a Katz ADL score = 0/6.

*Comparison OAC vs no OAC.

**Comparison OAC vs APT vs LMWH vs No therapy.

[a]There were the following missing values: MMSE = 49 missing; MNA-SF = 5 missing; Albumin = 7 missing; CHA_2DS_2VASc = 1 missing; HASBLED = 3 missing.

The results of the analysis for the association of clinical variables with OAC underuse at hospital discharge are reported in Table 2. In multivariable regression model, age > 90 years (OR = 2.57, CI = 1.28–5.16, p-value = 0.008), severe functional impairment (OR = 3.38, CI = 1.63–7.01, p-value = 0.001), polypharmacy (OR = 2.07, CI = 1.1–3.86, p-value = 0.023), HAS-BLED score (OR = 1.64, CI = 1.09–2.47, p-value = 0.019) and having at least one OAC contraindication (OR = 5.01, CI = 2.68–9.34, p-value < 0.001) were associated with OAC underuse.

Table 2. Factors associated with OAC underuse at discharge.

Characteristics		No OAC/n	% No OAC	Multivariate Analysis		
				OR	95%CI	p-value
Age:	<90 yrs	101/245	41.2	1		
	>90 yrs	34/60	56.7	2.57	1.28–5.16	0.008
Gender:	M	57/122	46.7	1		
	F	78/183	42.6	0.77	0.44–1.37	0.378
Severe dementia:	No	80/102	40.2	1		
	Yes	54/199	52.9	0.92	0.48–1.78	0.813
Severe functional impairment:	No	48/75	64.0	1		
	Yes	87/230	37.8	3.38	1.63–7.01	0.001
Malnutrition:	No	81/198	40.9	1		
	Yes	53/102	52.0	1.03	0.56–1.9	0.924
History of falls:	No	114/255	44.7	0.79	0.39–1.62	0.517
	Yes	21/50	42.0	1		
Charlson comorbidity index:				0.98	0.85–1.13	0.801
Stroke:	No	116/273	42.5	1		
	Yes	19/32	59.4	0.96	0.37–2.49	0.926
Congestive heart failure:	No	93/191	48.7	1		
	Yes	42/114	36.8	0.58	0.31–1.09	0.091
Polypharmacy (≥5):	No	93/221	42.1	1		
	Yes	42/84	50.0	2.07	1.1–3.86	0.023
HASBLED score:				1.64	1.09–2.47	0.019
Contraindication to OAC:	No	66/205	32.2	1		
	Yes	64/91	70.3	5.01	2.68–9.34	<0.001

Characteristics		No OAC/n	% No OAC	Multivariate Analysis		
				OR	95%CI	p-value
Discharge to Nursing home:	No	113/269	42.0	1		
	Yes	22/36	61.1	2.22	0.97–5.01	0.059

Abbreviations: OAC, Oral AntiCoagulant; BADL, Basic Activity of Daily Living; Severe dementiawas defined as a MMSE score ≤ 15/30 or as a CDR score ≥ 3/5. Severe functional impairmentwas defined as a Katz ADL score = 0/6.

Fig. 1 shows the results of a multivariable analysis with non-OAC subgroups as dependent variables. Contraindication to OAC was the only variable which was associated with all non-OAC subgroups: APT (OR = 3.33, CI = 1.54–7.21, p-value = 0.002), LMWH (OR = 4.89, CI = 2.03–11.74, p-value < 0.001) and no therapy (OR = 9.84, CI = 3.95–24.53, p-value <0.001), polypharmacy (OR = 2.35, CI = 1.09–5.06, p-value = 0.029), severe functional impairment (OR = 2.93, CI = 1.19–7.24, p-value = 0.019) and age >90 years (OR = 4.89, CI = 1.22–6.53, p-value = 0.016) were predictors of APT use rather than OAC. Severe functional impairment (OR = 5.56, CI = 2.05–15.13, p-value<0.001) and HAS-BLED score (OR = 1.82, CI = 1.01-3.28, p-value = 0.046) were predictors of LMWH use, while age >90 years (OR = 4.28, CI = 1.49–12.27, p-value = 0.006) was predictor of no antithrombotic treatment. Moreover, being female was predictor of OAC use rather than no therapy (OR = 0.34, CI = 0.13–0.84, p-value = 0.019).

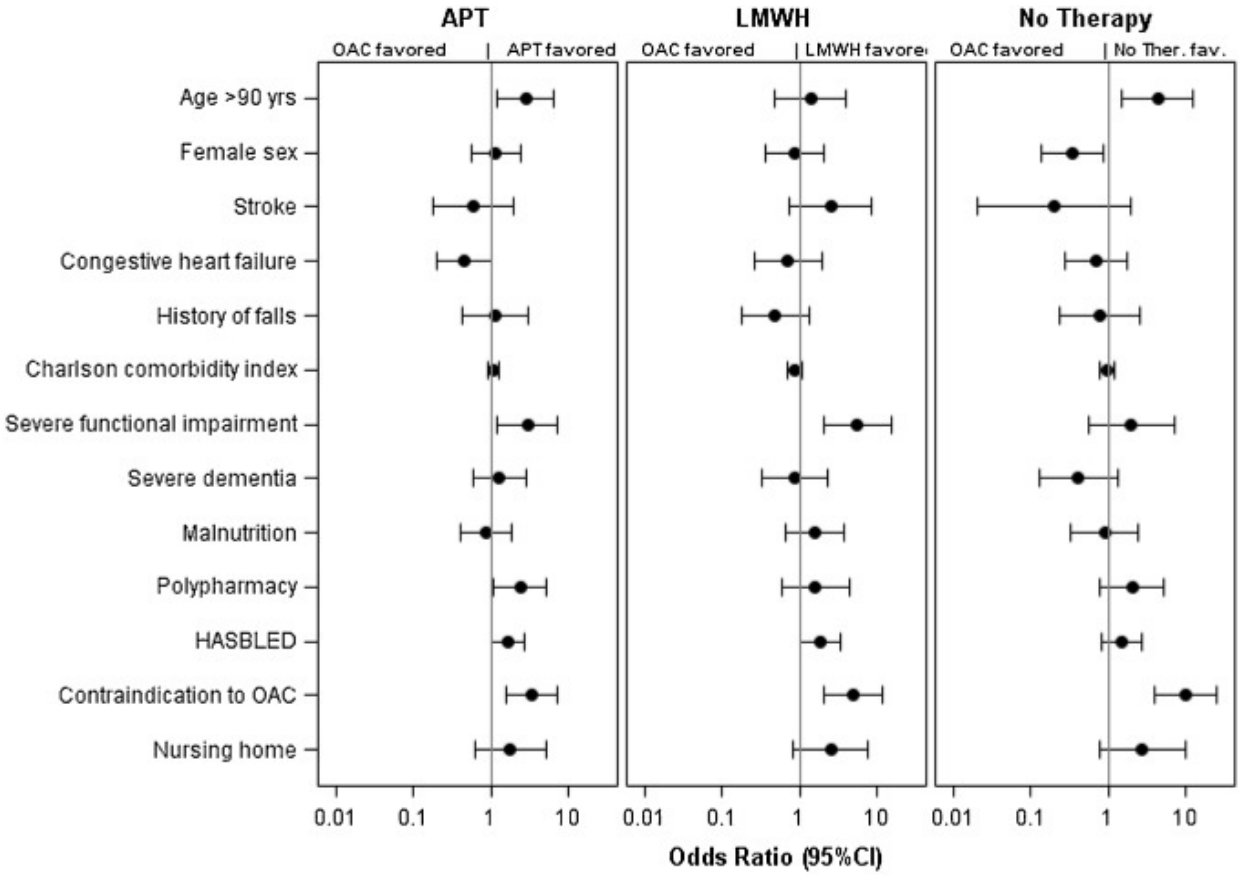

Fig. 1. Forest plots showing the results of multivariable regression analysis for the use of APT, LMWH or no thromboprophylaxis vs OAC at discharge.
Abbreviations: OAC, Oral AntiCoagulant; APT, Anti-Platelet Therapy; LMWH, Low Molecular Weight Heparin; OR, Odds Ratio; CI, Confidence Interval.

4. Discussion

In this retrospective study evaluating a cohort of older patients admitted to our AGU during a period of eighteen months, the prevalence of AF was high (24.6%). We found that, on admission, nearly half of the whole cohort was prescribed OAC and less than a third APT, while the others received either LMWH or no thromboprophylaxis. At discharge, a higher proportion of patients were prescribed OAC, while a lower proportion APT. The proportion of patients receiving LMWH or no antithrombotic drugs remained substantially unchanged. We also found that a mix of variables, which were different for each thromboprophylactic approach, influenced the attitude of prescribing physicians at discharge.

The rate of OAC utilization in our study confirmed that adherence to international guidelines was far from being optimal: in fact, only half of the patients were prescribed OAC before hospital admission and at discharge this proportion was only a bit higher. These findings are in substantial agreement with previous studies in community dwelling population, showing that only 30–60% of eligible patients are prescribed OAC (Ogilvie et

al., 2010; De Breucker, Herzog, & Pepersack, 2010; Di Pasquale et al., 2013). In a Turkish registry, only 37% of 631 patients with AF and age ≥75 years were on warfarin (Ertas et al., 2013), and in a Japanese registry, OAC was given to 53.1% of the patients (Akao et al., 2014). Analyzing the data of 81381 older patients in a UK database, Scowcfroft found that patients ≥ 80 years were significantly less likely to be prescribed warfarin than younger; in detail 32% of patients ≥ 80 years received warfarin compared with 57% aged 60–69 years, and 55% aged 70–79 years (Scowcroft, Lee, & Mant, 2013).

The use of non-OAC antithrombotic preventive approaches observed in our study deserves comments. The proportion of patients receiving APT was similar, if not lower, to previous studies of primary care (Tavassoli et al., 2013; Tulner et al., 2010; Bellelli, Guerini, Bianchetti, & Trabucchi, 2002), and its prescription rate was even lower at discharge. To our knowledge, only two studies assessed LMWH use in similar populations, finding 7.5-8% prescription on hospital admission (Maes et al., 2014; Marcucci et al., 2010) 26% at discharge[47] and other two studies found rates of no-prescription ranging from 11.2% to 44% (Tavassoli et al., 2013; Bellelli et al., 2002). Therefore, our findings on the use of these approaches may be considered in keeping with existing literature.

We found that the presence of at least one contraindication and high HAS-BLED score were predictors of OAC underuse. Only few studies assessed OAC contraindications (Tavassoli et al., 2013; Tulner et al., 2010) and hemorrhage risk scores in geriatric populations with AF (Sanchez-Barba et al., 2013; Maes et al., 2014), though none of them assessed both factors at the same time. In previous studies, contraindications were unrelated to OAC underuse, but an important difference between those and our study is that our study has been carried out in hospital while previous in outpatients (Tavassoli et al., 2013; Tulner et al., 2010). On the contrary, previous studies that assessed the hemorrhage risk scores have been carried out in hospital settings. One of these studies used HAS-BLED score, finding significant association with OAC underprescription (Sanchez-Barba et al., 2013), while the second used HEMORR$_2$HAGES score, finding that two items (namely, antiplatelet and ethanol abuse) were the main determinants (Maes et al., 2014). Importantly, the CHA$_2$DS$_2$VASc score was not different among groups in our study. This finding is in keeping with existing literature (Tavassoli et al., 2013;Perera et al., 2009; Tulner et al., 2010; Sanchez-Barba et al., 2013; Maes et al., 2014).

The finding that severe functional impairment was strongly associated with OAC underuse and predicted both APT and LMWH use indirectly suggests that AGU physicians used some information from CGA assessment to choice the thromboembolic prevention approach and also that they deemed ineffective OAC prescription when disability was severe. Because severe disability is a marker of reduced lifespan (Rozzini et al., 2005), it could be hypothesized that this approach reflects the feeling of AGU physicians that the risk/benefit ratio for these patients was unfavorable. If this could be a suitable

explanation, it remains to establish whether this approach may reflect malpractice or accuracy.

Other predictors of OAC underuse were age ≥90 years and polypharmacy. The finding that older age predicts OAC underuse is reported in both community dwelling (Tulner et al., 2010; Doucet et al., 2008) and hospital-based studies (Maes et al., 2014; Marcucci et al., 2010), and is therefore not novel in literature. However, it is of interest that being nonagenarians was associated in our population with an increased odd of APT prescription, a drug that is neither more effective for prevention nor safer for the risk of hemorrhage than OAC (Mant et al., 2007), and with an increased odd of no prescription of antithrombotic prevention treatments. No association was found between age ≥90 years and LMWH prescription. Polypharmacy is also a well-known predictor of OAC underuse in hospital populations (Perera et al., 2009; Marcucci et al., 2010). However, our study found that polypharmacy was associated with an increased odd of being prescribed APT but not with the prescription of LMWH or no antithrombotic prevention treatments. Future studies are expected to assess the reasons of these physicians' attitudes on this segment of population.

A strength of the study is that we used an extensive CGA to evaluate the patients' multiple bio-psychosocial domains (i.e. cognitive status, functional status, malnutrition, etc.), which is a novelty in comparison to previous research. Our sample size is larger than previous studies (Tavassoli et al., 2013; Tulner et al., 2010; De Breucker et al., 2010) and reflects a "real-world" population of hospitalized older patients. Especially this point deserves comments. Prescribing OAC for elderly patients with AF is often troublesome in clinical practice. In light of the discrepancy existing between the "ideal" and the "real" world, with only half of the eligible older patients with AF who actually receive OAC (Ogilvie et al., 2010; Bahri et al., 2015; De Breucker et al., 2010; Di Pasquale et al., 2013; Ertas et al., 2013; Akao et al., 2014; Scowcroft et al., 2013), it could be hypothesized that a number of factors, which are currently not included in common scoring systems, might play a relevant role in the physician's decision to prescribe OAC (Bungard, Ghali, Teo, McAlister, & Tsuyuki, 2000). For example, it has been reported that some physicians are reluctant on prescribing anticoagulation when they perceive the "futility" of OAC therapy in vulnerable elderly, and also that they are more prone to withhold these drugs when they believe that patients would refuse therapy or be noncompliant (Bungard et al., 2000). However, accomplishing these tasks (i.e., measuring futility and assessing noncompliance), is not always easy and the physician's clinical impression may fails if not supported by systematic assessments. The CGA has been created properly at this aim, to reduce the risk of misevaluating the complex and demanding needs of older patients (Rubenstein et al., 1991; Rubenstein & Rubenstein, 1991). By demonstrating that severe functional impairment is strongly associated with a reduced OAC use in elderly patients, our study

suggests that functional status is an important marker for physician's decision in prescribing OAC and should be therefore taken into account in future studies.
Several limitations are also worthy of comments. Firstly, this is a single-site and retrospective study, thus limiting the transferability of our findings to other settings. Secondly, we were not able to assess whether CGA can drive the decision-making processes on the thromboembolic prevention approaches in our patients, due to a small number of change in treatments from admission to discharge. Future studies are expected to this aim. Thirdly, about two-thirds of CHA_2DS_2-VASc and HAS-BLED scores have been obtained retrospectively, which may represent a source of possible bias. Another missing information is that we did not assess patient's willingness to treatment. Finally the small number of patients across the no OAC subgroups may limit the strength of our secondary analysis; nonetheless, it should be highlighted that such a distinction in more than two groups of patients is a novel approach in this field and might provide information regarding the use of APT, LMWH or no therapy that may be helpful to understand some important differences among groups.
In conclusion, our study suggests that the selection of antithrombotic prevention treatments in older patients with AF relies on a mix of clinical and geriatric variables, among which a severe impairment of functional status is particularly relevant.

Conflict of interest

All authors declare no financial and personal relationships with other people or organisations that could inappropriately influence this work.

Author contributions

Mazzone: study concept and design, recruitment of participants, acquisition of data, preparation of the manuscript. Bellelli: study concept and design, preparation of the manuscript Bo: revision of the manuscript. Lucenti: design and interpretation of data analyses, preparation of the manuscript. Galimberti: design and interpretation of data analyses, preparation of the manuscript. Annoni: revision of the manuscript. All authors read and approved the final manuscript.

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