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Atrial fibrillation and prediction of mortality by conventional clinical score systems according to the setting of care

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ABSTRACT

Background: Atrial fibrillation (AF) is associated with high morbidity and mortality, also among anticoagulated patients. Our aim was to evaluate the predictive role for long-term mortality of a series of risk stratification scores associated with cardiovascular or thromboembolic outcomes ($CHADS_2$, CHA_2DS_2-VASc, ATRIA, TIMI-AF), and bleeding complications (HAS-BLED) in an unselected population of patients with AF.
Methods: Single center, observational, prospective registry of consecutive patients with AF, undergoing clinical/echocardiographic evaluation in a University Hospital, as either in-patients or out-patients. We assessed the role of each single score as predictors of long-term survival according to clinical setting.
Results: We enrolled 1051 patients, mean age 72 ± 12 years, who were followed for 797 ± 298 days. All the tested scores showed a good performance in prediction of mortality, together with several clinical factors (older age, chronic heart failure, diabetes, renal impairment, previous transient ischemic attack, left ventricular ejection fraction). The values at C-statistics ranged between modest (0.608–0.684) of inpatients to good (0.708–0.751) in outpatients without any statistical difference between the scores, excepted a lower performance of HAD-BLED.
Conclusions: Risk scores currently adopted for decision making on starting oral anticoagulation provide good prediction of long-term survival in unselected AF patients, especially in the outpatient setting.

1. Introduction

Atrial fibrillation (AF) is associated with high morbidity and mortality, which is still evident among anticoagulated patients [1–5]. To improve effective clinical decision-making several clinical scoring systems (see Supplementary Table 1) have been developed to stratify the risk of thromboembolic events [6–8], bleeding complications [9] risk of adverse cardiovascular events [10] and the identification of patients for whom a therapeutic benefit of novel oral anticoagulants (NOACs) over Vitamin K antagonist (VKA) [11]. Previous studies have shown that the $CHADS_2$ and CHA_2 DS_2 –VASc scores may have some predictive role for survival of AF and non-AF patients both in inpatient and outpatient settings [12–17] but the adoption in non-AF patients has been criticized [18].

Our aim was to evaluate the predictive role for long-term mortality of a series of clinical risk stratification scores associated with cardiovascular or thromboembolic outcomes (ATRIA, $CHADS_2$, CHA_2DS_2-VASc, TIMI-AF), and bleeding complications (HAS-BLED) in an unselected population of patients with AF, also considering the site of enrolment (inpatient vs. outpatient setting).

2. Materials and methods

We performed a single center observational, prospective registry including consecutive patients with a diagnosis of AF referred to a tertiary teaching Hospital. The study design has been previously reported [19]. In brief, we enrolled patients with ≥1 ECG-proved episode of AF within 1 year before screening. Patients were included if ≥18 years old and basic echocardiographic data were available (i.e. left ventricular ejection fraction, left atrial diameter and quantification of valvular dysfunctions). The local ethical committee approved the study and written informed consent was obtained by all the participants. The investigation was conducted in accordance with the principles expressed in the Declaration of Helsinki.

Data collection was performed at patient inclusion (baseline) and at 1-year follow-up.

Baseline evaluation considered: (a) patient demographics, (b) medical history, (c) AF characteristics, (d) AF-related symptoms, (e) AF management strategy, (f) standard laboratory assay and (g) complete pharmacological therapy. For each patient we calculated ATRIA, $CHADS_2$, CHA_2DS_2-VASc, HAS-BLED, and TIMI-AF scores (Supplementary Table 1). The same evaluation was performed every 12 months for up to three years of follow-up. At each review check we also evaluated overall patient status and the events occurred since baseline, in particular: (a) hospital admissions, (b) cardiovascular interventions,

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Table 1
Baseline clinical characteristics of the enrolled cohort ($n = 1051$).

Characteristic		Out-Patients ($n = 304$)	In-patients ($n = 747$)	p
Male		198 (65.1%)	459 (61.4%)	n.s.
Age (years)		69.6 ± 11.8	72.7 ± 12.1	<0.001
BMI (kg/m^2)		26.8 ± 4.6	26.5 ± 4.7	n.s.
Main CV diagnosis (reason for access to medical intervention)	AF	139 (45.7%)	151 (20.2%)	<0.001
	Hypertension	32 (10.5%)	43 (5.8%)	
	Coronary artery disease	36 (11.8%)	158 (21.2%)	
	Valvular heart disease	37 (12.2%)	210 (28.1%)	
	Cardiomyopathy	33 (10.9%)	64 (8.6%)	
	Heart failure	14 (4.6%)	83 (11.1%)	
	Other	13 (4.3%)	38 (5.1%)	
Chronic heart failure		71 (23.4%)	406 (54.4%)	<0.001
	NYHA III-IV	13/71 (18.3%)	249/406 (61.3%)	<0.001
LVEF (%)		58 ± 13%	54 ± 15%	<0.001
Coronary artery disease		60 (19.7%)	285 (38.2%)	<0.001
Cardiomyopathy	Dilated	17 (5.6%)	47 (6.3%)	n.s.
	Hypertrophic	6 (2.0%)	18 (2.4%)	
	Restrictive	0 (0.0%)	6 (0.8%)	
	Other	0 (0.0%)	7 (0.9%)	
Diabetes		26 (8.6%)	176 (23.6%)	<0.001
Hypertension		210 (69.1%)	551 (73.8%)	n.s.
Hypercholesterolemia		135 (44.7%)	371 (49.8%)	n.s.
TIA		15 (5.0%)	49 (6.6%)	n.s.
Ischemic stroke		16 (5.3%)	43 (5.8%)	n.s.
Embolism		10 (3.3%)	40 (5.4%)	n.s.
Hemorragic stroke		3 (1.0%)	13 (1.7%)	n.s.
Major bleeding		12 (3.9%9	35 (4.7%)	n.s.
Minor bleeding		20 (6.6%)	58 (7.8%)	n.s.
Peripheral vascular disease		94 (30.9%)	387 (51.8%)	<0.001
eGFR < 45 ml/min		43 (14.1%)	204 (27.3%)	<0.001
eGFR < 60 ml/min		89 (35.7%)	373 (51.1%)	<0.001
Liver disease		10 (3.3%)	44 (5.9%)	n.s.
COPD		24 (7.9%)	142 (19.0%)	<0.001
Thyroid disease	Hypothyroidism	42 (13.8%)	101 (13.5%)	n.s.
	Hyperthyroidism	3 (1.0%)	22 (2.9%)	
Device therapy	PM	35 (11.5%)	83 (11.1%)	n.s.
	ICD	20 (6.6%)	43 (5.8%)	
	CRT-P	1 (0.3%)	4 (0.5%)	
	CRT-D	23 (7.6%)	17 (2.3%)	
AF type	Paroxysmal	98 (32.2%)	183 (24.5%)	<0.001
	Persistent	95 (31.2%)	202 (27.0%)	
	Permanent	110 (36.2%)	361 (48.3%)	
	Unknown	1 (0.3%)	1 (0.1%)	
Symptoms (EHRA score)	Never/EHRA 1	131 (43.1%)	377 (50.5%)	0.020
	EHRA 2–4	177 (56.9%)	370 (49.5%)	
Rate/Rhythm control	None (clinical monitoring)	44 (14.5%)	87 (11.6%)	<0.001
	Rate control	159 (52.3%)	524 (70.1%)	
	Rhythm control	101 (33.3%)	136 (18.2%)	
	Previous ECV	101 (33.4%)	154 (21.4%)	<0.001
	Previous ablations	26 (8.5%)	32 (4.2%)	n.s.
Prevention of thromboembolic events	Single AP	35 (11.5%)	43 (5.8%)	n.s.
	Double AP	1 (0.3%)	24 (3.2%)	
	OAC/DOAC	233 (76.6%)	492 (65.9%)	
	OAC/DOAC + AP	27 (8.9%)	122 (16.3%)	
	OAC/DOAC + Double AP	2 (0.6%)	48 (6.4%)	
	Use of AP	65 (21.4%)	237 (31.7%)	<0.001

AF = atrial fibrillation; AP = anti-platelet agent; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CRT-D = cardiac resynchronization therapy-defibrillator; CRT-P = cardiac resynchronization therapy-pacemaker; CV = cardiovascular; DOAC = Direct oral anticoagulant; ECG = electrocardiogram; ECV = electric cardioversion; eGFR = estimated glomerular filtration rate; EHRA = European Heart Rhythm Association; ICD = implantable cardioverter defibrillator; LVEF = Left ventricular ejection fraction; NYHA = New York Heart Association; OAC = oral anti-coagulant; PCV = pharmacologic cardioversion; PM = pacemaker; TIA = transient ischemic attack.

(c) instrumental evaluations. Between the two fixed face to face checks we performed telephonic surveillance (between months 3 to 9 after each check) to improve compliance to the protocol. The same was performed to exclude death or major clinical events for patients not performing the periodical face to face check. To classify the mode of death we performed parent interview and revision of death certificate and all the available clinical records by two different operators.

2.1. Statistical analysis

Continuous variables with normal distribution are expressed as means ± standard deviation (median and interquartile range (IQR) for continuous variables without normal distribution). Categorical variables are expressed as number of patients and frequencies/percentage. Comparisons between enrolment and follow-up data were performed using the paired Student's *t*-test for continuous normally distributed variables, $\chi 2$-test for categorical variables and non-parametric equivalent tests for other type of variables. Cox proportional hazards analysis was used to identify scores as independent predictors of overall mortality and the results are presented as hazard ratio (HR), confidence interval and p-value. Model building follows a backward-stepwise approach, the test of term significance is the Wald chi-square test with cutoff p value of 0.1 for removal and 0.05 for addition. The Harrell's C-statistic and the confidence intervals were used to assess the goodness of fit, or discriminatory value, of Cox regression models and to compare their predictive power. Kaplan–Meier curves for overall survival according to the various scoring systems were constructed. Data analysis was performed with the statistical software Stata/SE 14.2 for Windows (StataCorp LLC, College Station TX, USA) and SPSS 23.0 (SPSS Statistics/IBM Corp, Chicago IL, USA).

3. Results

We enrolled 1051 patients aged 72 ± 12 years. The main enrolment site was cardiology ward and day-hospital (71.1%) followed by outpatients clinic (28.9%). Baseline clinical and echocardiographic

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