

2MACE score predicts cardiovascular adverse events in real-world atrial fibrillation patients under rivaroxaban therapy. Data from EMIR study

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Background: Atrial Fibrillation (AF) patients have higher risk of major adverse cardiovascular events (MACEs). In 2015, the 2MACE score (2 points for metabolic syndrome and age ≥ 75 , and 1 point for myocardial infarction [MI] or revascularization, congestive heart failure [ejection fraction $\leq 40\%$] and thromboembolism [stroke or transient ischemic attack]) was described to stratify cardiovascular risk and 2MACE ≥ 3 was related with high risk of MACE in AF patients but a long-term validation in prospective patients under direct anticoagulants has not been performed yet.

The aim of this study was to analyse the incidence of cardiovascular events and to validate the 2MACE score as predictor of MACEs.

Methods: EMIR study [acronym from 'Estudio observacional para la identificación de los factores de riesgo asociados a eventos cardiovasculares Mayores en pacientes con fibrilación auricular no valvular tratados con un anticoagulante oral directo (Rivaroxaban)'] was an observational, multi-center, post-authorization and prospective study that involved AF patients under oral anticoagulation with rivaroxaban at least 6 months before enrolment. We analyzed baseline clinical characteristics and adverse events after 2.5 years of follow up: annual incidence of thromboembolic events, MACE (composite of nonfatal MI, coronary revascularization and cardiac death) and cardiovascular mortality were analyzed.

Results: We analyzed 1,433 patients (55.5% women, mean 74.2 \pm 9.7 years). 385 (26.9%) patients had 2MACE score ≥ 3 and of those high-risk patients, 42.1% had previous coronary disease, 12.5% had previous peripheral artery disease, 40.7% had diabetes mellitus, 39% heart failure and 50% had chronic kidney disease (GFR < 60 ml/min). After 2.5 (2.2–2.6) years of follow-up, we observed patients with 2MACE score ≥ 3 had higher rate of adverse events (Table), specially of higher rate of cardiovascular mortality and MACE. Patients with 2MACE score ≥ 3 had RR 4.09 (2.59–6.45; $p < 0.001$) for MACE. Indeed, patients with 2MACE score ≥ 3 had around 6-fold risk of cardiovascular death due heart failure than patients with 2MACE score < 3 (0.17%/year vs 1.09%/year; $p = 0.003$). 2MACE score had suitable predictive performance for MACE (AUC 0.638 [(0.534–0.742); $p = 0.010$]).

Conclusion: In a Real-world AF patients under rivaroxaban therapy from EMIR registry, the 2MACE score is a good predictor of long-term cardiovascular events, MACE and major bleeding. A 2MACE score ≥ 3 categorize patients at "high-risk" with almost 4-fold risk of MACE in a long-term follow-up.

	2MACE<3	2MACE \geq 3	p-value
MACE	16	18	0.001
Annual Rate (%/year)	0.68	2.18	
Fatal Heart Failure	4	9	0.003
Annual Rate (%/year)	0.17	1.09	
Acute Myocardial Infarction	3	2	0.771
Annual Rate (%/year)	0.13	0.24	
Cardiovascular Mortality	9	11	0.011
Annual Rate (%/year)	0.38	1.33	

Table 1. Adverse events according to 2MACE