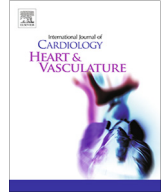




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Antithrombotic treatment pattern in newly diagnosed atrial fibrillation patients and 2-year follow-up results for dabigatran-treated patients in the Africa/Middle-East Region: Phase II results from the GLORIA-AF registry program

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ABSTRACT

Background: Data on the epidemiology and treatment of atrial fibrillation in the Africa/Middle East region are limited, and the use of novel oral anticoagulants and their effectiveness in real-world clinical practice has not been evaluated.

Methods and Results: This study used prospectively collected data from the Global Registry on Long-Term Oral Antithrombotic Treatment in Patients With Atrial Fibrillation (GLORIA-AF) to describe anticoagulant use and outcomes in Africa and the Middle East. Baseline characteristics of patients newly diagnosed with nonvalvular atrial fibrillation from Lebanon (242 patients, 40.3%), Saudi Arabia (236 patients, 39.3%), United Arab Emirates (87 patients, 14.5%), and South Africa (35 patients, 5.8%) were described, and clinical outcomes were investigated for all patients in this region who received dabigatran.

In newly diagnosed patients (having a diagnosis within the last three months) with nonvalvular atrial fibrillation in Africa and the Middle East, the observed uptake of non-vitamin K oral anticoagulants was high in the first years following their availability; dabigatran was the most commonly used antithrombotic agent (314/600 patients), and only 1.5% of patients did not receive any antithrombotic therapy. Use of dabigatran was associated with a high persistence rate (>88% at 24 months) and low incidence rates of stroke, myocardial infarction, major bleeding, and all-cause mortality after 2 years of follow-up. **Conclusions:** Data from GLORIA-AF reveal a change in the landscape for stroke prevention in the AME region, and the results were consistent with those observed in the global GLORIA-AF registry, as well as those of randomized clinical trials.

Clinical Trial Registration: NCT01937377 (<https://clinicaltrials.gov/ct2/show/NCT01937377>).

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1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the world and is a major risk factor for stroke, systemic embolism, and mortality [1,2]. Characteristics, treatment patterns, and long-term outcomes have been well reported for North American and European patients with AF [3,4]. Vitamin K antagonists (VKAs)

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² This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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were the cornerstone of treatment for AF prior to the availability of the newer non-VKA oral anticoagulants (NOACs), but because of their narrow therapeutic index, the need of regular monitoring and the fear of bleeding, VKAs are not given to almost half of patients with AF [5]. After their introduction in clinical practice, NOACs overcame some of the shortcomings of VKAs, simplifying patient management, and were proven to be at least equal or superior to VKAs with respect to prevention of embolic complications and bleeding risk [6–8]. Consequently, NOACs have become more frequently prescribed than VKAs, and their widespread acceptance and use has improved the overall anticoagulation rate of patients with AF [9,10]. Their effectiveness in the initial randomized clinical trials has since been confirmed in real-world studies that have replicated the results [11].

Unlike North America and Europe, only limited data are available on the epidemiology and treatment of AF in the Africa/Middle East (AME) region. In particular, the use of NOACs and their effectiveness in real-world clinical practice has not been evaluated. A recent review of AF in the AME region characterized this disease as “unmapped, underdiagnosed, and undertreated” [12]; thus, studies on AF patients within the AME region are needed to assess current practice, establish region-specific guidelines, and improve management of this arrhythmia.

The objectives of this study were to use prospectively collected data from the Global Registry on Long-Term Oral Antithrombotic Treatment in Patients With Atrial Fibrillation (GLORIA-AF) to describe baseline characteristics of patients newly diagnosed with nonvalvular AF in the AME region, and to investigate on-treatment clinical outcomes for AME patients who received dabigatran, the first NOAC available.

2. Methods

2.1. Design and study population

We evaluated AME patients enrolled in the GLORIA-AF registry, the design and rationale of which have been previously published [9,10]. In summary, GLORIA-AF is a comprehensive worldwide registry program on AF patients that prospectively enrolled patients 18 years or older, with newly (within the last 3 months) diagnosed nonvalvular AF and at risk of stroke (CHA₂DS₂-VASC [Congestive heart failure, Hypertension, Age \geq 75 years, Diabetes mellitus, Stroke/transient ischaemic attack/systemic embolism, Vascular disease, Age 65–74 years, Sex category (female)] score \geq 1). Phase II enrolled patients from November 2011 to December 2014 and were grouped in 5 regions: Asia, Europe, North America, Latin America, and AME. AF was diagnosed by 12-lead electrocardiography, Holter electrocardiography recording, electrocardiographic rhythm strip, or electrocardiogram from pacemakers or implantable cardioverter-defibrillator. Patients with mechanical valves, prior VKA therapy for > 60 days, an indication for VKA other than AF, AF owing to reversible causes, or a life expectancy < 1 year were excluded. Patients were recruited consecutively from outpatient settings, such as general practice, primary care, and specialist offices; community or university hospital clinics; and anticoagulation clinics. In Phase II of the GLORIA-AF program, patients' demographics and comorbidities; AF characteristics, CHA₂DS₂-VASC-score, HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding, Labile international normalized ratio, Elderly [age > 65 years], Drugs or alcohol concomitantly) score; AF management; and outcomes specific to dabigatran were recorded on standard electronic case report forms. Dabigatran (at doses of 75 mg, 110 mg, or 150 mg twice daily [BID]), VKA, or other antithrombotic agents were prescribed at the discretion of the treating physician according to local guidelines and standard clinical practice. Data quality was monitored on an ongoing basis by the

sponsor (Boehringer Ingelheim), with regular queries and frequent on-site auditing with data verification. Informed consent was obtained from all patients, and the study protocol was approved by the institutional ethics committees of participating sites.

2.2. Follow-Up and outcome

Patients who received dabigatran were prospectively followed for 2 years with clinic visits or phone calls at 3, 6, 12, and 24 months after enrollment. Prespecified outcome events were stroke (ischemic or hemorrhagic), transient ischemic attack, systemic embolism, pulmonary embolism, myocardial infarction, major bleeding events, life-threatening bleeding events, vascular death, and all-cause death. In addition, a composite endpoint of stroke, systemic embolism, myocardial infarction, life-threatening bleeding, and vascular death was analyzed. Patients who received at least one dose of dabigatran were included in the outcome analysis. Discontinuation of dabigatran was defined as suspension of the drug for > 30 days. Persistence on treatment was analyzed as the proportion of patients without dabigatran discontinuation during each follow-up visit. Follow-up for dabigatran patients ended at 2 years, including those who discontinued dabigatran or switched to another antithrombotic agent during this period.

2.3. Statistical analysis

Data were summarized by mean and standard deviation for continuous variables, and by frequencies and percentages for categorical variables. Crude incidence rates for outcomes of interest are shown per 100 patient-years and 2-sided 95% confidence intervals (95% CIs) based on the Poisson distribution and its relation to the χ^2 -distribution and were calculated during the dabigatran on-treatment period. Treatment interruptions < 30 days were disregarded for the analysis. Only descriptive results are provided; no statistical hypothesis tests were performed. Statistical analyses were performed using the SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Patients and AF characteristics

Phase II of the GLORIA-AF registry enrolled 15,641 patients at 984 centers in 44 countries [10,13]. Of these, 608 patients were enrolled in the AME region and 600 of them were eligible for analysis. Patients were enrolled in 4 AME countries: Lebanon, 242 patients (40.3%); Saudi Arabia, 236 patients (39.3%); United Arab Emirates, 87 patients (14.5%); and South Africa, 35 patients (5.8%).

Patients' baseline characteristics are summarized in Table 1. Mean (SD) age at enrollment was 67.7(12) years, and 52% were male. The most prevalent comorbidity was hypertension in 80.2% of patients, followed by diabetes mellitus in 42.0%, coronary artery disease in 33.3%, and congestive heart failure in 30.8%. Overall, 16.7% of patients had a prior myocardial infarction and 13.2% had a prior stroke. Mean (SD) creatinine clearance was 81.0 (38.3) mL/min.

AF was paroxysmal in 48.2% of the study population and persistent or permanent in 31.8% and 20.0% of them, respectively. Mean (SD) CHA₂DS₂-VASC-score was 3.6 (1.7) and 89.8% of patients had a score \geq 2. Mean (SD) HAS-BLED-score was 1.3 (0.9) and 83.3% of the participants had a score < 3.

The majority of patients were enrolled at university hospital outpatient clinics (39.0%), private specialist offices (24.8%), or community hospital outpatient clinics (23.8%), and the remainder were treated in anticoagulation clinics (11.8%) or in the offices of primary care physicians (0.5%).

Table 1
Patient Characteristics, All Phase II Eligible AME Patients and Dabigatran Dose Groups.

	All AME Patients	Dabigatran 150 mg BID	Dabigatran 110 mg BID	Dabigatran 75 mg BID	All Dabigatran*
Patients, n	600	111	193	6	314
Age, mean (SD), y	67.7 (12.4)	62.7 (11.3)	69.5 (11.2)	82.3 (5.0)	67.5 (12.0)
BMI, mean (SD) [†] , kg/m ²	30.25 (6.19)	31.10 (6.13)	30.04 (6.00)	26.78 (2.61)	30.27 (6.03)
Sex, male, n (%)	312 (52.0)	55 (49.5)	93 (48.2)	5 (83.3)	155 (49.4)
Type of AF, n (%)					
Paroxysmal	289 (48.2)	50 (45.0)	102 (52.8)	3 (50.0)	156 (49.7)
Persistent	191 (31.8)	35 (31.5)	59 (30.6)	2 (33.3)	99 (31.5)
Permanent	120 (20.0)	26 (23.4)	32 (16.6)	1 (16.7)	59 (18.8)
Categorization of AF, n (%)					
Symptomatic	157 (26.2)	29 (26.1)	51 (26.4)	2 (33.3)	82 (26.1)
Minimally symptomatic	278 (46.3)	54 (48.6)	97 (50.3)	1 (16.7)	154 (49.0)
Asymptomatic	165 (27.5)	28 (25.2)	45 (23.3)	3 (50.0)	78 (24.8)
Medical history, n (%)					
Previous stroke	79 (13.2)	11 (9.9)	31 (16.1)	1 (16.7)	44 (14.0)
Myocardial infarction	100 (16.7)	8 (7.2)	30 (15.5)	5 (83.3)	43 (13.7)
Coronary artery disease	200 (33.3)	26 (23.4)	74 (38.3)	6 (100.0)	108 (34.4)
Congestive heart failure	185 (30.8)	27 (24.3)	52 (26.9)	1 (16.7)	81 (25.8)
History of hypertension	481 (80.2)	89 (80.2)	161 (83.4)	4 (66.7)	257 (81.8)
Diabetes mellitus	252 (42.0)	43 (38.7)	80 (41.5)	2 (33.3)	126 (40.1)
Prior bleeding	24 (4.0)	2 (1.8)	4 (2.1)	1 (16.7)	8 (2.5)
Creatinine clearance, mean (SD) [‡] , mL/min	81.0 (38.3)	101.3 (37.6)	81.0 (31.4)	46.8 (15.9)	86.5 (35.2)
CHA ₂ DS ₂ -VASc, mean (SD)	3.6 (1.7)	3.0 (1.4)	3.8 (1.7)	4.5 (1.4)	3.5 (1.6)
CHA ₂ DS ₂ -VASc score, n (%)					
Score = 1	61 (10.2)	15 (13.5)	14 (7.3)	0 (0)	29 (9.2)
Score ≥ 2	539 (89.8)	96 (86.5)	179 (92.7)	6 (100.0)	285 (90.8)
HAS-BLED score, mean (SD)	1.3 (0.9)	0.9 (0.8)	1.3 (0.9)	1.8 (0.8)	1.2 (0.9)
HAS-BLED score category [§] , n (%)					
Low, score < 3	500 (83.3)	100 (90.1)	172 (89.1)	4 (66.7)	278 (88.5)
High, score ≥ 3	55 (9.2)	5 (4.5)	17 (8.8)	1 (16.7)	23 (7.3)

AF indicates atrial fibrillation; AME, Africa/Middle East; BID, twice daily; BMI, body mass index; CHA₂DS₂-VASc, Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, Stroke/transient ischaemic attack/systemic embolism, Vascular disease, Age 65–74 years, Sex category (female); HAS-BLED, Hypertension, Abnormal renal/liver function, Stroke, Bleeding, Labile international normalized ratio, Elderly (age > 65 years), Drugs or alcohol concomitantly; PPI, proton pump inhibitor; SD, standard deviation.

* Four patients (1.3%) were prescribed dabigatran at a dose other than 75 mg, 110 mg, or 150 mg BID.

† Data missing for 14 (2.3%) All AME patients and 9 (2.9%) dabigatran AME patients.

‡ Data missing for 132 (22.0%) All AME patients and 54 (17.2%) dabigatran AME patients.

§ Data missing for 45 (7.5%) All AME patients and 13 (4.1%) dabigatran AME patients.

3.2. Antithrombotic treatment pattern

Dabigatran was the most commonly used antithrombotic agent. It was prescribed to 315 patients and, of those, 314 patients received at least one dose of dabigatran (52.3%). Other antithrombotics prescribed were VKAs (31.7%), antiplatelets (10.7%), and other NOACs (3.8%). Nine patients (1.5%) did not receive antithrombotic therapy. Dabigatran was prescribed in 97.8% of cases by cardiologists, with the remainder having been prescribed by internists (2.2%). The most commonly prescribed dose of dabigatran was 110 mg BID (193 patients or 61.5%), with a mean (SD) duration of treatment of 22.4±(5.4) months. Dabigatran 150 mg BID was given to 111 patients (35.4%) for a mean duration of 20.6±(7.4) months, and dabigatran 75 mg BID was used in 6 patients (1.9%) for 18.5 (7.8) months. Four patients received dabigatran at doses different from those above for a mean duration of 4.2±(11) months.

Patients treated with dabigatran (pooled dabigatran at any dose) had similar characteristics and comorbidities compared with the overall cohort of AME patients on any treatment (Table 1). However, patients who received the 110-mg BID and 75-mg BID doses of dabigatran were older than those who received the 150-mg BID dose, had lower creatinine clearance, and higher CHA₂DS₂-VASc- and HAS-BLED-scores.

3.3. Effectiveness and safety outcomes

During the 2-year follow-up of dabigatran patients, the following events occurred: 3 S, of which 2 were ischemic and 1 was of unknown type; 2 myocardial infarctions; 1 major bleeding event (gastrointestinal with > 2-g/dL fall in hemoglobin); and 8

all-cause deaths, of which 2 were vascular deaths (Table 2). The crude incidence rates per 100 patient-years and 95% CIs of these events were 0.53 (0.11–1.56) for stroke, 0.36 (0.04–1.29) for myocardial infarction, 0.18 (0.00–0.99) for major bleeding, and 1.42 (0.61–2.80) for all-cause death. The crude incidence rate per 100 patient-years (95% CI) of the composite outcome of stroke, systemic embolism, myocardial infarction, life-threatening bleed, or vascular death was 1.07 (0.39–2.33).

3.4. Dabigatran persistence

Using Kaplan-Meier estimates, the probabilities and 95% CIs of continuing dabigatran treatment (persistence) were 93.2% (89.8%–95.5%) at 6 months, 92.2% (88.7%–94.7%) at 12 months, and 88.5% (84.3%–91.6%) at 24 months.

4. Discussion

To our knowledge, the GLORIA-AF registry is one of the largest prospective global registry studies to evaluate the clinical characteristics, treatments, and long-term outcomes of newly diagnosed AF patients after the introduction of NOACs in routine clinical practice. This sub-study evaluated the situation in the AME region where data on AF are scarce.

4.1. Comparison with the global GLORIA-AF registry

Patients included in this AME cohort had slightly different baseline demographics and clinical characteristics than those in the global registry. They were slightly younger, more often obese,

Table 2
Effectiveness and Safety Outcomes in Phase II Eligible Patients from AME Treated With Dabigatran: Crude Incidence Rates.

	No. of Patients With Event	PY	Crude IR per 100 PY (95% CI)
Stroke	3	563	0.53 (0.11–1.56)
Hemorrhagic stroke	0		
Ischemic stroke	2		
Unknown type	1		
Systemic embolism	0	563	0 (0–0)
Major bleeding	1	563	0.18 (0–0.99)
Life threatening	0		
Transfusion (2 + units of blood/red cells)	0		
Fall in hemoglobin of 2 g/dL	1		
Fatal bleeds	0		
Gastrointestinal	1		
Intracranial	0		
Myocardial infarction	2	561	0.36 (0.04–1.29)
All-cause death	8	563	1.42 (0.61–2.80)
Vascular death	2		
Nonvascular death	4		
Unknown	2		
Composite outcome (stroke, systemic embolism, myocardial infarction, life-threatening bleed, or vascular death)	6	561	1.07 (0.39–2.33)

AME indicates Africa/Middle East; CI, confidence interval; IR, incidence rate; PY, patient-years.

and had more co-morbidities such as history of hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, and prior myocardial infarction and stroke (Table 3). Their CHA₂DS₂-VASC-score and HAS-BLED-score categories however, were similar to those of the global cohort. Overall, oral anticoagulation rate was higher in AME patients (88% vs. 80% in the global cohort) with a preferential use of NOACs over VKA (table 3).

The 110 mg bid dose of dabigatran, was most commonly used in AME region, contrary to the global registry where the 150 mg bid dose was the most frequent one. This could be due to several reasons. The choice of the anticoagulant prescribed and its dose, was based solely on the decision of the treating physician. Patients in the 110 mg bid dose group, did not have lower risk of thromboembolic events or higher risk of bleeding, compared to those in the 150 mg bid dose group to justify reduced dosing (table 1). It is possible that physicians in the AME region might have leaned toward safety, by choosing a dose that was shown in the randomized clinical trial to cause less bleeding but that keeps the same efficacy compared to warfarin [6]. Another reason that could explain the more common use of the 110 mg bid dose in our cohort, is the fact that this dose is not approved for clinical use in the USA, leaving physicians with the 150 mg bid dose for effective anticoagulation. Despite the preferential use of reduced dabigatran dose in the AME cohort, the incidences of ischemic and thrombotic events were comparable to those of the global registry, where the rates (95% CI) of stroke and myocardial infarction were 0.63 (0.42, 0.92) and 0.47 (0.29, 0.72), respectively [13]. The incidence rates of major bleeding and death were lower in this sub-analysis compared with the global cohort (0.18 vs 1.12 and 1.42 vs 2.69, respectively), but the wide CIs, resulting from the low number of events in AME patients, overlap with those of the patients in the main study and do not allow for any conclusion regarding superiority [13].

4.2. Comparison with the randomized trial RE-LY

Our results are also in line with those of the randomized clinical trial, RE-LY, where the stroke incidence rates per 100 patient-years

Table 3
Comparison of selected demographic, clinical and treatment characteristics between patients of the AME cohort and those in the global registry.

	AME Patients	All GLORIA-AF
Patients, n	600	15,092
Age, y	67.7 (12.4)*	71 (64–78) †
BMI, mean (SD) †, kg/m ²	30.25 (6.19)*	27.5 (24.5–31.4) †
Sex, male, n (%)	312 (52.0)	8,225 (54.5)
Type of AF, n (%)		
Paroxysmal	289 (48.2)	8,059 (53.4)
Persistent	191 (31.8)	5,358 (35.5)
Permanent	120 (20.0)	1,675 (11.1)
Categorization of AF, n (%)		
Symptomatic	157 (26.2)	4,256 (28.2)
Minimally symptomatic	278 (46.3)	6,007 (39.8)
Asymptomatic	165 (27.5)	4,829 (32)
Medical history, n (%)		
Previous stroke	79 (13.2)	1,582 (10.5)
Myocardial infarction	100 (16.7)	1,600 (10.6)
Coronary artery disease	200 (33.3)	3,068 (20.3)
Congestive heart failure	185 (30.8)	3,647 (24.2)
History of hypertension	481 (80.2)	11,255 (74.6)
Diabetes mellitus	252 (42.0)	3,487 (23.1)
Prior bleeding	24 (4.0)	842 (5.6)
Creatinine clearance, mean (SD), mL/min	81.0 (38.3)	101.3 (37.6)
CHA ₂ DS ₂ -VASC score, n (%)		
Score = 1	61 (10.2)	2,093 (13.9)
Score ≥ 2	539 (89.8)	12,999 (86.1)
HAS-BLED score category ‡, n (%)		
Low, score < 3	500 (83.3)	11,927 (79)
High, score ≥ 3	55 (9.2)	1,376 (9.1)
Medications, n (%)		
VKA	190 (31.7)	4,878 (32.3)
Dabigatran	314 (52.3)	4,767 (31.6)
Other NOACs	23 (3.8)	2,420 (16)
Antiplatelet	64 (10.7)	1,833 (12.1)
None	9 (1.5)	1,182 (7.8)

* Mean (standard deviation).

† Median and (95% confidence interval).

‡ Data missing for 45 (7.5%) AME patients and for 1,789 (11.8%) patients in All GLORIA-AF.

were 1.01 and 1.44 and the major bleeding rates were 3.11 and 2.71 for the dabigatran 150-mg and 110-mg BID doses, respectively [6]. However, direct comparisons cannot be made for several reasons. Treatment in RE-LY was randomized, whereas patients in GLORIA-AF received 150 mg, 110 mg, or 75 mg of dabigatran BID based on the physician's decision. Patients' comorbidities, as well as CHA₂DS₂-VASC- and HAS-BLED-score, were different from those of RE-LY. That said, our results still demonstrate that in real life, dabigatran use is associated with high levels of effectiveness and safety.

4.3. Comparison with older registries in the Middle-East and Africa

The only multinational prospective registry that analyzed the baseline characteristics, treatments, and long-term outcomes of AF patients from the AME region is the Gulf Survey of Atrial Fibrillation Events (Gulf SAFE), which recruited between October 2009 and June 2010 and included 2043 consecutive patients with AF from Kuwait, Bahrain, Qatar, United Arab Emirates, Oman, and Yemen [14]. Inclusion criteria were newly diagnosed AF or AF of < 1 year in duration in patients being evaluated for various reasons in the emergency departments of 23 hospitals. NOACs were not approved at that time, and oral anticoagulants predominantly consisted of VKAs.

Compared with similar registries in the West [15] as well as to the current sub-analysis of GLORIA-AF, patients in the Gulf SAFE registry were on average a decade younger (mean age, 57 years), had lower median CHA₂DS₂-VASC scores (median score, 2), and had a lower rate of use of oral anticoagulants. Even in patients considered at high risk of stroke, use of VKAs was only 58% [15]. The 1-

year rates of stroke/transient ischemic attack and all-cause mortality were 4.2% and 13%, respectively. These rates were significantly higher (double rate of stroke and 67% higher rate of mortality) than those of a comparative AF cohort from the Darlington AF registry in the United Kingdom [15]. The higher incidence of events was attributed to the low rate of anticoagulant prescription in the Gulf SAFE registry, as well as to inadequate use of these drugs: only 50% of patients were monitored with regular international normalized ratio (INR) checks, and the mean time within the therapeutic INR window was 63.5% for those who had at least 3 INR checks across the 12 months of follow-up.

Our results reflect a change in the profile of patients with AF, along with better management of the disease, especially in terms of oral anticoagulation. Patients enrolled in our study had demographics and comorbidities that were much closer to those of their Western counterparts. This may be because our patients were recruited from hospitals' outpatient clinics or from private practitioner's offices rather than from emergency departments (as in Gulf SAFE). These referral centers are more likely to receive more complex patients. Overall, our patients had a higher risk of stroke than those of the Gulf SAFE registry but, paradoxically, had a much lower rate of thromboembolic events (3 Strokes out 314 (0.95%) dabigatran treated patients in 2 years follow-up). This is not only owing to the overall higher rate of prescription of oral anticoagulants, but is most likely owing to a shift toward the preferential use of NOACs. Dabigatran was the first approved and the first available NOAC in AME region, which explains its more frequent use compared to other NOACs at the time of the study. Contrary to Gulf SAFE, where the prevalence of VKA use was 50%, oral anticoagulants were prescribed to almost 88% of our patients, and NOACs were given to 56% of them. This "change in the landscape of stroke prevention" with a high and preferential use of NOACs eliminated some of the shortcomings of VKAs, such as compliance and time spent in therapeutic INR window, and contributed to equalizing the outcomes of AF patients across geographic regions.

4.4. Limitations and strengths

The findings of this study should be interpreted in the context of certain limitations. First, the observational design of the study means that it is subject to potential selection bias and unmeasured confounding. Second, findings from this sub-analysis may not be generalizable to the entire nonvalvular AF patient population of the participating country, as the study was restricted to patients with a CHA₂DS₂-VASc-score ≥ 1 . A third potential limitation is that patient recruiting sites were not randomly selected, but were selected to reflect the balance between general practices, specialist offices, community hospitals, university hospitals, outpatient care centers, and anticoagulation clinics, based on the percentage of sites that treated AF patients for stroke prevention; the majority of study centers were university hospitals or community hospitals, and this may have increased the apparent prevalence of patients treated with NOACs. Fourth, the outcomes were not adjudicated in this analysis of routine clinical practice, although extensive measures were taken to ensure high data quality and complete reporting, including on-site source data verification, regular review of aggregate data to mitigate quality concerns, and close and regular site contact to ensure comprehensive reporting. However, all 4 of these limitations equally apply to the global GLORIA-AF registry and were similar across all of the geographic regions it included. The comparison of our results with those of the global registry are, thus, valid. Finally, given the small number of events, it was not possible to compare outcomes between the 2 most commonly used doses of dabigatran—150 mg and 110 mg BID. Nonetheless, the effectiveness and safety of both doses are reassuring.

Our study had several strengths. It included a large prospective cohort of consecutive AF patients and is the only reported registry of dabigatran-treated patients in the AME region. The inclusion of newly diagnosed nonvalvular AF allows the evaluation of contemporary management of this disease. Over the long observation period of up to 2 years for dabigatran patients, with regular follow-up with physicians, alongside on-site monitoring, multiple standards for data quality assurance and review ensured event capture. The quality of the data is high, with an extremely low loss to follow-up in this observational setting; all variables were prospectively captured by well-trained individuals; and all events were evaluated by the sponsor.

5. Conclusion

In conclusion, results of the GLORIA-AF AME region sub-study reveal a change in the landscape for stroke prevention. In newly diagnosed nonvalvular AF patients, there is a high adoption of NOACs, especially dabigatran, seen in the first years after their availability. Use of dabigatran was associated with a high persistence rate (>88% at 24 months) and low incidence rates of stroke, myocardial infarction, major bleeding, and all-cause mortality after 2 years of follow-up. These results are consistent with those observed in the global GLORIA-AF registry, as well as those of randomized clinical trials.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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Data disclosure

The sponsor of the GLORIA-AF Registry Program (Boehringer Ingelheim) is committed to responsible sharing of clinical study reports, related clinical documents, and patient level clinical study data. Researchers are invited to submit inquiries via the following website: <https://trials.boehringer-ingelheim.com>.

Disclosures

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