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Atrial fibrillation outcomes in patients from Asia and non-Asia countries: insights from GARFIELD-AF

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ABSTRACT

Background Differences in the clinical outcomes and level of risk among Asian versus non-Asian patients with atrial fibrillation (AF) have been sparsely investigated.

Objective To provide a contemporary prospective comparison of outcomes for newly diagnosed patients with AF, between Asian and non-Asian regions.

Methods Six Asian countries (China, Japan, India, Singapore, South Korea and Thailand) and 29 countries outside Asia participated in the Global Anticoagulant Registry in the FIELD-AF (GARFIELD-AF) study. Newly diagnosed patients with AF, enrolled between 2010 and 2016, were followed up for≥2 years. The outcome studies were all-cause, cardiovascular and non-cardiovascular mortality, non-haemorrhagic stroke/systemic embolism (SE), major bleeding. The association of geographical region with clinical outcomes (event rates per 100 person-years) were estimated using multivariable Cox models.

Results 13 841/52 057 (26.6%) GARFIELD-AF participants were enrolled in Asia. Average age and prevalence of cardiovascular comorbidities were lower than in non-Asian countries and patients at high risk of stroke (ie, CHA_2DS_2-VASc≥2 excl. sex) were less frequently anticoagulated (60.1% vs 73.2%). Non-vitamin K oral anticoagulant (NOAC) was similar in both regions (~28%), though Asian patients were more frequently underdosed. Both Asian and non-Asian patients who received NOAC at enrolment experienced lower all-cause mortality and non-haemorrhagic stroke/SE compared with patients on other treatments or none.

All-cause mortality, non-cardiovascular mortality and major bleeding were less frequent in patients from Asia versus non-Asia (HR (95% CI): 0.62 (0.39 to 0.99), 0.52 (0.28 to 0.97), 0.58 (0.36 to 0.96), respectively). Associations of moderate-to-severe chronic kidney disease and vascular disease with increased risk of all-cause mortality were stronger in Asian versus non-Asian patients (interaction p values: 0.0250 and 0.0076, respectively). There was notable heterogeneity in oral anticoagulant (OAC) usage within the Asian countries.

Conclusions Patients in Asian countries had a lower risk of all-cause mortality and major bleeding compared to the rest of the world. NOAC had evident benefits for reducing mortality and stroke across populations. Further studies on sociocultural impacts on OAC outcomes are needed.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Observational studies in atrial fibrillation (AF) have shown that Asian populations with AF have a lower incidence risk of death compared with Caucasian populations and there were notable treatment differences.

WHAT THIS STUDY ADDS

⇒ This study explores the patient characteristics of the Asian population with AF in greater detail, drawing data from the largest registry of newly-diagnosed patients with AF, the Global Anticoagulant Registry in the FIELD-AF study. The study also examines the treatment patterns and 2-year clinical outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results from this study provide a balanced assessment to treating physicians on the risks and benefits of anticoagulation treatment for AF.

Trial registration number ClinicalTrials.gov NCT01090362.

BACKGROUND

Atrial fibrillation (AF) is the most commonly encountered cardiac arrhythmia, posing significant risks for stroke, heart failure and cardiac-related deaths. Even though the current prevalence of AF is already high, it is projected to increase considerably in the coming years. By 2060, it is estimated that AF will affect 14.4 million people in Europe and 7.56 million in the USA.[1] The situation is particularly concerning in the Asia-Pacific region where the number of people affected by AF is expected to increase 10-fold to 72 million by 2050 due to an ageing population,[2] making AF a significant public health concern.

There is strong evidence from a range of studies indicating that ethnic Asians have a

significantly lower risk of developing AF compared with Caucasians.[3–6] Additionally, a study from the Asia-Pacific Heart Rhythm Society Atrial Fibrillation Registry reported lower rates of cardiovascular morbidity and all-cause mortality among patients with AF in Asian cities compared with the EurObservational Research Programme population.[7] Genetic studies have also revealed that individuals of European ancestry are at a higher risk of AF compared with African Americans.[8 9] However, data are still lacking that would enable a contemporary prospective comparison of outcomes for newly diagnosed AF between Asian and non-Asian regions.

The Global Anticoagulant Registry in the FIELD-AF (GARFIELD-AF) is the largest worldwide prospective study of adult patients with newly diagnosed non-valvular AF.[10 11] Previous GARFIELD-AF studies have noticed differences between Asian and non-Asian regions. A lower risk of death within 1 month from AF diagnosis was observed among patients enrolled in Asia compared with patients enrolled in European countries.[12] Other studies pointed out that patients receiving antiplatelet monotherapy were more frequently Chinese compared with Caucasian[13] and a different international normalised ratio distribution in Asian patients treated with vitamin K antagonists (VKAs) compared with patients from other regions.[14]

In the current study, we aimed to investigate the characteristics of patients from Asian and non-Asian countries, describe their treatment patterns, assess the occurrence of 2-year clinical outcomes and identify possible reasons for these differences.

METHODS

Data collection

GARFIELD-AF Study (registration ClinicalTrials.gov NCT01090362) is an observational, multicentre, prospective cohort study which enrolled newly diagnosed patients with AF from March 2010 to August 2016, with an intended minimum follow-up of 2 years. A total number of 52 057 participants were prospectively enrolled from 35 countries. Patients were enrolled into five consecutive cohorts of approximately 10 000 patients each. The six participating countries from Asia were China, India, Japan, Singapore, South Korea and Thailand.

Data for this report were extracted from the study database in June 2019. For the follow-up programme, patients were contacted at 4 monthly intervals by telephone or postal mail. Data were examined for completeness and accuracy by the coordinating centre. In accordance with the study protocol, 20% of all data submitted electronically were monitored against source documentation.[15]

Clinical outcomes included in this study were all-cause, cardiovascular and non-cardiovascular mortality, non-haemorrhagic stroke/systemic embolism (SE) and major bleeding.

Non-haemorrhagic stroke or SE was defined as a composite of ischaemic stroke, unknown type of stroke and SE. Major bleeding was classified by investigators as defined by the International Society on Thrombosis and Haemostasis.[16] Major bleeds, including intracranial bleeds, were defined as a combined endpoint of haemorrhagic stroke and any major bleed. Minor or non-major clinically relevant bleeds that required transfusion, occurred in a critical site, or were fatal bleeds, were reclassified as major bleeds. Outcomes were investigator-reported, but a comprehensive audit and quality control system that included onsite audits and remote quality control measures was enacted in GARFIELD-AF.

Demographics and baseline characteristics of medical history, detailed AF-related information and treatment strategy were recorded in the screening step. Occurrences of clinical events, healthcare utilisation and hospitalisation were recorded during follow-up visits.

Statistics

Continuous variables are expressed as mean±SD and categorical variables as frequency and percentage. Distribution of baseline characteristics is reported for patients with available information, without imputation procedures performed for patients with missing data. No formal statistical tests were performed to compare the distribution of baseline characteristics across regions.

The occurrence of clinical events was described using the number of events and person-time event rate (per 100 person-years) with a 95% CI. We estimated person-year rates using a Poisson model. Time at risk was initiated from the date of enrolment. For the estimation of event rates, follow-up was truncated at the first event occurrence, death, loss to follow-up or 2 years after enrolment, whichever occurred first. Only the first occurrence of each event was taken into account.

HRs were estimated using Cox proportional hazards models. Adjustments were made for the following confounding factors: age, sex, ethnicity, type of AF, heart failure, vascular disease, hypertension, prior stroke/transient ischaemic attack (TIA)/SE, prior bleeding, diabetes, moderate-to-severe chronic kidney disease, baseline anticoagulation and antiplatelet therapy. A robust covariance estimate was included to account for correlation within countries. Interactions between the region of enrolment and selected clinical characteristics, or anticoagulation at baseline, were assessed using Cox models including the interaction effect of these variables.

Only complete cases were presented in descriptive tables. Multiple imputation was applied for the estimation of the region associations with outcomes.[17] Final estimates were obtained by combining results across five imputed data sets.

Data analysis was performed at the Thrombosis Research Institute using SAS Enterprise Guide V.8.3 (SAS Institute, Cary, North Carolina, USA).

RESULTS

A total number of 52 057 patients were recruited through all five cohorts of the GARFIELD-AF registry between

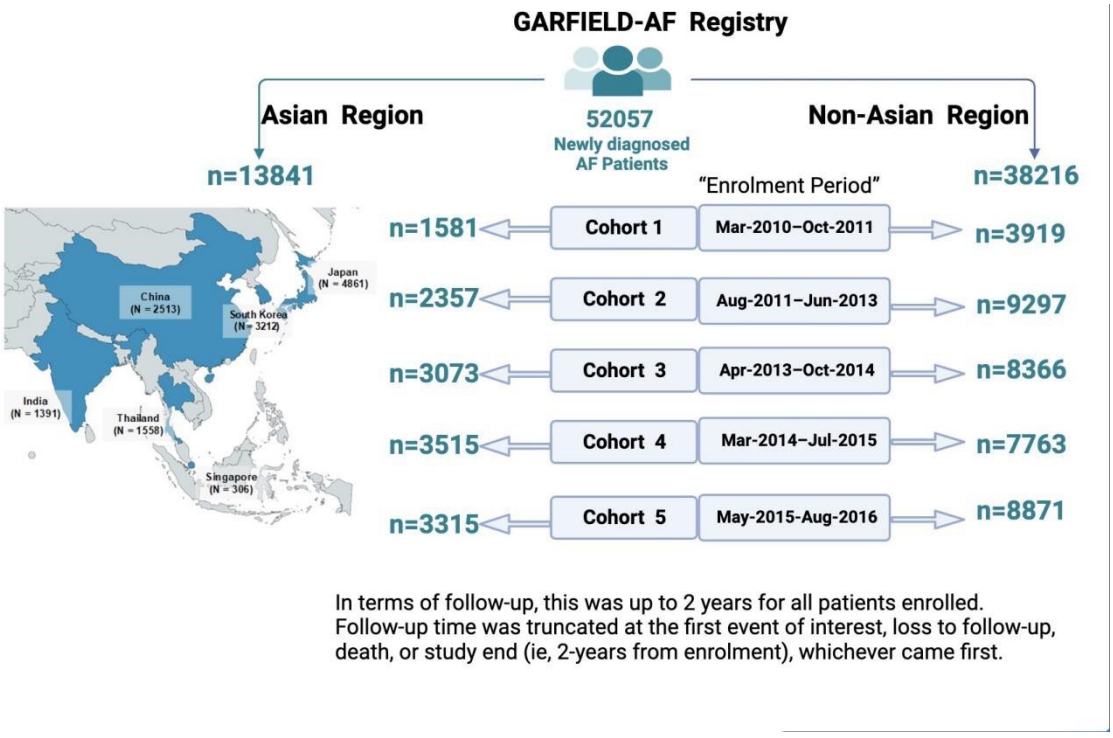

Figure 1 Flowchart for the selection of the study population. Figure describes the enrolment of patients with AF from Asian and non-Asian countries in the GARFIELD-AF study. Patients were enrolled across five cohorts, with enrolment periods from 2010 to 2016. The Asian countries where patients were enrolled are depicted in the map. AF, atrial fibrillation; GARFIELD-AF, Global Anticoagulant Registry in the FIELD-AF.

March 2010 and August 2016 and followed up for 2 years (figure 1). Among them, 13 841 (26.6%) patients were enrolled in Asia and 38 216 (73.4%) were enrolled in other regions of the world. Six Asian countries participated in GARFIELD-AF: Japan (n=4861), South Korea (n=3212), China (n=2513), Thailand (n=1558), India (n=1391) and Singapore (n=306).

Baseline patient characteristics

Detailed baseline characteristics of the population are reported in table 1. The average age was 67.8 and 70.3 years old for Asian and non-Asian AF groups, respectively. Asian and non-Asian populations had a similar percentage of male patients (59% and 55%, respectively). Interestingly, 27.7% of Asians had hypercholesterolaemia, while the percentage was higher at 46.7% among non-Asian patients. The prevalence of hypertension was also higher among non-Asian patients compared with Asian patients (79.4% vs 67.9%). The majority of patients with AF were recruited from cardiology departments, comprising 83.7% Asian and 59.2% of non-Asian patients. Patients treated in a hospital care setting were 73.2% of Asian and 53.0% of non-Asian.

Patient outcomes

In the GARFIELD-AF registry, Asian patients experienced lower occurrence of outcomes than non-Asian patients. Online supplemental table 1 summarises the event rates (per 100 person-years) through 2-year follow-up. The rate ratios (95% CI) between Asian and non-Asian countries were 0.59 (0.54 to 0.65) for all-cause mortality, 0.83 (0.72 to 0.97) for non-haemorrhagic stroke/SE and 0.62 (0.53 to 0.73) for major bleeding.

After adjustment for confounding factors, the risk for all-cause mortality within a 2-year follow-up was lower for patients enrolled in Asian countries compared with patients in the rest of the world (HR (95% CI): 0.62 (0.39 to 0.99)). The associations were of similar magnitude for cardiovascular and non-cardiovascular mortality (0.50 (0.24 to 1.03) and 0.52 (0.28 to 0.97)), respectively. Major bleeding was less frequent among patients enrolled in Asian countries (0.58 (0.36 to 0.96)), while the risk of non-haemorrhagic stroke/SE was not found to be significantly different between the two regions (table 2).

Moderate-to-severe chronic kidney disease and vascular disease had a stronger detrimental effect with regard to mortality in Asian compared with non-Asian patients (p value for interaction 0.0250 and 0.0076, respectively), as shown in online supplemental table 2. The risk of major bleeding increased more than twofold among Asian patients receiving oral anticoagulant (OAC), whereas the effect was milder among non-Asians (p value for interaction 0.0029). The latter finding might be partly due to the very low major bleeding rates among non-anticoagulated Asian patients.

Patients from Asia experienced a lower rate of events compared with patients from non-Asian countries, independently of the treatment they were assigned at baseline. Non-vitamin K oral anticoagulant (NOAC)-treated

Table 1 Baseline characteristics for Asia and non-Asia patients

Baseline characteristics	Asia (n=13 841)	Non-Asia (n=38 216)
Sex, n (%)		
Female	5631 (40.7)	17 373 (45.5)
Male	8210 (59.3)	20 842 (54.5)
Age at AF diagnosis, mean (SD)	67.8 (11.9)	70.3 (11.3)
Race/ethnicity, n (%)		
White	13 (0.1)	31 998 (86.6)
Hispanic/Latino	0 (0.0)	3397 (9.2)
Asian	13 809 (99.8)	487 (1.3)
Black/mixed/other	16 (0.1)	1056 (2.9)
Vital signs, mean (SD)		
BMI (kg/m²)	24.5 (3.9)	29.1 (5.8)
Pulse (bpm)	86.7 (23.5)	91.8 (27.7)
Systolic BP (mm Hg)	129.5 (19.4)	135 (19.8)
Diastolic BP (mm Hg)	77.9 (13.5)	80.4 (12.6)
Type of AF, n (%)		
Paroxysmal	5167 (37.3)	9140 (23.9)
Persistent	2509 (18.1)	5251 (13.7)
Permanent	1110 (8.0)	5526 (14.5)
New onset (unclassified)	5054 (36.5)	18 294 (47.9)
Care setting specialty, n (%)		
Cardiology	11 586 (83.7)	22 614 (59.2)
Internal medicine	1651 (11.9)	7724 (20.2)
Primary care/general practice	445 (3.2)	6957 (18.2)
Neurology	127 (0.9)	746 (2.0)
Geriatrics	31 (0.2)	170 (0.4)
Care setting location, n (%)		
Hospital	10 130 (73.2)	20 233 (53.0)
Office	3354 (24.2)	12 233 (32.0)
Emergency room	342 (2.5)	5419 (14.2)
Anticoagulation clinic/thrombosis centre	14 (0.1)	325 (0.9)
Medical history, n (%)		
Hypertension	9366 (67.9)	30 264 (79.4)
Hypercholesterolaemia	3750 (27.7)	17 219 (46.7)
Diabetes	2980 (21.5)	8570 (22.4)
Congestive heart failure	3083 (22.3)	8673 (22.7)
Vascular disease	2637 (19.2)	10 191 (26.9)
Prior stroke/TIA/SE	1376 (10.2)	4304 (11.7)
Moderate-to-severe CKD	1052 (7.8)	4305 (11.7)
Prior VTE	81 (0.6)	1274 (3.4)
Prior bleeding	222 (1.6)	1094 (2.9)
Dementia	246 (1.8)	518 (1.4)
Cirrhosis	96 (0.7)	198 (0.5)
Lifestyle factors, n (%)		
Heavy alcohol consumption	367 (3.2)	663 (2.0)
Current smoker	1596 (13.0)	3608 (10.3)
Treatment at baseline, n (%)		
NOAC±AP	3534 (25.7)	10 583 (28.2)
VKA±AP	4128 (30.0)	16 074 (42.8)
AP only	3811 (27.7)	6956 (18.5)
None	2287 (16.6)	3961 (10.5)
Risk scores, mean (SD)		
CHA_2DS_2-VASc	2.9 (1.6)	3.4 (1.6)
HAS-BLED*	1.3 (0.9)	1.4 (0.9)
GARFIELD-AF Score for mortality†	5.1 (5.9)	7.8 (7.7)
GARFIELD-AF Score for stroke‡	1.9 (1.5)	2.0 (1.5)
GARFIELD-AF Bleeding Score§	1.6 (1.1)	2.0 (1.5)

*The risk factor 'Labile INRs' is not included in the HAS-BLED score as it is not collected at baseline. As a result, the maximum HAS-BLED score at baseline is 8 points (not 9).
†Represents the expected risk of mortality within 2 years.
‡Represents the expected risk of non-haemorrhagic stroke/systemic embolism within 2 years.
§Represents the expected risk of major bleeding within 2 years.
AF, atrial fibrillation; AP, anti platelet ; BMI, body mass index; BP, blood pressure; CHA2DS2-VASc, Congestive heart failure, Hypertension, Age (greater than or equal to 75), Diabetes, Stroke/TIA/thromboembolism, Vascular disease, Age (65-74), sex category (female); CKD, chronic kidney disease; GARFIELD-AF, Global Anticoagulant Registry in the FIELD-AF; INRs, international normalised ratios; NOAC, non-vitamin K oral anticoagulant; SE, systemic embolism; TIA, transient ischaemic attack; VKA, vitamin K antagonist; VTE, venous thromboembolism.

patients experienced a lower occurrence of all-cause mortality and non-haemorrhagic stroke/SE compared with patients on VKAs, antiplatelets only or no antithrombotic, both in Asian and non-Asian countries (online supplemental table 3).

NOAC dosing differed substantially between Asian and non-Asian regions. For instance, only 9.6% of patients

Table 2 Unadjusted and adjusted HRs by region of enrolment (ref.: non-Asia)

Outcome	Asia versus non-Asia (ref.)	
	Unadjusted HR (95% CI)	Adjusted* HR (95% CI)
All-cause mortality	0.59 (0.38 to 0.92)	0.62 (0.39 to 0.99)
Cardiovascular mortality	0.49 (0.25 to 0.98)	0.50 (0.24 to 1.03)
Non-cardiovascular mortality	0.53 (0.35 to 0.81)	0.52 (0.28 to 0.97)
Non-haemorrhagic stroke/SE	0.83 (0.65 to 1.06)	0.85 (0.44 to 1.62)
Major bleeding	0.62 (0.42 to 0.90)	0.58 (0.36 to 0.96)

*HR adjusted by age, sex, ethnicity, type of AF, heart failure, vascular disease, hypertension, prior stroke/TIA/SE, prior bleeding, diabetes, moderate-to-severe CKD, baseline anticoagulation and antiplatelet therapy.
AF, atrial fibrillation; CKD, chronic kidney disease; ref., reference; SE, systemic embolism; TIA, transient ischaemic attack.

Table 3 Distribution of NOAC daily dose among GARFIELD-AF patients (Cohorts 3–5) in patients who received NOAC at baseline in Asia and non-Asia countries

NOAC daily dose (%)	Asia	Non-Asia	P value
Rivaroxaban			
Missing	119	114	
10 mg	363 (39.3)	69 (1.9)	<0.0001
15 mg	459 (49.7)	751 (20.3)	
20 mg	89 (9.6)	2782 (75.4)	
>20 mg	12 (1.3)	89 (2.4)	
Apixaban			
Missing	110	104	
2.5 mg	22 (2)	14 (0.6)	<0.0001
5 mg	463 (41.2)	535 (24)	
10 mg	638 (56.8)	1682 (75.4)	
Dabigatran			
Missing	48	66	
<150 mg	13 (2.5)	28 (1.6)	<0.0001
150 mg	34 (6.5)	57 (3.2)	
220 mg	326 (62.6)	591 (32.8)	
300 mg	148 (28.4)	1125 (62.5)	
Edoxaban			
Missing	35	1	
15 mg	2 (1)	1 (1)	<0.0001
30 mg	152 (76.8)	26 (24.8)	
60 mg	41 (20.7)	78 (74.3)	
120 mg	3 (1.5)	0 (0.0)	

GARFIELD-AF, Global Anticoagulant Registry in the FIELD-Atrial Fibrillation; NOAC, non-vitamin K oral anticoagulant.

from Asia received a 20 mg daily dose of rivaroxaban, compared with 75.4% of patients from the non-Asia region. Some Asian country-specific guidelines also recommend lower doses, such as in Japan where 15 mg/day is the standard. Differences between Asia and non-Asia were still present but smaller for apixaban (56.8% vs 75.4% received 10 mg daily, respectively) (table 3).

Treatment distribution also differed between Asian and non-Asian enrolments. Patients who underwent only antiplatelet therapy and patients without any antithrombotic therapy accounted for 39.9% of total patients with AF in Asia, but the percentage was only 26.8% among non-Asian patients (online supplemental figure 1).

Within Asia, the treatment strategies vary among countries. The use of NOACs seemed to be common among Japanese patients but not nearly as much in other countries. In India and China, more than half of the population at high risk of stroke was not receiving any form of anticoagulation (figure 2).

The event rates in each Asian country showed notable heterogeneity, though some populations were rather small. All-cause mortality varied from 1.01 (per 100 person-years) in South Korea to 6.55 (per 100 person-years) in India, while major bleeding events were relatively rare in India and China compared with other Asian regions (online supplemental table 4).

To further determine the variability between the countries, we used the event rate of Japan as a reference to compare the primary outcomes across the other Asian countries included in the study. Patients with AF enrolled in China, India and Thailand were associated with higher rates of all-cause mortality compared with Japan. Patients with AF from Singapore had higher rates of non-haemorrhagic stroke/SE and from South Korea were associated with higher rates of major bleeding, respectively, when compared with patients from Japan (online supplemental figure 2).

DISCUSSION

In this global prospective study of recent onset AF, Asian patients had lower rates of all-cause mortality and major bleeding than non-Asians during a 2-year follow-up.

Previous studies have shown heterogeneity in terms of OAC uptake and risks of clinical outcomes in Asian versus non-Asian patients with AF. Notably, a post hoc analysis of data from the Global Registry on Long-Term Oral Antithrombotic Treatment in Patients With Atrial Fibrillation (GLORIA-AF) registry showed that (1) Asian patients with AF were more frequently undertreated with OAC and NOAC and had higher rates of OAC discontinuation, (2) there was marked variability in OAC prescription among the subgroups and (3) Asians exhibited lower risks of clinical outcomes.[6] An analysis of the Asia-Pacific-Heart-Rhythm-Society Registry (APHRS-AF) indicated that Asian females were often undertreated with rhythm control drugs. However, a Cox regression analysis showed no gender-related differences in clinical outcomes among Asian patients with AF.[18] Other studies have also found that prevalence of AF and incidence of new-onset AF are lower in Asian than non-Asian populations (ie, prevalence in Asia 0.5–1.9%, non-Asia 1.4–4.9%;[19] incidence of AF in Asian population was 5.38 (95% CI, 4.53 to 6.24) per 1000 patient-years,[20] compared with 6.4–8.1 per 1000 person-years in non-Asians.[21 22]

In a large hospital-based cohort in California, Dewland *et al* reported patients with white racial background had an increased risk of AF compared with those of black, Asian or Hispanic backgrounds.[3] Furthermore, the Bio-Repository of DNA in Stroke (BRAINS) study showed that South Asian patients with ischaemic stroke had a significantly lower prevalence of AF compared with their white British counterparts.[23] A similar observation was also made by a British study in the Bradford Metropolitan District.[24] Our findings are consistent with these studies, showing that Asian patients experience a lower rate of all-cause mortality, non-haemorrhagic stroke/SE and major bleeding compared with non-Asians.

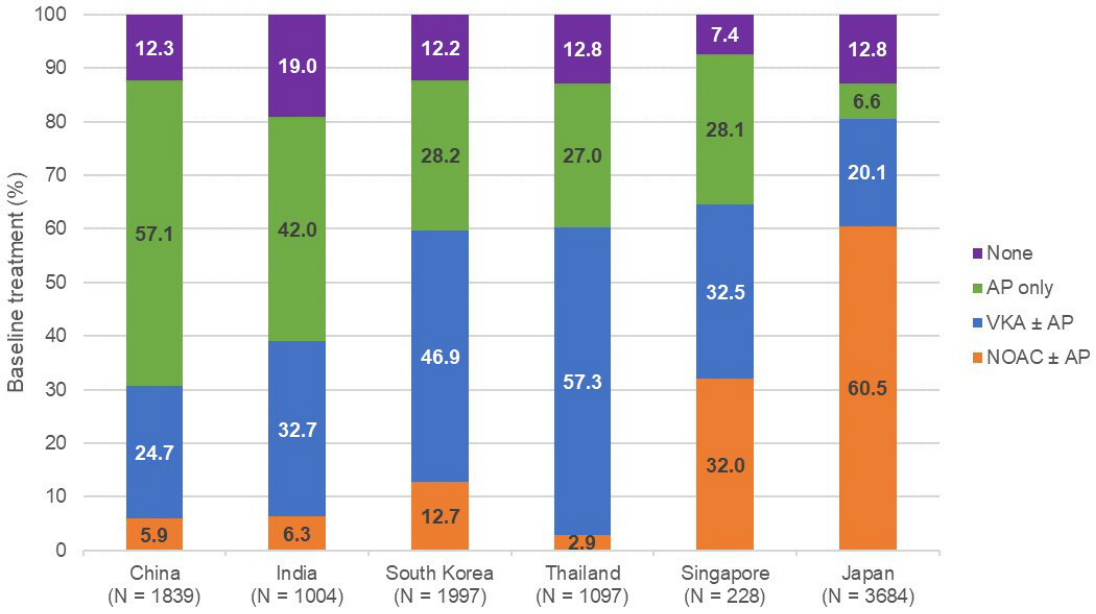

Figure 2 Distribution of baseline treatment in patients with CHA2DS2-VASc≥2 (excl. sex) enrolled in Asian countries by country. The treatment groups at baseline are described for the six Asian countries that are included in this study. The total enrolment from each country are presented in parentheses below each column. NOAC, non-vitamin K oral anticoagulant; VKA, vitamin K antagonist.

There have also been contrary reports as well of increased prevalence of stroke-relation complications in Asian patients compared with non-Asians. A systematic review using census data from the USA and the UK showed that the risk for ischaemic stroke in South Asians was 55% and 41% greater compared with the white population, in men and women, respectively.[25] Similarly, the large ecological epidemiological study using the UK-Biobank and the Korean National Health Insurance Service-Health Screening data sets showed that, in a healthy population, at 5-year follow-up, East Asians from Korea had a 3.5-fold higher incidence of primary outcome (ischaemic and haemorrhagic strokes) compared with Caucasians from the UK. However, the incidence of AF during the follow-up was significantly lower among East Asians than among Caucasians from the UK.[26] These results underscore the need for further investigation to examine the racial difference in the prevalence of AF and its associated health complication.

The GARFIELD-AF research group previously developed a model to effectively identify risk factors associated with stroke in AF population.[27] We subsequently took these selected risk factors and compared their association with primary and secondary outcomes between Asian and non-Asian populations. Our analysis confirmed that age, heart failure, chronic kidney disease, vascular disease, prior stroke/TIA/SE, prior bleeding and diabetes are all risk factors for the above outcomes in both groups. Chronic kidney and vascular disease may have a greater impact on mortality in the Asian population. However, these results must be interpreted with caution as the analysis was not adjusted for multiple testing. The results must be considered as exploratory and need further confirmation.

The relationship of risk factors to AF does not vary substantially by race,[28] although the prevalence of risk factors varies according to race in most studies including CHARGE-AF (Cohorts for Heart and Aging Research in Genomic Epidemiology) and MESA (Multi-Ethnic Study of Atherosclerosis).[29–32] Asian patients with AF share similar risk factor profiles as non-Asians, except that more Asians have a history of previous stroke.[2]

To further illustrate the possible reasons which may cause different outcomes, we revealed the presence of an intergroup interaction in the treatment of OAC for secondary outcomes, suggesting potential racial/ethnic differences in the responsiveness to OAC treatment. In this initial report on the real-world use and impact of OAC, prevention of SE appeared to be better in non-Asian than Asian populations. However, when receiving anticoagulation, the increase in major bleeding risk among Asians was higher than non-Asians. These findings are in line with previous studies showing that East Asians have a greater tendency than other populations towards bleeding in the presence of anticoagulation therapy.[33–35] On similar lines, the Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48 (ENGAGE-AF-TIMI-48) study also showed that, in Asian patients with AF, the risk of major bleeding was higher compared with non-Asians.[36] The reasons underlying this increased risk are not entirely clear. Lower body mass index and differences in concomitant medications have been suggested as potential reasons for the difference in the bleeding profile. Whether genetic

factors also contribute to the differences needs further investigation. We observed that among patients who did not receive any OAC or antiplatelet therapy, Asians had significantly lower event rates than non-Asians for any outcome occurrence. Patients of the same racial or ethnic background often share similar genetic profiles and environmental exposures. These factors can contribute to the observed variations in the incidence, presentation and outcomes of AF among different racial and ethnic groups. Additionally, racial and ethnic disparities and biases may also have a significant impact. Disparities in access to healthcare, socioeconomic status and education which are often associated with race and ethnicity can influence disease awareness, potentially leading to underdiagnosis and inadequate treatment.[37]

Strengths and limitations

GARFIELD-AF is, to date, the largest observational and non-randomised registry in the newly diagnosed AF population which enhances the generalisability of the findings to real-world clinical practice. Other notable strengths include a large multinational patient sample, detailed audited baseline information and a follow-up of at least 2 years.

GARFIELD-AF patients from the Asian region represent only a small proportion of its total AF population. Therefore, despite the lack of strict inclusion criteria and the selection from different care settings, the representativeness of each country cannot be guaranteed. Although lower average age and lower prevalence of comorbidities in Asian patients were considered, we cannot exclude an influence of unobserved confounders on the multivariable regression estimates. For example, socioeconomic factors and treatment changes over the follow-up period were not accounted for in this analysis. Finally, adverse event recognition was left to investigators' judgement and not centrally adjudicated. Nevertheless, to minimise errors, 20% of electronic Case Report Forms (eCRFs) were audited.

CONCLUSIONS

In this large data set comprising patients diagnosed with recent onset non-valvular AF, Asian patients experienced lower occurrences of mortality and major bleeding. The results validate previous studies done in this population. Treatment patterns were substantially different between Asia and non-Asian regions, with patients at high risk of stroke enrolled in Asian countries receiving anticoagulation less frequently and at lower doses compared with the rest of the world.

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Contributors C-YC, T-YL and X-JZ contributed equally and share the first authorship. Z-CJ and X-HF contributed equally to the work as corresponding authors. SV was the primary statistician. This work was conceptualised and the analysis was overseen by the working group comprising of C-YC, Z-CJ, SV, JC and KP. GK and AKK managed the funding for this study. All authors reviewed and approved the manuscript. AKK is the guarantor of this manuscript.

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