Do baseline characteristics account for geographical variations in event rates in patients with newly diagnosed atrial fibrillation? The GARFIELD-AF registry

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BACKGROUND AND CONTEXT

- Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting 1–2% of the general population and there are an estimated 30 million individuals affected worldwide[1]
- Studies in specific regions have shown wide variations in the management and outcomes of patients with AF. These variations may be influenced by baseline characteristics including gender and ethnicity[2-8]
- Prior to the Global Anticoagulant Registry in the FIELD–Atrial Fibrillation (GARFIELD-AF) there were not large-scale multinational contemporary data to define the characteristics of patients with AF, their management and their outcomes
- GARFIELD-AF has recruited >57,000 patients from 35 countries, and has the potential to define the relationship between baseline characteristics and outcomes across diverse patient populations and practice patterns

AIM

- **To define geographical variations in all-cause mortality, stroke/systemic embolism (SE) and major bleeding in patients with newly diagnosed non-valvular AF and to determine whether this variation is accounted for by baseline risk factors**

METHODS

- GARFIELD-AF has broad inclusion criteria. Eligible patients are ≥18 years with newly diagnosed (≤6 weeks' duration) non-valvular AF and ≥1 additional investigator-determined stroke risk factor(s)
- Baseline characteristics and 1-year event rates were analysed for 39,898 consecutive patients who were enrolled between Mar 2010 and Sep 2015 in 35 countries
- We fitted a two-level mixed Weibull model on patients' time-to-event nested for each country. The effect of including different patient-level baseline characteristics in the model was evaluated. A random intercept for each country was specified and adjusted for variables as defined in Figure 1
- To identify country effects greater or less than the mean global event rate, empirical Bayes means of the posterior distribution of the random coefficients were estimated

RESULTS

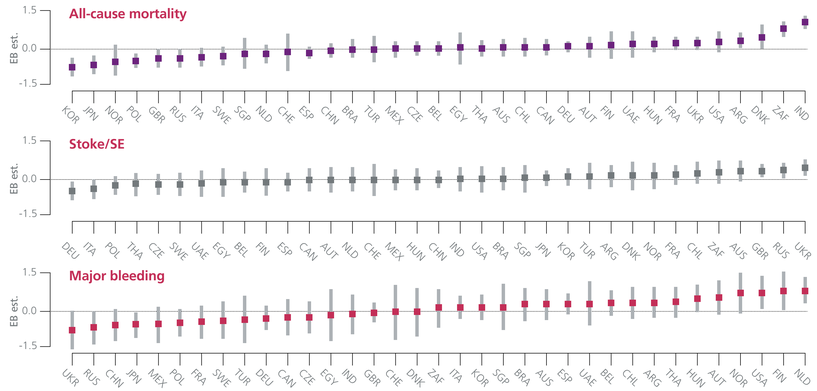
Baseline characteristics

- There were wide variations in baseline characteristics between regions and countries (Table 1)
  - In particular, there was wide variability in the reporting of vascular disease (including coronary artery disease [CAD]), as well as congestive heart failure (%), diabetes and current smoking (Table 1, median and quartile values)
  - Relative to patients in Europe and North America, patients from Asia with newly diagnosed AF were younger and less likely to have a history of CAD or a history of bleeding; although the calculated risk of bleeding (according to HAS-BLED) was similar across all regions (Table 1)
  - Relative to patients in Europe, Asia and Latin America, patients from North America were less likely to have a history of congestive heart failure

Unadjusted event rates

- Unadjusted (crude) mortality rates after 1 year's follow-up differed by country, ranging from <1 to 12.6 per 100 patient-years (average: 4.6 per 100 patient-years). Unadjusted rates of stroke/SE averaged 1.4 per 100 patient-years (range: <1 to 3.2 per 100 patient-years) and for major bleeding 1.1 per 100 patient-years (range: <1 to 2.8 per 100 patient-years)

FIGURE 1. Event rates by country (0.0 = global mean) after adjustment of all factors in Model 2



Fixed effects included in the models: gender, age group, diabetes, hypertension, congestive heart failure, vascular disease, previous stroke*, previous bleed**, ethnicity, smoke, type of atrial fibrillation, moderate-to-severe chronic kidney disease. *Not included in the model for major bleeding. **Not included in the model for stroke/systemic embolism (SE).

ARG, Argentina; AUS, Australia; AUT, Austria; BEL, Belgium; BRA, Brazil; CAN, Canada; CHE, Switzerland; CHL, Chile; CHN, China; CZE, Czech Republic; DEU, Germany; DNK, Denmark; EGY, Egypt; ESP, Spain; FIN, Finland; FRA, France; GBR, United Kingdom; HUN, Hungary; IND, India; ITA, Italy; JPN, Japan; KOR, South Korea; MEX, Mexico; NLD, Netherlands; NOR, Norway; POL, Poland; RUS, Russia; SGP, Singapore; SWE, Sweden; THA, Thailand; TUR, Turkey; UAE, United Arab Emirates; UKR, Ukraine; USA, United States of America; ZAF, South Africa. EB, empirical Bayes estimate.

TABLE 1. Baseline characteristics of patients (n=39,898) in different regions and inter-country variation

	Europe (n= 23,092)	Asia (n= 11,117)	North America (n=1133)	Latin America (n=3329)	Other countries (n=1227)	Inter-country variation		
						Median	1st quartile	3rd quartile
Mean age, yr (SD)	70.7 (10.9)	67.4 (12.0)	71.3 (11.7)	69.8 (12.0)	68.5 (12.1)	69.8	66.7	71.5
Women, %	45.3	41.0	47.2	48.0	42.2	45.0	40.8	47.1
Mean BMI, kg/m² (SD)	28.9 (5.5)	24.7 (4.1)	30.2 (7.2)	28.6 (5.6)	30.8 (7.4)	28.9	27.9	29.6
Congestive heart failure, %	20.0	19.8	15.4	20.8	17.8	16.7	13.1	20.2
Coronary artery disease, %	23.3	17.5	23.3	14.7	26.2	19.0	13.9	25.9
Acute coronary syndromes, %	10.0	7.2	12.7	8.8	16.4	9.7	7.8	12.4
Stroke/TIA, %	11.9	10.8	10.9	11.8	16.5	11.6	9.4	13.9
Systemic embolism, %	0.7	0.4	0.7	1.3	1.2	0.5	0.3	1.0
PE/DVT, %	3.5	0.6	4.4	2.2	5.0	2.5	1.3	4.4
History of bleeding, %	2.7	1.7	5.1	4.2	3.5	2.7	1.9	3.5
History of hypertension, %	80.2	68.4	76.3	80.9	76.6	75.9	70.4	85.1
Vascular disease, %	15.7	11.3	17.4	14.8	21.0	16.0	12.3	18.6
Carotid occlusive disease, %	3.8	1.7	3.1	2.6	2.1	2.3	1.5	3.9
Diabetes mellitus, %	21.3	21.7	25.3	24.0	23.0	21.3	17.7	26.6
Moderate-to-severe CKD, %	12.0	7.6	8.6	7.1	12.4	9.4	5.8	13.0
Cirrhosis, %	0.5	0.6	0.7	0.4	0.4	0.5	0.2	0.8
Dementia, %	1.3	1.7	2.1	1.1	2.4	1.0	0.6	1.6
Current smoker, %	10.2	12.8	12.2	8.4	10.4	9.8	7.3	11.6
Risk score, mean (SD)								
CHA_2DS_2-VASc	3.3 (1.6)	2.9 (1.6)	3.3 (1.5)	3.3 (1.6)	3.3 (1.6)	3.1	3.0	3.4
HAS-BLED	1.4 (0.9)	1.4 (0.9)	1.6 (0.9)	1.5 (0.9)	1.6 (1.1)	1.5	1.3	1.6

BMI, body mass index; CKD, chronic kidney disease; DVT, deep vein thrombosis; PE, pulmonary embolism; SD, standard deviation; TIA, transient ischaemic attack.

TABLE 2. Inter-country variation in 1-year clinical outcomes

	All-cause mortality		Stroke/SE		Major bleeding	
Model	**Variance**	**95% CI**	**Variance**	**95% CI**	**Variance**	**95% CI**
1	0.17	0.10; 0.30	0.10	0.05; 0.24	0.36	0.18; 0.73
2	0.16	0.09; 0.28	0.09	0.04; 0.21	0.30	0.13; 0.69

Model 1: gender, age group, diabetes, hypertension, congestive heart failure, vascular disease, previous stroke*, previous bleed**. Model 2: Model 1 + ethnicity, smoking, type of atrial fibrillation, moderate-to-severe chronic kidney disease. *Not included in the model for major bleeding. **Not included in the model for stroke/SE. CI, confidence interval; SE, systemic embolism.

Event rates after adjustment for baseline characteristics

- After adjusting for CHA_2DS_2-VASc-related baseline characteristics and previous bleed (Model 1), inter-country variance in mortality was 0.17 (95% confidence interval: 0.10 to 0.30) (Table 2)
- With further adjustment for ethnicity, smoking, type of AF and moderate-to-severe chronic kidney disease (Model 2), the variance between countries in mortality decreased by 6%, to 0.16 (0.09 to 0.28) (Table 2)
- **Having adjusted for all key variables (Model 2), the geographical variation in stroke/SE, mortality and major bleeding remained significant (p<0.0001 likelihood ratio test comparing the models with the one-level Weibull regression; Figure 1)**
- Despite risk adjustment, we observed lower mortality in Eastern Asia (Japan and South Korea) and higher mortality in countries such as India and South Africa
- Variations in adjusted rates of stroke/SE and major bleeding remained after risk adjustment. These were not concordant with mortality rates for the respective countries. Some of the variation in major bleeding may be related to ascertainment of this endpoint

CONCLUSIONS

Following the diagnosis of AF, there were marked geographical variations in outcomes

The variations persisted after adjusting for CHA_2DS_2-VASc risk factors and other commonly reported baseline characteristics (ethnicity, smoking, type of AF and moderate-to-severe chronic kidney disease)

Other factors, including variation in practice patterns/system of care between countries, as well as other patient-related factors (determined by genetic variance or lifestyle)[9] may be responsible for the substantial differences in the rates of mortality, stroke/SE and major bleeding

Further investigation into the role of practice patterns and factors beyond those in CHA_2DS_2-VASc is warranted to minimise adverse outcomes

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DECLARATION OF INTEREST

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http://www.tri-london.ac.uk/garfield/ESC-2016/ESC_2016_posters

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