Vitamin K antagonist control for patients with nonvalvular atrial fibrillation in Eastern and Southeastern Asia: An analysis of event rates from GARFIELD-AF

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BACKGROUND

- Vitamin K antagonist (VKA) therapy is effective in preventing thromboembolism in atrial fibrillation (AF)[1,2]
- However, the intensity of anticoagulation, measured by the international normalised ratio (INR), needs to be maintained within a narrow therapeutic range.[3] An INR below the therapeutic range increases the risk of thromboembolism, whereas an INR above the therapeutic range increases the risk of bleeding
- International guidelines for AF differ in their recommended target INR range: European and American guidelines recommend a target of 2.0–3.0,[4,5] while the Asia Pacific Heart Rhythm Society and Japanese Circulation Society recommend an INR of 2.0–3.0 for all patients with AF except those aged ≥70 years, for whom 1.6–2.6 is recommended[6,7]

PURPOSE

- To identify the INR range with the lowest rates of stroke/systemic embolism (SE), major bleeding and all-cause mortality for VKA-treated patients with newly diagnosed nonvalvular AF from Eastern (E) and Southeastern (SE) Asia, using data from the Global Anticoagulant Registry in the FIELD–Atrial Fibrillation (GARFIELD-AF)

METHODS

- GARFIELD-AF is an ongoing, international, observational registry of consecutively recruited patients aged ≥18 years with newly diagnosed (≤6 weeks' duration) nonvalvular AF and ≥1 additional investigator-determined stroke risk factor(s)[8]
- INR values during 1-year follow-up for patients in E and SE Asia (China, Japan, Korea, Singapore, Thailand) receiving VKA at baseline, with or without antiplatelet therapy, were analysed
- INR values after an event and those after discontinuation or interruption of VKA were not included
- The analysis included only patients with ≥3 INR values
- Time in each INR level was estimated using linear interpolation according to Rosendaal's method,[9] only if the interval between consecutive INR readings did not exceed 90 days; intervals exceeding 90 days were excluded
- INR-related crude 1-year rates (per 100 person-years) of stroke/SE and major bleeding, occurring within 30 days of the last INR measurement, were analysed using a Poisson model
- Incidence rate ratios (IRRs), relative to the reference group with an INR of 1.6–2.0, were estimated

RESULTS

- A total of 9632 patients were recruited in E and SE Asia between May 2010 and Sep 2015. Of these, 1835 (19.1%) received VKA (with or without antiplatelet therapy) at baseline and had ≥3 INR values during 1-year follow-up
- The mean (standard deviation) age at diagnosis was 67.8 (11.2) years and 41.7% of patients were female (Table 1). The mean CHA_2DS_2-VASc score was 3.0 (1.5) and mean HAS-BLED score was 1.3 (0.9)
- The mean INR was 2.0 (0.9); 35.8% of INR values were <1.6, 24.5% were 1.6–2.0, 23.8% were 2.0–2.6 and 15.8% were >2.6
- During 1-year follow-up, the lowest rates of stroke/SE, major bleeding and all-cause mortality were observed at the INR values of 1.6–2.0 (Table 2)
- Most strokes were primary ischaemic (Table 3)
- IRRs tended toward an increase in the risk of stroke/SE with INR values of <1.6, 2.0–2.6 and >2.6, and the risk of major bleeding was considerably increased with an INR of >2.6, although numbers of events were low (Table 2, Figure 1)

TABLE 1. Baseline characteristics of patients who received vitamin K antagonist and had ≥3 international normalised ratio values during

	All patients (n=1835)
Age at diagnosis, years, mean (SD)	67.8 (11.2)
Women, %	41.7
Medical history, %	
Congestive heart failure	24.8
Coronary artery disease	9.4
Acute coronary syndromes	3.9
Stroke/transient ischaemic attack	13.4
Systemic embolism	0.7
History of bleeding	1.2
History of hypertension	73.2
Diabetes mellitus	24.1
Moderate-to-severe CKD	9.2
Risk score, mean (SD)	
CHA_2DS_2-VASc	3.0 (1.5)
HAS-BLED	1.3 (0.9)

CKD, chronic kidney disease; SD, standard deviation.

TABLE 2. Rates and incidence rate ratios for clinical outcomes during the first year of follow-up according to international normalised ratio

Outcome	INR	Number of events	Person-years	Rate (95% CI), per 100 person-years	IRR	95% CI
Stroke/SE	<1.6	8	289.7	2.8 (1.4; 5.5)	7.9	1.0; 62.9
	1.6–2.0	1	284.8	0.4 (0.1; 2.5)	1 (ref)	-
	2.0–2.6	5	274.6	1.8 (0.8; 4.4)	5.2	0.6; 44.4
	>2.6	1	143.1	0.7 (0.1; 5.0)	2.0	0.1; 31.8
	Overall*	15	1211.3	1.2 (0.8; 2.1)	-	-
Major bleeding	<1.6	2	289.3	0.7 (0.2; 2.8)	2.0	0.2; 21.8
	1.6–2.0	1	285.7	0.4 (0.1; 2.5)	1 (ref)	-
	2.0–2.6	4	274.4	1.5 (0.6; 3.9)	4.2	0.5; 37.3
	>2.6	8	143.0	5.6 (2.8; 12.0)	16.0	2.0; 127.8
	Overall*	15	1212.2	1.2 (0.8; 2.1)	-	-
All-cause mortality	<1.6	4	290.6	1.4 (0.5; 3.7)	4.0	0.4; 35.3
	1.6–2.0	1	286.5	0.4 (0.1; 2.5)	1 (ref)	-
	2.0–2.6	3	275.4	1.1 (0.4; 3.4)	3.1	0.3; 30.0
	>2.6	3	143.5	2.1 (0.7; 6.5)	6.0	0.6; 57.6
	Overall*	11	1216.1	0.9 (0.5; 1.6)	-	-

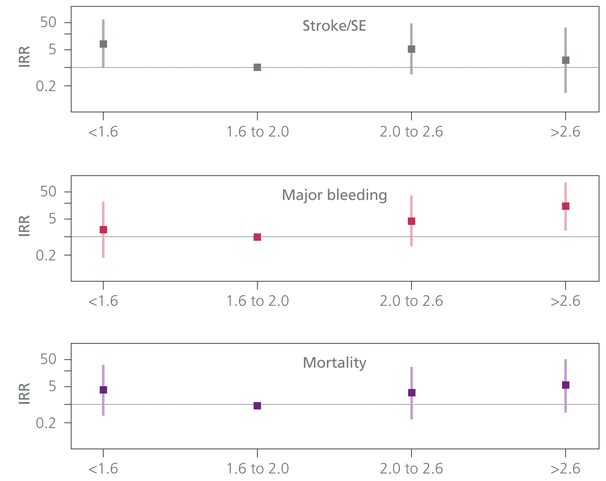
*The sum of person-years for different INR levels is not the same as the overall person-years due to consecutive INR values with an interval of >90 days. CI, confidence interval; INR, international normalised ratio; IRR, incidence rate ratio; SE, systemic embolism.

TABLE 3. Type of stroke during the first year of follow-up according to international normalised ratio

INR	Primary ischaemic	Primary haemorrhagic	Unknown	Total
<1.6	6*	1	1	8
1.6–2.0	1	0	0	1
2.0–2.6	2	3	0	5
>2.6	1	0	0	1
Overall	10	4	1	15

*Includes two secondary haemorrhagic ischaemic strokes.
INR, international normalised ratio.

FIGURE 1. Incidence rate ratios and 95% confidence intervals for clinical outcomes during the first year of follow-up according to international normalised ratio (reference group: 1.6 to 2.0)



INR, international normalised ratio; IRR, incidence rate ratio; SE, systemic embolism.

CONCLUSIONS

This prospective analysis of patients with newly diagnosed nonvalvular AF from Asia suggests that the lowest rates of stroke/SE and major bleeding occur at the INR level of 1.6–2.0, which does not contradict the regional practice of a lower INR than in non-Asian countries. More data are required to determine whether there are significant differences in outcomes among Asian patients with different INR levels.

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REFERENCES

1. Atrial Fibrillation Investigators. Arch Intern Med. 1994;154(13):1449-57. 2. Connolly SJ et al. Circulation. 2008;118(20):2029-37. 3. Hylek EM et al. N Engl J Med. 2003;349(11):1019-26. 4. Camm AJ et al. Europace. 2012;14(10):1385-413. 5. January CT et al. J Am Coll Cardiol. 2014;64(21):e1-76. 6. JCS Joint Working Group. Circ J. 2014;78(8):1997-2021. 7. Ogawa S et al. J Arrhythmia. 2013;29(3):190-200. 8. Kakkar AK et al. Am Heart J. 2012;163(1):13-19.e1. 9. Rosendaal FR et al. Thromb Haemost. 1993;69(3):236-9.

DECLARATION OF INTEREST

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

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