Differences in two-year outcomes according to type of atrial fibrillation: results from the GARFIELD-AF registry

Dan Atar[1], Jean-Yves Le Heuzey[2], Gabriele Accetta[3], Jean-Pierre Bassand[4], A. John Camm[5], Ramon Corbalan[6], Harry Gibbs[7], Samuel Z. Goldhaber[8], Shinya Goto[9], Paul Jones[3], Gloria Kayani[3], Frank Misselwitz[10], Janina Stepinska[11], Alexander G.G. Turpie[12], Ajay K. Kakkar[13], for the GARFIELD-AF Investigators

[1]Oslo University Hospital Ullevål and University of Oslo, Oslo, Norway, [2]Georges Pompidou Hospital, René Descartes University, Paris, France, [3]Thrombosis Research Institute, London, UK, [4]Thrombosis Research Institute, London, UK and University of Besançon, Besançon, France, [5]St. George's University of London, London, UK, [6]Catholic University School of Medicine, Santiago, Chile, [7]The Alfred Hospital, Melbourne, Australia, [8]Brigham and Women's Hospital and Harvard Medical School, Boston, USA, [9]Tokai University, Kanagawa, Japan, [10]Bayer AG, Pharmaceuticals, Berlin, Germany, [11]Institute of Cardiology, Warsaw, Poland, [12]McMaster University, Hamilton, Canada, [13]Thrombosis Research Institute and University College London, London, UK

BACKGROUND

- The type of atrial fibrillation (AF) has not been established as a major predictor of stroke or death, with conflicting reports in the literature[1-4].
- Therefore, AF burden, defined according to each type of AF, has not been factored into the guidance for clinical decision making[5,6].

PURPOSE

- To analyse outcomes over 2 years after diagnosis of AF by type of AF and by antithrombotic therapy.

METHODS

- The Global Anticoagulant Registry in the FIELD–Atrial Fibrillation (GARFIELD-AF) is a prospective non-interventional study designed to reflect patient management according to local practice.
- Adults (≥18 years) with newly diagnosed (≤6 weeks' duration) AF and ≥1 investigator-determined risk factor(s) for stroke were enrolled[7].
- We analysed baseline characteristics, antithrombotic therapy, and 2-year incidence of outcomes in patients classified as having paroxysmal, persistent, or permanent AF.
- All patients listed as 'new' or without a classification at baseline were assigned the type of AF listed at the 4-month time point, where available.
- Hazard ratios (HRs) were estimated using a Cox proportional hazard regression model and adjusted for anticoagulant (AC) treatment and the following baseline factors: age, gender, race, smoking, diabetes, hypertension, stroke/transient ischaemic attack/systemic embolism (SE), history of bleeding, cardiac failure, vascular disease, moderate-to-severe chronic kidney disease, and heavy alcohol consumption (only in the model for major bleeding).

RESULTS

PATIENT CHARACTERISTICS

- We analysed 28 628 patients enrolled from 32 countries in Mar 2010–Oct 2014.
- 10 473 (48.5%) patients were classified as having paroxysmal AF, 6020 (27.9%) persistent AF, and 5117 (23.7%) permanent AF; 7018 patients were classed as having new-onset or unknown type of AF.
- Patients with permanent AF had slightly higher CHA_2DS_2-VASc and HAS-BLED scores than those with paroxysmal or persistent AF, and they were most likely to be ≥75 years of age (Table 1).
- Compared to patients with other AF types, those with paroxysmal AF were less likely to be obese, or to have left ventricular ejection function <40% or severe heart failure (New York Heart Association Class III/IV), but they were as likely to have history of vascular disease (stroke/transient ischaemic attack, carotid occlusive disease, acute coronary syndromes) (Table 1).

Table 1. *Baseline characteristics of patients according to type of atrial fibrillation*

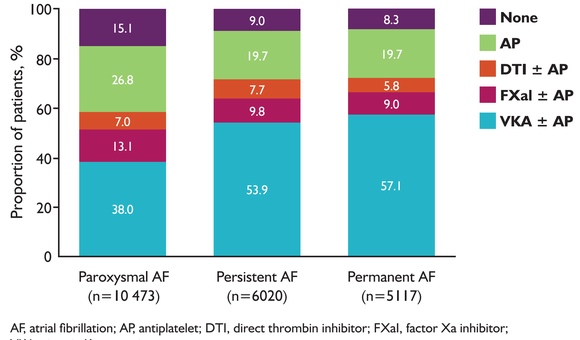
	Paroxysmal AF (n=10 473)	Persistent AF (n=6020)	Permanent AF (n=5117)
Age			
≥75 years, %	33.6	34.3	48.3
Mean (SD)	68.5 (11.7)	69.1 (10.9)	72.6 (10.6)
Women, %	47.3	40.4	43.8
BMI ≥30 kg/m^2, %	26.8	30.9	33.2
Medical history, %			
NYHA Class III–IV CHF	25.2	33.0	38.8
Acute coronary syndromes	9.4	8.3	9.6
LVEF <40%	6.0	12.0	14.4
Stroke/transient ischaemic attack	12.2	10.7	13.5
Carotid occlusive disease	2.9	2.8	4.1
Systemic embolism	0.6	0.7	0.8
History of bleeding	2.6	2.6	3.1
History of hypertension	76.6	77.2	79.4
Diabetes mellitus	20.2	22.1	23.1
Moderate-to-severe CKD	9.7	9.9	13.3
Risk score, mean (SD)			
CHA_2DS_2-VASc	3.1 (1.6)	3.1 (1.6)	3.5 (1.5)
HAS-BLED	1.4 (0.9)	1.4 (0.9)	1.6 (0.9)

AF, atrial fibrillation; BMI, body mass index; CHF, congestive heart failure; CKD, chronic kidney disease; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD, standard deviation.

ANTITHROMBOTIC THERAPIES

- Patients with paroxysmal AF were less likely to receive AC therapy, with or without antiplatelet (AP) therapy, and more likely to receive AP therapy only or no antithrombotics, versus patients with persistent or permanent AF (Figure 1).

Figure 1. *Antithrombotic therapy at diagnosis according to type of atrial fibrillation*



AF, atrial fibrillation; AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist.

CLINICAL OUTCOMES

- Incidence rates of adverse events during 2-year follow-up are shown in Table 2.

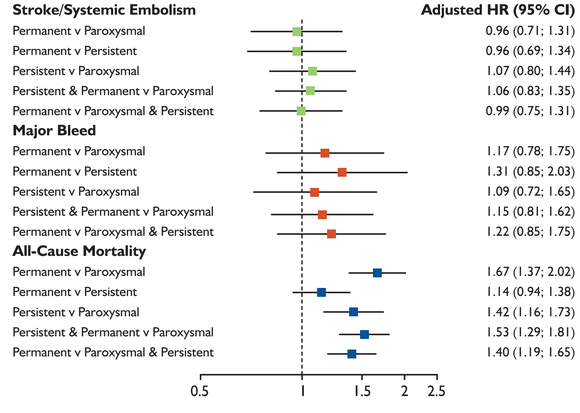
Table 2. *Incidence event rates during 2-year follow-up in patients with different types of atrial fibrillation*

Rate per 100 person-years (95% CI)	Paroxysmal AF (n=10 473)	Persistent AF (n=6020)	Permanent AF (n=5117)
Stroke/systemic embolism	1.26 (1.11; 1.43)	1.39 (1.18; 1.63)	1.82 (1.56; 2.12)
Major bleeding	0.73 (0.61; 0.86)	0.76 (0.61; 0.94)	1.07 (0.87; 1.30)
All-cause mortality	2.80 (2.57; 3.05)	3.82 (3.47; 4.21)	5.89 (5.41; 6.41)

AF, atrial fibrillation; CI, confidence interval.

- Compared to patients with paroxysmal AF, those with persistent or permanent AF had higher risks of all-cause mortality, stroke/SE, and major bleeding. After adjustment for AC treatment and baseline factors, significant differences in type of AF only remained for all-cause mortality (Figure 2).
- Adjusted HRs also showed that mortality is significantly less in paroxysmal vs permanent and persistent AF (Figure 2).
- For all outcomes, no statistically significant interaction was found between type of AF and AC therapy (all p>0.10).

Figure 2. *Adjusted hazard ratios for 2-year clinical outcomes according to type of atrial fibrillation*



Hazard ratios were adjusted for anticoagulant treatment and baseline factors: age, gender, race, smoking, diabetes, hypertension, stroke/transient ischaemic attack/systemic embolism, history of bleeding, cardiac failure, vascular disease, moderate-to-severe chronic kidney disease, and heavy alcohol consumption (only for major bleeding).

CI, confidence interval; HR, hazard ratio.

LIMITATIONS

- Of the 28 628 patients available, type of AF was missing for 7018 (24.5%).

CONCLUSIONS

- Patients with paroxysmal AF were less likely to be prescribed AC therapy (with or without AP therapy) than those with persistent or permanent AF.
- Persistent and permanent AF were associated with higher mortality risk compared with paroxysmal AF, but had similar adjusted risks of stroke/SE and major bleeding during 2 years of follow-up.
- We found no statistically significant interaction between type of AF and AC therapy for clinical outcomes.

CLINICAL IMPLICATIONS

The finding of similar adjusted stroke rates in patients with paroxysmal AF as compared to those with persistent or permanent AF has several implications:

- It emphasises the need for early detection of silent and unnoticed paroxysmal AF.
- It underscores the recommendation to apply the same stroke prevention strategies to paroxysmal AF as to the other types of AF.

ACKNOWLEDGEMENTS

We thank the physicians, nurses, and patients involved in the GARFIELD-AF registry. SAS programming support was provided by Jagan Allu (Thrombosis Research Institute, London, UK). Editorial assistance was provided by Emily Chu (Thrombosis Research Institute, London, UK).

REFERENCES

1. Banerjee A, et al. *Int J Cardiol* 2013; 167(6): 2682-7.
2. Vanassche T, et al. *European Heart Journal* 2015; 36(5): 281-7a.
3. Steinberg BA, et al. *European Heart Journal* 2015; 36(5): 288-96.
4. Senoo K, et al. *Stroke* 2015; 46(9): 2523-8.
5. Kirchhof P, et al. *European Heart Journal* 2016; 37(38): 2893-962.
6. January CT, et al. *Circulation* 2014; 130(23): 2071-104.
7. Kakkar AK, et al. *Am Heart J* 2012; 163(1): 13-19 e1.

DECLARATION OF INTEREST

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG (Berlin, Germany).

DA: Personal fees from Bayer Healthcare, BMS/Pfizer, Boehringer-Ingelheim, MSD; J-YLH: Personal fees from Boehringer Ingelheim, Bayer, BMS/Pfizer, Daiichi Sankyo, Servier, Meda; GA: None; J-PB: None; AJC: Personal fees from Bayer, Boehringer Ingelheim, Pfizer/BMS, Daiichi Sankyo; RC: None; HG: Personal fees from Pfizer, Bayer, Boehringer Ingelheim; SZG: Grants from BiO2 Medical, Boehringer-Ingelheim, Bristol Meyers Squibb, BTG EKOS, Daiichi Sankyo, National Heart Lung and Blood Institute of the National Institutes of Health, Janssen, Thrombosis Research Group, personal fees from Bayer, Boehringer-Ingelheim, Bristol Meyers Squibb, Daiichi Sankyo, Janssen, Portola; SG: Personal fees from Bayer, AstraZeneca, grants from Sanofi, Pfizer, Ono; PJ: None; GK: None; FM: Employee of Bayer AG; JS: Grants from Bayer, personal fees from Bayer, Boehringer Ingelheim, BMS/Pfizer, Novartis, Servier, Amgen, Sanofi, expert witness for Boehringer Ingelheim; AGGT: Personal fees from Bayer Healthcare, Janssen Pharmaceutical Research & Development LLC, Astellas, Portola, Takeda; AKK: Research support from Bayer AG, personal fees from Bayer AG, Boehringer-Ingelheim Pharma, Daiichi Sankyo Europe, Janssen Pharma, Sanofi SA.

TRI Thrombosis Research Institute

www.garfieldregistry.org

Poster presented at the ESC Congress, Barcelona, Spain; 26–30 August 2017

AF Garfield global anticoagulant registry in the field