Similar clinical outcomes of asymptomatic and symptomatic patients with newly diagnosed atrial fibrillation: results from GARFIELD-AF

Harry Gibbs[1], Ben Freedman[2], Marten Rosenqvist[3], Wael Al Mahmeed[4], Giuseppe Ambrosio[5], A. John Camm[6], Stuart J. Connolly[7], Haiyan Gao[8], Barry Jacobson[9], Carlos Jerjes-Sanchez[10], Gloria Kayani[8], Ali Oto[11], Elizaveta Panchenko[12], Hany Ragy[13], Ajay K. Kakkar[14], for the GARFIELD-AF Investigators

[1]The Alfred Hospital, Melbourne, Australia, [2]Heart Research Institute, Charles Perkins Centre, University of Sydney, Sydney, Australia, [3]Karolinska Institutet, Danderyd University Hospital, Stockholm, Sweden, [4]Heart and Vascular Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates, [5]University of Perugia School of Medicine, Perugia, Italy, [6]St. George's University of London, London, UK, [7]McMaster University, Hamilton, Canada, [8]Thrombosis Research Institute, London, UK, [9]Johannesburg Hospital, University of the Witwatersrand, Johannesburg, South Africa, [10]Instituto de Cardiologia y Medicina Vascular, TecSalud, Tecnológico de Monterrey, Monterrey, Mexico, [11]Hacettepe University, Ankara, Turkey, [12]Cardiology Research and Production Center, Moscow, Russia, [13]Hayat Hospital, Cairo, Egypt, [14]Thrombosis Research Institute and University College London, London, UK

BACKGROUND

- Atrial fibrillation (AF) is often associated with heart failure and adverse outcomes such as stroke and all-cause mortality, which can be reduced with appropriate interventions[1,2].
- The incidental diagnosis of asymptomatic AF is relatively common, especially in elderly patients[3]. Asymptomatic AF appears to be associated with increased stroke risk, although it is unclear whether this is to the same extent as in those with symptoms[3].
- The Global Anticoagulant Registry in the FIELD–Atrial Fibrillation (GARFIELD-AF) provides an opportunity to investigate prospectively the outcomes of a large cohort of patients with newly diagnosed AF, including some with asymptomatic AF. Reflecting the non-interventional design of this registry, patients are managed according to usual care and treatment with anticoagulants is not mandated.

PURPOSE

- To compare the characteristics, treatment, and 1-year outcomes of asymptomatic vs symptomatic AF in patients with newly diagnosed AF.

METHODS

- GARFIELD-AF is an ongoing, international, non-interventional disease registry of consecutively recruited patients aged ≥18 years with newly diagnosed (≤6 weeks' duration) non-valvular AF and ≥1 investigator-determined stroke risk factor(s)[4].
- We analysed baseline characteristics, antithrombotic therapy, and 1-year incidence of outcomes in asymptomatic and symptomatic patients.
- Hazard ratios (HRs) were estimated using a Cox proportional hazard regression model and adjusted for differences in baseline variables.

RESULTS

PATIENT CHARACTERISTICS

- 39 898 patients were enrolled into GARFIELD-AF from 35 countries from Mar 2010–Sep 2015.
- We analysed the 36 968 patients with data on symptoms of AF at enrolment; 28 843 (78.0%) presented with symptoms (palpitations, shortness of breath, chest pain/discomfort, dizziness, tiredness, sweating, fainting, other) and 8125 (22.0%) were asymptomatic.
- Compared with symptomatic patients, the asymptomatic patients were more often more men, older, and had lower prevalence of congestive heart failure (CHF), and of New York Heart Association Class III–IV CHF (Table 1).
- The two groups had similar median CHA_2DS_2-VASc and HAS-BLED scores (Table 1).
- Fewer asymptomatic patients were diagnosed in a hospital or emergency room and more in an office setting (Table 1).

Table 1. *Baseline characteristics of asymptomatic and symptomatic patients with newly diagnosed atrial fibrillation*

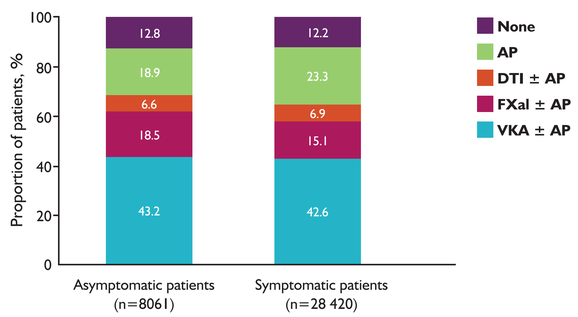
	Asymptomatic patients (n=8125)	Symptomatic patients (n=28 843)
Age at diagnosis, years, median (IQR)	73.0 (65.0 to 79.0)	70.0 (62.0 to 78.0)
Men:women	1.9	1.1
Medical history, %		
Congestive heart failure	11.7	23.2
NYHA Class III–IV	17.1	34.9
Coronary artery disease	16.8	22.5
Stroke/transient ischaemic attack	15.8	10.1
Systemic embolism	1.0	0.6
History of bleeding	3.0	2.6
History of hypertension	75.2	77.2
Diabetes mellitus	22.6	21.6
Moderate-to-severe CKD	12.8	11.8
Risk score, median (IQR)		
CHA_2DS_2-VASc	3.0 (2.0 to 4.0)	3.0 (2.0 to 4.0)
HAS-BLED	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)
Care setting location at diagnosis, %		
Anticoagulation clinic/thrombosis centre	1.0	0.7
Emergency room	4.3	13.6
Hospital	52.6	60.7
Office	42.2	25.0

CKD, chronic kidney disease; IQR, interquartile range; NYHA, New York Heart Association.

ANTITHROMBOTIC THERAPIES

- The prescribing of antithrombotic therapies following AF diagnosis was similar in asymptomatic and symptomatic patients, with 68.3% and 64.6% receiving anticoagulant therapy (with or without antiplatelet therapy), respectively (Figure 1).

Figure 1. *Antithrombotic therapy at diagnosis in asymptomatic and symptomatic patients with atrial fibrillation*



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

CLINICAL OUTCOMES

- The incidence rates of stroke/systemic embolism (SE), major bleeding, and all-cause mortality during 1-year follow-up in asymptomatic and symptomatic AF are shown in Table 2. Rates of stroke/SE, major bleeding, and all-cause mortality in asymptomatic patients were similar to those observed in patients with symptomatic AF.

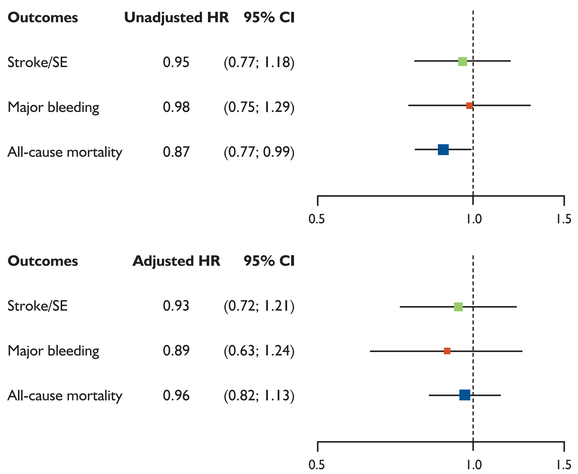
Table 2. *Incidence event rates during 1-year follow-up in asymptomatic and symptomatic patients with atrial fibrillation*

Rate per 100 person-years (95% CI)	Asymptomatic patients (n=8125)	Symptomatic patients (n=28 843)
Stroke/systemic embolism	1.40 (1.16; 1.69)	1.47 (1.34; 1.62)
Major bleeding	0.86 (0.68; 1.10)	0.88 (0.78; 1.00)
All-cause mortality	3.81 (3.40; 4.28)	4.38 (4.14; 4.63)

CI, confidence interval.

- Unadjusted and adjusted HRs showed no difference in the rate of stroke/SE or of major bleeding in asymptomatic and symptomatic patients (Figure 2).
- Unadjusted HRs showed slightly lower all-cause mortality in asymptomatic patients, although this difference was not present after adjustment for baseline characteristics (Figure 2).

Figure 2. *Hazard ratios for 1-year clinical outcomes for patients with asymptomatic vs symptomatic atrial fibrillation*



Hazard ratios were adjusted for age group, gender, race, smoking, diabetes, hypertension, previous stroke/transient ischaemic attack/systemic embolism, history of bleeding, cardiac failure, vascular disease, moderate-to-severe renal disease, anticoagulant treatment, type of atrial fibrillation, and alcohol consumption.

Reference group: patients with symptomatic atrial fibrillation.

CI, confidence interval; HR, hazard ratio; SE, systemic embolism.

CONCLUSIONS

- One-fifth of patients newly diagnosed with AF were asymptomatic. Two-thirds of asymptomatic patients were men.
- Prescribing of antithrombotic therapies was similar in asymptomatic and symptomatic patients.
- After accounting for differences in baseline characteristics, adjusted 1-year mortality, stroke/SE, and major bleeding were also similar in each group.

CLINICAL IMPLICATIONS

- Asymptomatic newly diagnosed AF is not benign and should be treated as for symptomatic AF.
- Because patients who are asymptomatic at presentation have incidentally detected AF, their prognosis will mimic that of screen-detected AF. Our results of similar adverse prognosis in such patients as those who are symptomatic support the likely benefit of screening for AF.
- Further research into the value of population screening for asymptomatic AF is warranted.

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. Stewart S, et al. *Am J Med* 2002; 113(5): 359-64.
2. Andersson T, et al. *Eur Heart J* 2013; 34(14): 1061-67.
3. Freedman B, et al. *Circulation* 2017; 135(19): 1851-67.
4. 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).

H Gibbs: Personal fees from Pfizer, Bayer, Boehringer Ingelheim; BF: Speakers' fees and advisory board honoraria from Bayer Pharma AG, Boehringer Ingelheim, BMS/Pfizer; MR: Consultant/research grants/lectures for Bayer, Bristol-Myers Squibb, Boehringer Ingelheim, Pfizer, Abbott, Medtronic, Zenicor; WAM: None; GA: Personal fees from Merck, Menarini, Angelini, Behring; AJC: Personal fees from Bayer, Boehringer Ingelheim, Pfizer/BMS, Daiichi Sankyo; SJC: Research grants and consulting fees from Bayer, Boehringer Ingelheim, BMS, Pfizer, Portola, Janssen, Sanofi, Medtronic, St. Jude, Abbott; H Gao: None; BJ: Personal fees from Bayer HealthCare, Sanofi-Aventis; CJ-S: Personal fees from Bayer, Boehringer Ingelheim, Pfizer; GK: None; AO: None; EP: Personal fees from Sanofi, Takeda, Boehringer Ingelheim, Pfizer, Bristol-Myers Squibb, Bayer, AstraZeneca; HR: None; 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