Outcomes after rhythm versus rate control in patients with atrial fibrillation: the international prospective GARFIELD Registry

Eivind Berge[1], Dan Atar[1], Jean-Yves Le Heuzey[2], Stuart Connolly[3], David A. Fitzmaurice[4], A. John Camm[5], Petr Jansky[6], Sophie K. Rushton-Smith[7], Gloria Kayani[7], Ajay K. Kakkar[7], for the GARFIELD Investigators

[1]Oslo University Hospital Ulleval, and University of Oslo, Inst of Clinical Medicine, Norway; [2]AP-HP – European Hospital Georges Pompidou, Department of Cardiology, and René Descartes University, Paris, France; [3]McMaster University, Hamilton, Canada; [4]University of Birmingham, Birmingham, UK; [5]St George's University of London, London, UK; [6]University Hospital Motol, Prague, Czech Republic; [7]Thrombosis Research Institute, London, UK

BACKGROUND

- Randomized trials and registries, such as AFFIRM[1] and RecordAF,[2] have demonstrated no difference in risks of cardiovascular clinical events between atrial fibrillation (AF) patients assigned to either rate or rhythm control therapy.
- In comparison, a population-based observational study conducted in >57,000 Quebec patients aged ≥65 years with a discharge diagnosis of AF showed that, in comparison with rate control, the use of rhythm control therapy was associated with lower risks of both long-term death (>5 years)[3] and stroke/transient ischaemic attack (TIA),[4] particularly among those at moderate to high risk of stroke.

PURPOSE

To determine whether rhythm control confers clinical benefits over rate control in patients with newly diagnosed non-valvular AF.

METHODS

- GARFIELD is an ongoing, international, prospective, observational study of consecutively recruited adults (≥18 years) with newly diagnosed (≤6 weeks previously) non-valvular AF and ≥1 additional investigator-determined stroke risk factor(s).[5] Such risk factors were not prespecified in the study protocol, nor were they limited to those in risk-stratification schemes such as $CHADS_2$[6] or CHA_2DS_2-VASc.[7]
- Investigator sites were representative of the distribution of AF care settings in each country.
- A total of 10,614 patients were recruited into cohort 1 at 540 randomly selected sites in 19 countries over a 2-year period; of these patients, 5089 were recruited retrospectively as a validation cohort, and 5525 were recruited prospectively, and comprise the study population for this analysis.
- Patients were classified as being on either rate or rhythm control at baseline; those simultaneously prescribed rhythm and rate control drugs were classified as on rhythm control.
- A Cox proportional hazards model was used to determine the effects of rhythm versus rate control on clinical outcomes at 1 year after AF diagnosis. Outcomes of all-cause death and stroke/systemic embolism (SE) were adjusted for antithrombotic treatments and components of the CHA_2DS_2-VASc score. The outcome of major bleed[8] was adjusted for antithrombotic treatments and components of the HAS-BLED score.[9]

RESULTS

- Of the 5525 adults enrolled prospectively, 2107 (38.1%) were on rhythm control and 2754 (49.8%) were on rate control therapy only. Of the rhythm control patients, 1.6% (n=33) were simultaneously receiving beta-blocker medication.
- Patients in the rhythm control group were on average younger and had lower stroke and bleed risk scores (Table) and were less likely to have antithrombotic treatments initiated at AF diagnosis (Figure 1).

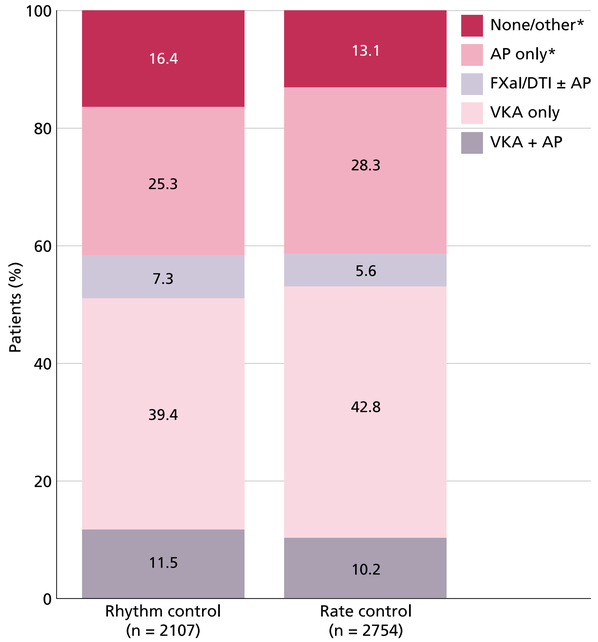
TABLE Patient baseline characteristics according to rhythm or rate control.

	Rhythm control (n = 2107)	Rate control (n = 2754)	P value*
Women, %	42.3	45.5	0.026
Age, median (IQR) years	69 (60–77)	72 (64–79)	<0.001
BMI, mean±SD, kg/m²	27.3±5.0	27.3±5.7	0.80
Pulse, mean±SD, bpm	88.1±26.9	90.2±25.8	0.011
Smoking status (current/previous), %	34.0	34.9	0.53
Medical history, %			
Congestive heart failure	17.5	25.5	<0.001
Hypercholesterolaemia	40.1	35.0	<0.001
Hypertension	77.1	78.1	0.39
Acute coronary syndromes	10.4	10.3	0.85
Coronary artery disease	18.8	20.4	0.16
Family history of premature cardiac disease	17.0	18.2	0.32
Diabetes mellitus	21.7	22.7	0.42
Stroke or TIA	11.5	13.1	0.082
Cirrhosis	0.4	0.9	0.046
Peripheral artery disease	7.0	6.6	0.61
Carotid occlusive disease	3.3	3.5	0.69
Systemic embolism	0.6	0.6	0.83
Bleeding	2.7	3.5	0.12
Heavy alcohol consumption	2.1	2.8	0.11
PE or DVT	2.6	3.0	0.40
Renal dysfunction (GFR <60 mL/min)	11.4	12.6	0.25
Type of AF, %			<0.001
New	41.4	47.1	
Paroxysmal	34.2	17.4	
Persistent	16.1	17.7	
Permanent	8.4	17.8	
Risk scores†, mean±SD			
$CHADS_2$	1.7±1.1	2.0±1.1	<0.001
CHA_2DS_2-VASc	3.0±1.6	3.3±1.6	<0.001
HAS-BLED‡	1.3±0.9	1.5±0.9	<0.001

BMI, body mass index; DVT, deep vein thrombosis; GFR, glomerular filtration rate; IQR, interquartile range; PE, pulmonary embolism; SD, standard deviation; TIA, transient ischaemic attack.
*Analysis of variance or chi-squared test as appropriate.
†Calculated retrospectively.
‡Based on 1408 rhythm and 1789 rate patients; excluding international normalized ratio.

- The rate of all-cause death was lower in the rhythm control group; while rates of stroke/SE and major bleeds were similar (Figure 2). After adjustment, rhythm control was associated with a statistically significantly lower risk of death.

FIGURE 1 Antithrombotic treatment initiated at AF diagnosis: rhythm versus rate control. P<0.001 by chi-squared test.



AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist. *Includes patients who received a heparin, heparinoid or other anticoagulant.
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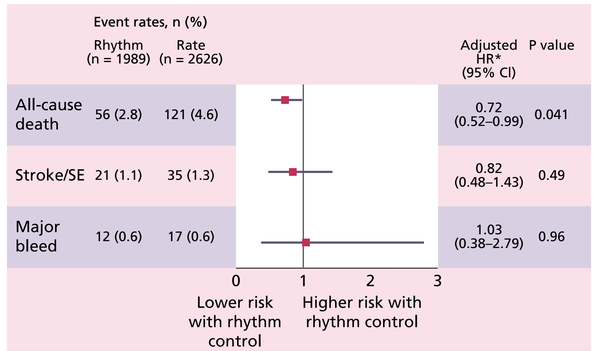
FIGURE 2 Outcomes at 1 year after AF diagnosis in patients on rhythm versus rate control.



CI, confidence interval; HR, hazard ratio; SE, systemic embolism.
*Estimated from Cox proportional hazards model with appropriate adjustment.

CONCLUSIONS

- In this multinational observational study, patients with newly diagnosed non-valvular AF and ≥1 stroke risk factor who were treated with rhythm control were younger and had lower risk scores than those treated with rate control.
- After adjustment, rhythm control was associated with a reduced risk of death compared with rate control. The two groups differed in many respects, however, and we may not have been able to adjust for residual confounding. These results must therefore be interpreted with caution.

DECLARATION OF INTEREST

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