An International Observational Prospective Survey Assessing the Control of Atrial Fibrillation in Asia-Pacific: Results of the Record-AFAP Registry

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ABSTRACT: A prospective 1-year observational survey was designed to assess the management and control of atrial fibrillation (AF) in eight countries within the Asia-Pacific region. Patients ($N = 2,604$) with recently diagnosed AF or a history of AF ≤1 year were included. Clinicians chose the treatment strategy (rhythm or rate control) according to their standard practice and medical discretion. The primary endpoint was therapeutic success. At baseline, rhythm- and rate-control strategies were applied to 35.7% and 64.3% of patients, respectively. At 12 months, therapeutic success was 43.2% overall. Being assigned to rhythm-control strategy at baseline was associated with a higher therapeutic success (46.5% vs 41.4%; $P = 0.0214$) and a lower incidence of clinical outcomes (10.4% vs 17.1% $P < 0.0001$). Patients assigned to rate-control strategies at baseline had higher cardiovascular morbidities (history of heart failure or valvular heart disease). Cardiovascular outcomes may be less dependent on the choice of treatment strategy than cardiovascular comorbidities.

KEYWORDS: atrial fibrillation, sinus arrhythmia, rate control, rhythm control, cardiac glycosides, Record-AFAP

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia; it is progressive, often worsening over time, and its prevalence increases with age.[1] Prevalence in Asians is lower than in Caucasians, but due to the large aged population in Asia, its overall disease burden remains high.[2] Disease profiles and CHADS2 index (congestive heart failure, hypertension, age = 75 years, diabetes mellitus, stroke) distributions in patients with AF are similar in both Asian and Western populations, although there is a higher prevalence of valvular heart diseases among Asians.[3]

Management of AF involves two key objectives: prevention of thromboembolic stroke, and symptom management. In addition to anticoagulant therapy, initial symptom management involves either the control of ventricular response (rate control) or restoration and maintenance of sinus rhythm (rhythm control).[4] Rhythm control aims to revert AF to normal sinus rhythm using electrical direct-current defibrillation, anti-arrhythmic drugs, or a combination of both, while rate control focuses on controlling the ventricular rate while leaving the heart in AF rhythm by using rate-slowing medication.

Randomized comparative trials have demonstrated equal efficacy of rate- and rhythm-control strategies,[5–10] suggesting that there is no advantage of rhythm control over rate control with respect to major cardiovascular (CV) outcomes. In randomized controlled trials, however, clinicians are confined by the parameters set out in the protocol: during the course of the study, they have no scope to amend their treatment approach as they would in a real-world setting. By contrast, registry studies describe what happens in real-world practice, with clinicians treating patients according to their individual characteristics.

The REgistry on Cardiac rhythm disORDers (Record-AF) was the first worldwide prospective observational study designed to trace the influence of clinicians' choices of rate- versus rhythm-control strategy for consecutive patients with first onset or recent recurrent AF.[11] Results based on data from 5,171 patients recruited between May 2007 and April 2008 showed the rhythm-control strategy to be associated

with superior therapeutic success and less rapid progression to permanent AF.[12] In Record-AF, the Asia-Pacific region contributed minimal (12.3%) patient data. Therefore a separate study, Record-AF Asia-Pacific (Record-AFAP), was conducted in eight countries across this region from April 2009 to July 2010.[13]

Methods

Record-AFAP was a prospective observational survey of the management of recently diagnosed AF patients. Its primary objective was to prospectively assess the real-world management of AF over a 12-month period in patients attending general or specialist practices and to compare clinical outcomes in patients treated with rhythm versus rate control. Full details of the study methodology have been published previously.[13] The study was approved by the relevant ethics committee in each of the institutions that recruited participants into the registry and was performed in accordance with the Declaration of Helsinki.

Participating clinicians were randomly selected to provide a representative sample based upon the expertise and healthcare structure of each participating country. Consecutive patients (aged ≥18 years) presenting with newly diagnosed AF or a history of AF ≤1 year (treated or not; in sinus rhythm or AF at inclusion) eligible for pharmacological treatment of AF by rhythm- or rate-control agents were included in the study after providing informed consent. Data were collected at baseline (visit 1) and during routine follow-up visits at 6 months (visit 2) and 12 months (visit 3). During the 12 months from recruitment to the end of study (visit 3), treatment including the choice of medication, dosage, and titration was documented by the clinicians according to their standard practice and medical discretion, without randomization.

The co-primary endpoints at 12 months' follow-up were the rate of therapeutic success and the incidence of clinical outcomes in rhythm- versus rate-control strategies. Therapeutic success was a composite endpoint where the patients were required to meet all of the following three criteria: 1) patients assigned to rhythm-control strategy at inclusion visit and observed with an ECG status of sinus rhythm, or patients assigned to rate-control strategy at inclusion visit with an observed resting heart rate of ≤80 beats/minute (bpm) at 12-month follow-up visit; 2) no clinical outcomes during the follow-up period (CV death, hospitalization for transient ischemic attack, myocardial infarction, hospitalization or prolongation of hospitalization for arrhythmic or pro-arrhythmic events, other CV events or major complications of ablative procedure); and (3) no crossover between rhythm-control or rate-control treatment strategies during the study. Patients for whom insufficient data were available to determine therapeutic success [missing rhythm status assessment at 12 months, rhythm assessment conducted outside of study visit window (12 ± 3 months), or withdrew prematurely from the study] were excluded from the efficacy analyses.

Secondary endpoints included the determination of the therapeutic success rate for each AF pharmacological drug class, which was analyzed using the methodology as for therapeutic success. Health status, resource utilization, and information on suspected adverse reactions to AF treatments were also analyzed. Health-related quality of life was assessed at baseline and 12 months using the self-administered EQ-5D questionnaire.[14]

Five regions of interest were selected for the study: Australia, China, Korea, Taiwan, Thailand, and a group of other Asian countries (Malaysia, Hong Kong, and Philippines). Data from 384 evaluable patients in each geographic unit of interest were required to estimate a therapeutic success rate of 50% at 1 year with a significance of 0.05% and 95% confidence intervals (CI). With an expected loss to follow-up rate of 25%, a total of 2,560 enrolled patients and 1,920 evaluable patients were needed.

Only patients with baseline and post-baseline assessment were included in the statistical analyses. Descriptive data were summarized using mean and standard deviation, and categorical data as number counts and percentages. Univariate between-group comparisons were undertaken using a Chi-squared test. Adjusted odds ratios (ORs) were computed using a logistic regression model adjusting for a number of covariates (sex, age group, prior duration of AF, and CV risk factors) and presented with their associated 95% CI. Significant covariates (defined as those with a *P*-value ≤0.2) were retained in the regression model by adopting a backwards selection process.

Results

The study was conducted in multiple hospital sites in eight countries across Asia-Pacific (Australia, 21 sites; China, 17 sites; Hong Kong, 4 sites; Korea, 26 sites; Malaysia, 9 sites; Philippines, 2 sites; Taiwan, 19 sites; and Thailand, 27 sites).

Baseline patient characteristics and patient management have been described elsewhere,[15] and are summarized in Table 1. At baseline, rate control was the preferred strategy (64.3%, 1,675/2,604). There was regional variation in AF management strategy, with more patients assigned to rhythm-control strategies in Korea and Taiwan. The majority of patients had at least one CV risk factor or comorbidity; however, with the exception of heart failure and valvular heart disease, this did not influence the choice of treatment. Rhythm-control strategies were more likely to be used in younger patients, recently diagnosed AF, or paroxysmal AF, than rate-control strategies. Patients allocated to rate control more often had persistent AF, tended to be in AF at baseline, and were more likely to have an existing CV risk factor or comorbidity. Among the comorbidities, valvular heart disease, heart failure, stroke, and myocardial infarction were significantly more prevalent in patients in the rate-control group. Those allocated to rhythm control tended to be more symptomatic than those who received rate control. Pharmacological conversion and electrical cardioversion had been

Table 1. Baseline patient characteristics and cardiovascular risk factors (intent to treat population).

VARIABLE	RHYTHM-CONTROL STRATEGY (*n* = 929)	RATE-CONTROL STRATEGY (*n* = 1,675)	TOTAL (n = 2,604)	*P* VALUE*
Age (years)	63.3 ± 13.1	64.9 ± 13.2	64.4 ± 13.2	
Sex; male	582 (62.6)	990 (59.1)	1,572 (60.4)	
Ethnicity				
Chinese	406 (43.7)	546 (32.6)	952 (36.6)	<0.05
Korean	244 (26.3)	209 (12.5)	453 (17.4)	<0.05
Caucasian	157 (16.9)	270 (16.1)	427 (16.4)	
Thai	42 (4.5)*	468 (27.9)	510 (19.6)	<0.05
Other	80 (8.6)	182 (10.9)	262 (10.1)	
Body mass index (kg/m^2)	(n = 906) 25.6 ± 4.2	(n = 1,636) 25.3 ± 5.1	(n = 2,542) 25.4 ± 4.8	
Waist circumference (cm)	(n = 864) 89.8 ± 11.5	(n = 1,589) 89.3 ± 13.3	(n = 2,543) 89.5 ± 12.7	
History of:				
Hypertension	527 (56.7)	989 (59.0)	1,516 (58.2)	
Dyslipidaemia	319 (34.3)	635 (37.9)	954 (36.6)	
Valvular heart disease	147 (15.8)	444 (26.5)	591 (22.7)	<0.0001
Coronary artery disease	192 (20.7)	312 (18.6)	504 (19.4)	
Heart failure	133 (14.3)	521 (31.1)	654 (25.1)	<0.0001
Diabetes	150 (16.1)	309 (18.4)	459 (17.6)	
Stroke	64 (6.9)	158 (9.4)	222 (8.5)	0.026
Myocardial infarction	46 (5.0)	118 (7.0)	164 (6.3)	0.035
Transient ischemic attack	25 (2.7)	67 (4.0)	92 (3.5)	
Symptomatic peripheral artery disease	16 (1.7)	36 (2.1)	52 (2.0)	
Carotid stenosis	15 (1.6)	19 (1.1)	34 (1.3)	
Atrial fibrillation on baseline ECG	304 (32.7)	1053 (62.9)	1357 (52.1)	<0.0001
First atrial fibrillation diagnosis	170 (18.3)	369 (22.0)	539 (20.7)	
Diagnosis in previous year	759 (81.7)	1306 (78.0)	2065 (79.3)	
Paroxysmal atrial fibrillation	614 (66.1)	571 (34.1)	1185 (45.5)	<0.0001
Persistent atrial fibrillation	145 (15.6)	735 (43.9)	880 (33.8)	<0.0001
Symptomatic atrial fibrillation	320 (34.4)	469 (28.0)	789 (30.3)	

Notes: Data are presented as mean ± SD or n (%). *Chi-squared test.
Abbreviation: ECG, electocardiography.

performed more frequently in the year prior to enrollment in those patients assigned to rhythm-control strategies.

Primary efficacy analysis. Efficacy analyses were carried out on the full analysis dataset, which comprised the intention to treat (ITT) population ($N = 2,604$) minus patients where the 12-month follow-up data was not available ($n = 19$) and patients who were assessed outside the visit window (12 ± 3 months) or withdrew prematurely from the study ($n = 174$). At 12 months, 2,271 patients were assessable, the majority of whom had been assigned to a rate-control strategy (64.3% vs 35.7%). The composite endpoint of therapeutic success, as defined in Methods, was achieved by 981 (43.2%) patients overall and by a significantly higher proportion of patients assigned to rhythm-control strategy than to rate-control strategy (Fig. 1). The unadjusted odds of achieving therapeutic success were higher in the rhythm-control group than in the rate-control group (OR: 1.23, 95% CI: 1.03–1.46, $P = 0.022$). Multivariate logistic regression analyses with backward selection procedure was performed using the CV risk factors of family history of premature CV disease, history of arterial hypertension, dyslipidemia, heart failure, peripheral arterial disease with ischemic symptoms, stroke, transient ischemic attack, and duration (months) since first diagnosis of AF. The OR of therapeutic success increased to 1.24 (95% CI: 1.03–1.51, $P = 0.026$) after adjusting for these risk factors. The incidence of clinical outcome events was lowest in the rhythm-control group (10.4% vs 17.1%, $P < 0.0001$). The odds of having a clinical outcome event were lower in the rhythm-control group than in the rate-control group (unadjusted OR: 0.56, 95% CI: 0.43–0.75, $P < 0.0001$; adjusted OR: 0.68, 95% CI: 0.50–0.94, $P = 0.018$).

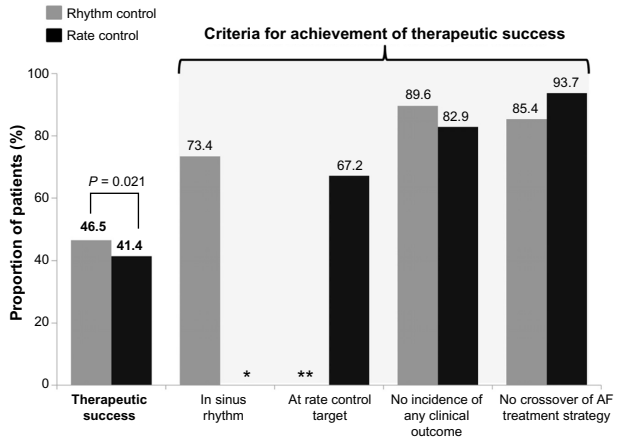

Figure 1. Therapeutic success at 12-month follow up.
Notes: *34.9% of patients in the rate-control group were in sinus rhythm after 1 year. **79.7% of patients in the rhythm control group were at rate control target after 1 year.

Logistic regression modeling was used to determine the predictive probability of CV risk factors on the occurrence of clinical events. AF control significantly reduced the risk of CV death (OR: 0.11, 95% CI: 0.02–0.85, $P = 0.035$) and the rate of hospitalization (OR: 0.59, 95% CI: 0.36–0.97, $P = 0.034$). The presence of arterial hypertension (OR: 4.33, 95% CI: 1.25–15.02, $P = 0.021$) and heart failure (OR: 3.07, 95% CI: 1.32–7.15, $P = 0.009$) both significantly increased the risk of CV death. The presence of stroke or myocardial infarction and previous myocardial infarction or previous heart failure all significantly increased hospitalization risk ($P < 0.05$).

Secondary efficacy analysis. Analysis of success rate by pharmacological drug class showed that all drug classes (65.7% vs 57.5%, $P < 0.001$) and heart-rate-lowering calcium channel blockers (66.3% vs 50.7%, $P = 0.02$) had a significantly higher success rate in patients assigned to rhythm control compared to those assigned to rate control. The converse was found for cardiac glycosides, with a significantly higher success rate in those assigned a rate-control strategy (54.0% vs 34.2%, $P = 0.001$). In all other drug classes, the success rate did not differ significantly between the two treatment strategies. Analyses of ORs yielded similar inferences.

Atrial fibrillation status at follow-up. At 12-month follow-up, data on rhythm status was available in 79.2% (1,814/2,290) patients (Table 2). Among the patients selected for the rate-control strategy, 65.1% were documented to be in AF (vs 69.3% at baseline). No patients had permanent AF at study inclusion, but this had occurred in 24.9% (452/1,814) of patients by the time of the 1-year follow-up.

Treatment strategies and adverse events. Approximately one-third of patients (rhythm control 338/839, 40.3%; rate control 532/1,565, 34.0%) had any modification to their AF treatment after inclusion in the study. Almost all of these patients (rhythm control 90.2%, rate control 91.5%) had a pharmacological modification, and of these, 77 (9.7%) received a pharmacological conversion. Electrical cardioversion occurred in 92 (11.6%) of patients, 7.7% underwent catheter ablation, 3.8% had a pacemaker inserted, and 1.5% underwent surgical therapy for AF. The mean time to initial electrical cardioversion was 85 days for the rhythm-control group and 91 days for the rate-control group.

The majority of patients [rhythm control 764 (82.2%), rate control 1464 (87.4%)] were receiving treatment for thromboembolic prevention at baseline. Most were prescribed aspirin [498, (65.2%) in the rhythm-control group and 819 (55.9%) in the rate-control group] or warfarin [271 (35.3%) in the rhythm control group and 685 (46.8%) in the rate control group]. A small proportion of patients were receiving a range of other antiplatelet agents, which included clopidogrel ($n = 198$) and enoxaparin ($n = 38$). The rate-control group had higher proportion of patients with CHADS2 score ≥2. Anticoagulant or antiplatelet medications differed significantly between rhythm- and rate-control strategies in the CHADS2 ≤1 subgroup, while in the CHADS2 >1 subgroup the difference between in two treatment strategies was not statistically significant. The mean time to permanent discontinuation of warfarin treatment was 130 days (range 5–340, median 120) and 156 days (range 1–453, median 146) in the rhythm- and rate-control group, respectively. Physician decision was the major reason for permanently stopping treatment. Warfarin

Table 2. AF status at 12-month follow-up.

	RHYTHM-CONTROL STRATEGY ($n = 618$)	RATE-CONTROL STRATEGY ($n = 1,196$)	TOTAL ($n = 1,814$)
Sinus rhythm	452 (73.1)	417 (34.9)	860 (47.4)
AF	166 (26.9)	779 (65.1)	945 (52.1)
Paroxysmal AF	479 (77.5)	445 (37.2)	924 (50.9)
Persistent AF	86 (13.9)	352 (29.4)	438 (24.1)
Permanent AF	53 (8.6)	399 (33.4)	452 (24.9)
Symptoms at the time of visit*	237 (38.3)	377 (31.5)	614 (33.8)

Notes: Values, *N* (%). *At the time of the baseline visit, 30.3% of patients were symptomatic (34.3% in the rhythm-control and 28.0% in the rate-control group).
Abbreviation: AF, atrial fibrillation.

was temporarily discontinued or reversed in 178 patients due to bleeding, physician decision, patient decision, or planned/unplanned surgery and procedures.

Based on patient reported outcomes (EQ-5D questionnaire), both treatment groups had a high proportion of patients with "no problems" at baseline and 12 months, and there were no significant changes from baseline in either group. Analyses of health economic outcomes revealed no significant differences between treatment groups in work absenteeism, unscheduled cardiologist visits, or hospitalizations (for either CV or non-CV related events).

After 1 year, the majority (90.8%) of patients maintained the initial treatment strategy to which they had been assigned at baseline. At the end of 1 year, 88.2% of patients were receiving antithrombotic medication (up from 85.0% at baseline). Overall, 28.9% of patients reported experiencing at least one treatment-related adverse event during the 12-month follow-up period, most commonly general side effects (15.3%) and cardiac side effects (9.4%), predominantly palpitations (Table 3).

Discussion

The Record-AFAP study has followed the treatment of AF in more than 2,000 patients from eight countries across the Asia-Pacific region. It has found that, in general, clinicians in this region prefer rate-control strategies. There were some significant regional differences. The preference for rhythm-control strategies in the Taiwanese and Korean centers is most likely to have been influenced by the fact that the majority of investigators in these countries were electrophysiologists; there is no clear reason as to why Thai cardiologists had a preference for rate-control strategies. The preference for a rate-control strategy was mostly in patients who had persistent AF who had little in the way of symptoms. Comorbidities did not appear to strongly influence the choice of treatment strategy, and more patients in the rhythm-control group had undergone prior pharmacological conversion.

Our primary endpoint, therapeutic success at 1 year, was achieved in 43.2% of patients. Although the rate of success was significantly higher in those patients initially assigned to a rhythm-control strategy, around one-third of patients had changed their pharmacological AF treatment since baseline. Failure to achieve an observed resting heart rate of ≤80 bpm in those patients assigned to rate-control strategy appears to be the driving force behind the higher therapeutic success rate in the rhythm-control group, but a resting heart rate of <80 bpm may have been an overly conservative estimate of therapeutic success. This cut-off of ≤80 bpm was chosen as the protocol definition of adequate rate control in the global AF study[12]; and it was selected based on data available at the time the original protocol was developed, which was primarily a comparison of data from the AFFIRM study (which used a cut-off of ≤80 bpm) and RACE trials (which used a cut-off of ≤100 bpm), which showed no difference in outcomes. While subsequent data have indicated that a higher rate might have been more appropriate, this was not published until after the protocol had been established and data collection had begun. Post hoc analyses at different resting heart rate cut-off points have not been undertaken, limiting the interpretation of our results.

We found a significantly higher incidence of clinical outcome events in the rate-control group (17.1% vs 10.4%). The rate-control patients had a higher burden of CV morbidities than the rhythm-control patients, but logistic regression modeling did not reveal strong predictive CV risk factors by the treatment group, suggesting that comorbidities (hypertension, heart failure) may have more of an impact on CV outcomes than does the choice of treatment strategy. Additionally, although baseline AF status was not used as a factor in the logistic regression models, the data suggest that it may have been a significant confounder in our dataset.

No patients were in permanent AF at baseline. Almost one-quarter of patients had progressed to permanent AF during the 12-month follow-up period of our study. Permanent AF was reported predominantly in those patients assigned to a

Table 3. Adverse events related to AF treatment since baseline.

	RHYTHM-CONTROL STRATEGY (*n* = 839)	RATE-CONTROL STRATEGY (*n* = 1,565)	TOTAL (*n* = 2,404)
Any adverse event	264 (31.5)	431 (27.5)	695 (28.9)
Gastrointestinal intolerance	56 (6.7)	73 (4.7)	129 (5.4)
Cardiac side effects	86 (10.3)	139 (8.9)	225 (9.4)
Palpitation	*65 (7.7)*	*82 (5.2)*	*147 (6.1)*
ECG modification	49 (5.8)	51 (3.3)	100 (4.2)
Sinus bradycardia	*39 (4.6)*	*31 (2.0)*	*70 (2.9)*
Organ toxicities	33 (3.9)	26 (1.7)	59 (2.5)
General side effects	123 (14.7)	244 (15.6)	367 (15.3)
Bleeding related to OAC	24 (2.9)	74 (4.7)	98 (4.1)

Note: All values, *n*/*N* (%).
Abbreviations: ECG, electocardiography; OAC, oral anticoagulant.

rate-control strategy (33.4% vs 8.6%; rhythm-control strategy) and a higher proportion of patients in this group were in AF at the end of the follow-up period (65.1% vs 26.9%; rhythm-control strategy). These results appear to suggest that use of a rate-control strategy may be associated with an increased likelihood of progression to permanent AF.

The present analysis is limited to the pooled results from all eight participating countries in the Record-AFAP registry. A more in-depth review of individual country data may yield further insights into inter-country variations in the management of AF; this will be possible only if the country-specific sample sizes are of sufficient power to enable meaningful statistical analyses. Various aspects of the design of this observational registry limit its ability to derive firm conclusions regarding differences in event rates between the rhythm- and rate-control strategies, and the results can be considered to be only hypothesis-generating. These limitations include the lack of randomization, the differences in the therapeutic success criteria for each treatment strategy, and the arbitrary nature of including AF control as a key component of the therapeutic success. Our study follow-up was limited to only 12 months and therefore does not account for potential differences between strategies in the long term.

Our study was a separate stand-alone study using the same methodology as the global RECORD AF trial.[12] Although it is not a subanalysis of data from the global RECORD AF trial, nor is the study designed to enable statistical comparison with the global Record-AF dataset, observational differences in strategy allocation and therapeutic success rates are noteworthy. In the global RECORD AF trial, rhythm- and rate-control strategies were applied to 54.9% and 45.1% of patients, respectively, at study inclusion.[12] Differences by ethnicity were observed – among Asian patients allocation to rate-control strategy (14.4%) was higher than rhythm-control strategy (5.8%) – but no explanations were given. In our study, allocation to rate-control strategy (63.5%) was again higher than rhythm-control strategy (36.5%). While the choice of individual physician's treatment strategy is influenced by a number of factors, one explanation could be the smaller proportion of symptomatic patients at baseline: 30.3% in our study versus 80.7% in the global dataset.

In both studies, the composite endpoint of therapeutic success was met more frequently in those patients assigned to a rhythm-control strategy. Post hoc analyses of the global data have shown that, once the cut-off value for resting heart rate was relaxed (≥90 bpm), this difference was neutralized.[12] Overall, therapeutic success rates were lower in our study (43.2%) than in the global Record-AF study (54.1%); the difference was largely driven by the lower proportion of patients who had achieved AF control (in sinus rhythm in rhythm-control strategy or resting heart rate of ≤80 bpm in rate-control strategy) in our study. Specific factors contributing to this difference are not clear. The only notable difference in treatments prescribed is that the use of beta-blockers in patients assigned a rhythm-control strategy is lower in our dataset (34.5%) than in the global dataset (51.2%). In our study, as in the global study, history of heart failure was the predominant factor influencing adverse clinical outcomes.

Rate and rhythm control are both acceptable strategies for AF management, as there is no long-term advantage in restoration of sinus rhythm compared with rate control. Choice of therapy should be guided by safety and efficacy with regard to CV outcomes[3] and tailored to account for individual patient characteristics (eg, age, AF type, and CV comorbidities). However, symptomatic status should be the major consideration as to whether to adopt a rate or rhythm approach.[16,17] Clinicians should ideally assess the benefits of maintaining sinus rhythm and whether it should be sought in minimally symptomatic AF patients. Available evidence suggests that rate control may be an appropriate strategy in older patients with minor symptoms, while rhythm-control may be used in patients who are symptomatic despite adequate rate control.[18]

Based on the available data at the time, 80 bpm was chosen as the definition of adequate rate control in our study protocol, and this was chosen to allow comparison with the global RECORD AF study. The results of the RACE (Rate Control Efficacy in Permanent Atrial Fibrillation) II trial, which showed lenient (<110 bpm) control to be noninferior to strict (<80 bpm) control,[19] have resulted in the suggestion that lenient rate control may be a reasonable strategy in patients with permanent AF and stable ventricular function.[20] Almost one-third of patients randomized to the strict control group in the RACE II study failed to reach their predefined target heart rate, casting doubt as to the clinical meaningfulness of the results. An exploratory analysis of the RACE II data using a composite CV morbidity and mortality outcome has shown that those patients who achieved strict heart rate control did not do better than those who failed to reach their target.[21] Mean heart rates in the lenient group were 93 ± 8 bpm after the dose adjustment phase and 85 ± 13 bpm at the end of the follow-up period. The corresponding values in the successful strict control group were 72 ± 7 and 75 ± 14 bpm, respectively. Questions still remain as to whether outcomes might have been worse had those patients in the lenient group had a resting heart rate of 110 bpm. Although a more lenient strategy may be adequate in some patients, stricter rate control remains appropriate in patients who are symptomatic. Catheter ablation or atrioventricular (AV) node ablation and pacemaker should be reserved for patients who remain symptomatic despite optimal medical therapy.[3]

Conclusion

Our study provides real-world insight into the management of AF. After 12 months' follow-up of newly diagnosed AF patients across eight countries in the Asia-Pacific region, there were significant differences in the assigned strategies at baseline (preference for rate-control), therapeutic success rates (higher with rhythm-control strategies), and incidence of

clinical cardiovascular outcomes (lower with rhythm-control strategies). The majority of patients received antithrombotic medication. There were no differences in patient-reported outcomes or economic analyses. Despite a preference for rate-control strategies, in our study AF appeared to be better controlled with rhythm-control strategies. However, due to the short (12 months) duration of our follow-up, longer term outcomes remain unknown. Rate-control patients had a higher burden of CV comorbidities (history of heart failure or valvular heart disease) than the rhythm group; CV comorbidities and baseline AF status may be more important predictors of CV outcomes than the choice of treatment strategy.

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Author Contributions

The authors of this manuscript form the basis of a National Co-Ordinating Committee set up to provide input into the protocol, to liaise with local ethics committees and to provide a focal point of expertise within each participating country. Conceived and designed experiments: JA, JGC, SAC, THF, RO, AK, CS, HD. Analysis and interpretation of data: JA, JGC, SAC, THF, RO, AK, CS, HD. Initial drafting of the manuscript: JA. Critical revision of the manuscript for important intellectual content: JGC, SAC, THF, RO, AK, CS, HD. All authors reviewed and approved of the final manuscript.

REFERENCES

1. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. *Arch Intern Med*. 1995;155(5):469–73.
2. Tse HF, Wang YJ, Ahmed Ai-Abdullah M, et al. Stroke prevention in atrial fibrillation – an Asian stroke perspective. *Heart Rhythm*. 2013;10(7):1082–8.
3. Chiang CE, Zhang S, Tse HF, Teo WS, Omar R, Sriratanasathavorn C. Atrial fibrillation management in Asia: from the Asian expert forum on atrial fibrillation. *Int J Cardiol*. 2013;164(1):21–32.
4. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: full text: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 guidelines for the management of patients with atrial fibrillation) developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Europace*. 2006;8(9):651–745.
5. Wyse DG, Waldo AL, DiMarco JP, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med*. 2002;347(23):1825–33.
6. Roy D, Talajic M, Nattel S, et al; Atrial Fibrillation and Congestive Heart Failure Investigators. Rhythm control versus rate control for atrial fibrillation and heart failure. *N Engl J Med*. 2008;358(25):2667–77.
7. Van Gelder IC, Hagens VE, Bosker HA, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med*. 2002;347(23):1834–40.
8. Carlsson J, Miketic S, Windeler J, et al; STAF Investigators. Randomized trial of rate-control versus rhythm-control in persistent atrial fibrillation: the Strategies of Treatment of Atrial Fibrillation (STAF) study. *J Am Coll Cardiol*. 2003;41(10):1690–6.
9. de Denus S, Sanoski CA, Carlsson J, Opolski G, Spinler SA. Rate vs rhythm control in patients with atrial fibrillation: a meta-analysis. *Arch Intern Med*. 2005;165(3):258–62.
10. Opolski G, Torbicki A, Kosior DA, et al; Investigators of the Polish How to Treat Chronic Atrial Fibrillation Study. Rate control vs rhythm control in patients with nonvalvular persistent atrial fibrillation: the results of the Polish How to Treat Chronic Atrial Fibrillation (HOT CAFE) Study. *Chest*. 2004;126(2):476–86.
11. Le Heuzey JY, Breithardt G, Camm J, et al. The RecordAF study: design, baseline data, and profile of patients according to chosen treatment strategy for atrial fibrillation. *Am J Cardiol*. 2010;105(5):687–93.
12. Camm AJ, Breithardt G, Crijns H, et al. Real-life observations of clinical outcomes with rhythm- and rate-control therapies for atrial fibrillation RECORDAF (Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation). *J Am Coll Cardiol*. 2011;58(5):493–501.
13. Amerena J, Chen SA, Sriratanasathavorn C, et al. An observational, prospective survey assessing the control of atrial fibrillation in Asia Pacific: rationale and design of the RecordAF-AP registry. *Clin Med Insights Cardiol*. 2011;5:1–6.
14. The EuroQol Group. *EQ-5D: A Standardised Instrument for Use as a Measure of Health Outcome*. 2010. Available at: www.euroqol.org/. Ref Type: Internet Communication.
15. Amerena J, Chen SA, Sriratanasathavorn C, et al. Insights into management of atrial fibrillation in Asia Pacific gained from baseline data from REgistry on cardiac rhythm disORDers (RecordAF-Asia Pacific [AP]) registry. *Am J Cardiol*. 2012;109(3):378–82.
16. Anderson JL, Halperin JL, Albert NM, et al. Management of patients with atrial fibrillation (compilation of 2006 ACCF/AHA/ESC and 2011 ACCF/AHA/HRS recommendations): a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;61(18):1935–44.
17. Frankel G, Kamrul R, Kosar L, Jensen B. Rate versus rhythm control in atrial fibrillation. *Can Fam Physician*. 2013;59(2):161–8.
18. Teme T, Goldberger J. Atrial fibrillation practice patterns among cardiac electrophysiologists and cardiologists. *Cardiol J*. 2013;21(3):293–8.
19. Van Gelder IC, Groenveld HF, Crijns HJ, et al. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med*. 2010;362(15):1363–73.
20. Wann LS, Curtis AB, Ellenbogen KA, Estes NA, et al. Management of patients with atrial fibrillation (compilation of 2006 ACCF/AHA/ESC and 2011 ACCF/AHA/HRS recommendations): a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;127(18):1916–26.
21. Groenveld HF, Crijns HJ, Tijssen JG, et al. Rate control in atrial fibrillation, insight into the RACE II study. *Neth Heart J*. 2013;21(4):199–204.