Treatment strategies and subsequent changes in the patient-reported quality-of-life among elderly patients with atrial fibrillation

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Abstract Background Rhythm-control strategy, including catheter ablation (CA) application, constitutes an integral part of atrial fibrillation (AF) management. However, elderly patients are underrepresented in clinical trials, and reports on patient-reported outcome of various rhythm-control treatments remain limited. Therefore, we aimed to investigate the application of a rhythm-control strategy for elderly patients with AF.

Methods Using a prospective, multicenter Japanese registry, we analyzed 733 patients with AF aged ≥70 years who completed the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) questionnaire at baseline and 1-year visit. Improvement in patient-reported quality-of-life (QOL) was assessed according to their initial treatment strategy.

Results A total of 321 patients (43.8%) were managed with rhythm-control strategy, of which 125 (17.1%) received treatment with antiarrhythmic drugs (AADs) alone and 196 (26.7%) underwent CA. Compared with the rate-control group, the rhythm-control group was younger and less likely to have comorbid conditions but had lower baseline AFEQT-overall summary (OS) scores (71.8 [standard deviation 20.3] vs. 80.0 [standard deviation 16.1]; $P < .001$). After the first year, AFEQT-OS scores improved regardless of treatment strategies (ie, rate- or rhythm-control). After adjusting for confounders, CA implementation and a lower baseline AFEQT score were associated with meaningful improvement in QOL (changes in AFEQT-OS score ≥5). QOL improvement among subgroups of rhythm-control patients with AADs alone was not clinically meaningful.

Conclusions In contemporary Japanese clinical practice, rhythm-control strategy is widely implemented in elderly patients with AF, and CA use is associated with improvement in QOL in carefully selected patients. (Am Heart J 2020;222:83-92.)

Atrial fibrillation (AF) can be a highly symptomatic condition that can lead to significant impairments in quality-of-life (QOL)[1,2] In recent years, a wide range of treatment options has become available to improve the QOL in patients with AF. However, limited information exists about the application of these treatments in elderly patients, partly due to exclusion of patients with older age and comorbidities from randomized clinical trials. For example, in the Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) trial, the median age of enrolled patients was 67 years (interquartile range [IQR] 62 to 72). Furthermore, prior studies on rhythm-control therapies in elderly patients consist of a narrow description of QOL, mainly due to the lack of validated AF-specific QOL assessments.[3,4]

Given the increased incidence of AF in an aging society, investigating QOL following treatment in elderly patients is necessary. AF prevalence is expected to significantly increase in the coming years. Current census projections for 2050 suggest that the number of Americans, Europeans, and Japanese with AF will increase by 2-fold to 3-fold.[1] To appropriately identify candidate patients for rhythm-control strategy, a comprehensive and subjective approach to determine the patient's QOL is needed, particularly for patients who are underrepresented in trials (eg, elderly and/or non-Whites).

As AF incidence and its arsenal of treatments continue to expand, the comprehensive nature of clinical

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Submitted August 28, 2019; accepted January 15, 2020.

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0002-8703

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https://doi.org/10.1016/j.ahj.2020.01.011

registries can provide important insights into the clinical management of AF. The multicenter Keio Interhospital Cardiovascular Studies-Atrial Fibrillation (KiCS-AF) registry prospectively collects information about the treatment and health status of patients with newly diagnosed AF in Japan. It also provides a unique opportunity to examine the lack of information in this area. We aimed to investigate the real-world application of rhythm-control strategy among elderly patients with AF and quantitatively assessed the degree of improvement in patient-reported QOL according to their initial treatment strategy.

Materials and methods

Data sources

We extracted patient-based data from the KiCS-AF registry between September 2012 and December 2017. The KiCS-AF is a multicenter registry-based retrospective cohort study designed to collect clinical variables and outcome data from consecutive patients with AF who were newly diagnosed at or were referred to an outpatient clinic at each of the 11 participating hospitals within the Tokyo Metropolitan Area of Japan (Saitama, Tochigi, Chiba, Kanagawa, and Tokyo Prefecture). Dedicated clinical research coordinators are assigned to each hospital, and data on approximately 150 variables are collected for each patient. The KiCS-AF registry ensures data traceability by tracking the staff who approved the data and data-entry personnel at the participating institutions. It also validates data consistency via inspections of the participating institutions. Additionally, the database administrators provide on- and off-site training systems to guide the clinical research coordinators on how to input data consistently.

Details of the design of this registry have been described previously.[5,6] In brief, data on patient backgrounds, symptoms, prior and current drug use (including oral anticoagulants), electrocardiography and echocardiography results, and blood sampling test results were collected from the medical records. To recruit treatment-naive patients, only patients with a diagnosis of AF within 6 months prior to the initial visit were enrolled. We limited the enrollment of patients with AF to those who had a new diagnostic coding for AF within the previous 6 months. Yearly follow-up examinations were performed for all patients by mail, phone interviews, and chart reviews. Patients completed the Atrial Fibrillation Effect on Quality-of-Life (AFEQT; http://www.afeqt.org) questionnaire during clinic visits or by mail. Trained study personnel subsequently transcribed the completed AFEQT questionnaires and updated the status of comorbidities, medication use, catheter ablation (CA), and intercurrent adverse events (all-cause mortality, stroke, bleeding).

Information disclosure

The institutional review board at each hospital approved the study protocol, and all participants provided written informed consent. Almost all patients agreed to participate. For example, the refusal rate was 2.9% at the core center (Keio University Hospital). The KiCS-AF steering committee was responsible for overall study guidance, including the study protocol, data collection forms, data analysis, and interpretation of the results. Before launching the KiCS-AF registry, information about the objectives of the study and its social significance was provided for clinical trial registration with the University Hospital Medical Information Network (UMIN 000022229). This Network is recognized by the International Committee of Medical Journal Editors as an "acceptable registry" according to a statement issued in September 2004.

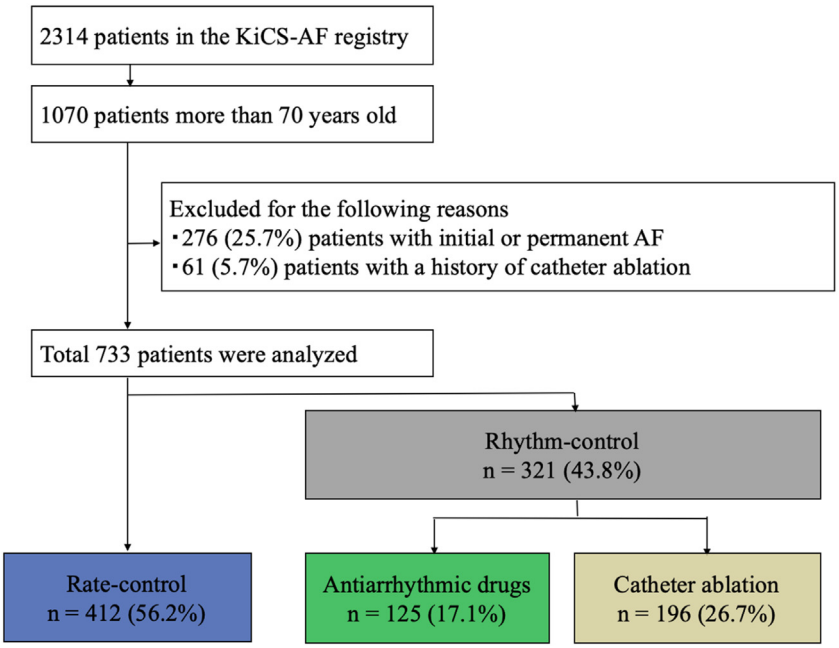
Study design

The KiCS-AF registry contained 2564 patients during the study period, and 1-year follow-up data were available for 2314 (90.2%) patients. We initially excluded 1244 patients who were< 70 years of age. Of the remaining 1070 patients, 276 (25.7%) with first detected or new-onset AF and permanent AF were excluded, because no treatment recommendations are available for first detected or new-onset AF, and rhythm-control interventions are not pursued in patients with permanent AF.[7] We also excluded 61 (5.7%) patients with a prior CA to avoid bias related to recurrence of symptoms associated with CA. Finally, 733 patients aged ≥70 years (11 hospitals) were included in this study (**Supplemental Figure 1**). These patients were divided into two groups according to the provided care within a 1-year study period: (1) rate-control group, comprising patients who had never been prescribed antiarrhythmic drugs [AADs] (AADs include procainamide, quinidine, cibenzoline, disopyramide, aprindine, mexiletine, pilsicainide, flecainide, propafenone, sotacor, amiodarone, and bepridil) and did not undergo CA, and (2) rhythm-control group, comprising patients who were prescribed AADs or underwent CA. Furthermore, the rhythm-control group was divided into two groups according to whether patients were treated with CA or were not treated with CA. The CA group comprised patients who underwent CA, and the AAD group comprised patients who were prescribed AADs and did not undergo CA within 1 year of registration (Figure 1).

Assessment of symptom burden and patient concern/satisfaction

Patients completed a detailed questionnaire about their perception of QOL and treatment at baseline and 1 year using the internationally validated AFEQT. The development and validation of AFEQT have been previously

Figure 1



Study flow chart KiCS-AF, Keio Interhospital Cardiovascular Studies-Atrial Fibrillation registry.

described.[8] The AFEQT is a 20-item questionnaire that quantifies 4 domains of AF-related QOL, including symptoms, daily activities, treatment concern, and treatment satisfaction by using a 7-point Likert response scale. An overall summary score can be calculated from the first three domains and ranges from 0 to 100 (100, best possible health status [no impairment]; 0, worst health status). Recent analysis has suggested that a 5-point change in the AFEQT Overall Summary (AFEQT-OS) score is observed among patients who change by 1 European Heart Rhythm Association (EHRA) functional status class, which is a clinically important difference.[9] A previous study compared the EHRA symptom classification in AF and AFEQT; it showed that the mean AFEQT-OS score in patients classified as EHRA class 1 (eg, no symptom) is 78.4 (standard deviation [SD] 19.0).[10] Thus, in the current study, we regarded patients with AFEQT-OS scores ≥80 as those with preserved QOL and patients with AFEQT-OS scores <80 as those with impaired QOL <80. A culturally and linguistically translated version of the AFEQT for Japan was used.

Statistical analysis

We compared baseline characteristics between each group, including patient demographics, symptoms, AF history, prior and current medical therapies, electrocardiograms, echocardiograms (left ventricular ejection fraction and left atrial diameter), and blood sampling test results. To examine how each strategy affected elderly patients' QOL, we compared AFEQT-OS score and its four individual domain scores at both baseline and 1-year follow-up within each group. To define patient and treatment factors associated with QOL more completely, we performed prespecified subgroup analyses based on baseline AFEQT-OS score (ie, 80 or more and lower than 80).

Continuous variables are presented as median and IQR, and categorical variables are expressed as numbers and percentages. Unless otherwise indicated, AFEQT, $CHADS_2$ (congestive heart failure or left ventricular dysfunction, hypertension, age ≥75 years, diabetes, and stroke), CHA_2DS_2-VASc (congestive heart failure or left ventricular dysfunction, hypertension, age ≥75 years, diabetes, stroke including vascular disease, age 65 to 74 years, and gender category [female]), and HAS-BLED (hypertension, renal impairment [estimated glomerular filtration rate (eGFR) <60 ml/min], liver impairment [aspartate aminotransferase, alanine aminotransferase more than 3-fold the upper limit], stroke history, prior major bleeding or predisposition to bleeding, labile international normalized ratio, elderly [>65 years], drugs/alcohol concomitantly) scores are reported as mean (SD). Group differences were evaluated using the Wilcoxon rank-sum test or Student's *t*-test for continuous variables and the chi-squared test for categorical variables. We defined change in AFEQT-OS score within 1

year as AFEQT-OS score at 1-year minus AFEQT-OS score at baseline. A positive change represents improved QOL, and a negative change implies worsening QOL. A series of paired *t* tests were conducted to compare the changes in AFEQT scores within each group.

To evaluate the association between each treatment strategy and change in QOL, changes in AFEQT-OS score within the 1-year study period were compared between each group by using analysis of covariance adjusted for baseline AFEQT-OS scores. In addition, a general linear mixed model was constructed to adjust AFEQT-OS scores for observed differences between each group, which included age (per 1-year increase), gender, body mass index (per 1-point increase), prior heart failure, hypertension, diabetes mellitus, stroke (cerebral infarction or transient ischemic attack), coronary artery disease, and type of AF. Furthermore, to explore the factors associated with meaningful improvement in QOL among elderly patients with AF, defined as a 5-point increase in the AFEQT-OS score, we constructed a logistic regression model. Our independent variable, patients with meaningful improvement in QOL or not, was entered as a categorical variable in the regression model. It was adjusted for clinically relevant variables: age (per 1-year increase), gender, prior heart failure, hypertension, diabetes mellitus, stroke, baseline AFEQT-OS score (per 10-point increase), use of oral anticoagulants, use of antiarrhythmic drugs, and treatment with CA within the 1-year study period. Odds ratios (ORs) are shown with 95% confidence intervals (CIs). In addition, participating hospitals were included based on a random effect to account for clustering of patients by site in these models.

There were missing data for less than 2% of all candidate variables. The complete case method was adopted to address the missing data in the statistical analysis. In addition, a sensitivity analysis was performed to exclude patients with preserved QOL at baseline (eg, patients with AFEQT-OS score ≥80), as these patients might be not eligible to experience improvement, making the interpretation of changes in AFEQT scores difficult. All *P*-values were 2 sided with a significance threshold of $P < .05$. Statistical analysis was performed using IBM SPSS Statistics 24.0 (IBM Corp, Armonk, NY).

Results

Baseline characteristics

Of the 733 elderly patients with AF extracted from the KiCS-AF registry, 321 (43.8%) patients were managed with rhythm-control strategy (Figure 1). Patient characteristics of each group are shown in Table I and Figure 2. Compared with the rhythm-control group, the rate-control group was older (78 [IQR 74-82] years vs. 74 [IQR 72-77.5] years; $P < .001$) and more often had high CHA_2DS_2-VASc score (3.73 [SD 1.42] vs. 3.12 [SD 1.50]; $P < .001$). Patients with paroxysmal AF were more likely to be managed with rhythm-control strategy (233 [56.6%] for the rate-control group vs. 230 [71.7%] for the rhythm-control group; $P < .001$). Among the patients in the rhythm-control group, 196 (26.7%) underwent CA within 1 year after their referral, and 125 (17.1%) were treated with AAD alone. The CA group was younger (73 [IQR 71-76] years vs. 76 [IQR 73-80] years; $P < .001$), more likely to be male (129 [65.8%] vs. 62 [49.6%]; $P = .004$), and had lower CHA_2DS_2-VASc scores (2.86 [SD 1.31] vs. 3.53 [SD 1.69]; $P = .001$) than the AAD group.

QOL in the rate- vs. rhythm-control group

The rhythm-control group had lower AFEQT-OS score at baseline compared with the rate-control group (71.8 [SD 20.3] vs. 80.0 [SD 16.1]; $P < .001$). The rhythm-control group also had significantly lower domain score at baseline, including symptoms, daily activities, treatment concerns, and treatment satisfaction (Table II; $P < .05$ for all group differences).

The mean changes in AFEQT-OS score from baseline to 1-year follow-up were 10.2 (SD 1.10) for the rhythm-control group and 2.56 (SD 0.71) for the rate-control group ($P < .001$ for both groups, but no significant changes in the AFEQT daily activities subscales in the rate-control group; Table II). In crude analysis, the changes in mean AFEQT-OS score among the rhythm-control group were significantly higher than those among the rate-control group ($P < .001$ for group differences). However, after adjusting for clinically relevant factors, the change in difference was not significant (5.05 [95% CI, 3.68-6.42] vs. 7.02 [95% CI, 5.45-8.60]; $P = .078$; Table III). Notably, in the subgroup analysis, patients with preserved QOL (ie, AFEQT-OS score ≥ 80 at baseline) showed no improvement in AFEQT-OS score in neither rate- nor rhythm-control strategy (**Supplemental Table I**).

QOL in the rhythm-control group: CA vs. AAD group

At baseline visit, no significant differences were found in AFEQT-OS score between the CA and AAD groups (72.7 [SD 20.6] for the CA group vs. 70.5 [SD 19.9] for the AAD group; $P = .25$). No significant differences were also found in scores of four individual domains (Table II; $P > .05$ for all groups). After 1 year, both CA and AAD groups showed improvement in AFEQT-OS scores (Table II), albeit the improvement in the AAD group did not reach the prespecified threshold of clinically meaningful improvement in QOL (ie, changes in AFEQT-OS score ≥ 5). The CA group showed quantitatively more improvement in AFEQT-OS score than did the AAD group ($P < .001$ for group differences). The trend persisted after adjusting for clinically relevant factors or excluding patients with preserved QOL at baseline (3.88 [95% CI 1.21-6.55] vs. 14.2 [95% CI 12.1-16.3]; $P < .001$; Table III).

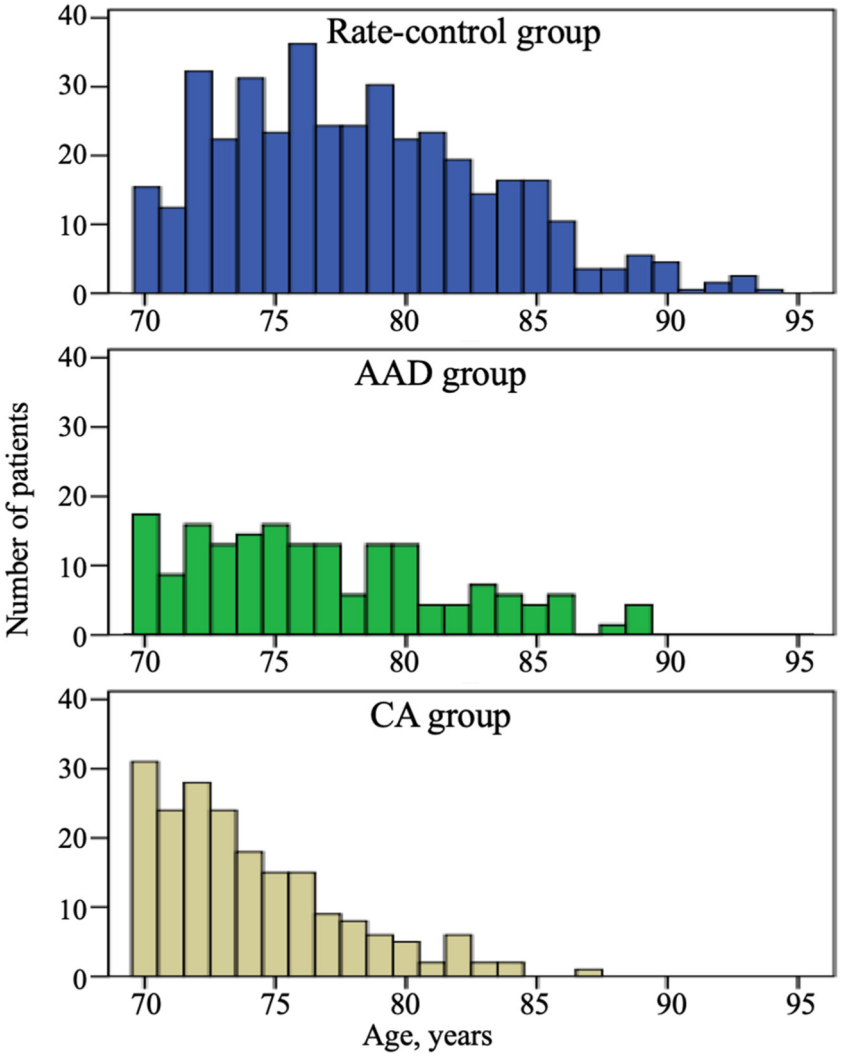
Table I. Baseline characteristics stratified by treatment strategy.

	Rate-control group (n = 412)	Rhythm-control group (n = 321)	*P*	Rhythm-control group		*P*
				AAD group (n = 125)	CA group (n = 196)	
Age, median (IQR), y	78 (74-82)	74 (72-77.5)	**<.001**	76 (73-80)	73 (71-76)	**<.001**
Male, %	225 (54.6)	191 (59.5)	**.18**	62 (49.6)	129 (65.8)	**.004**
BMI, median, kg/m2 (IQR)	22.8 (21.0-25.0)	22.7 (20.7-24.9)	**.47**	22.9 (20.9-24.9)	22.5 (20.6-24.9)	**.79**
Medical history						
Smoking	41 (10.0)	27 (8.4)	**.46**	11 (8.8)	16 (8.2)	**.84**
Hypertension	283 (68.7)	204 (63.6)	**.14**	82 (65.6)	122 (62.2)	**.54**
Diabetes mellitus	88 (21.4)	45 (14.0)	**.010**	21 (16.8)	24 (12.2)	**.25**
Dyslipidemia	160 (38.8)	124 (38.6)	**.95**	45 (36.0)	79 (40.3)	**.44**
Congestive heart failure	98 (23.8)	33 (10.3)	**<.001**	20 (16.0)	13 (6.6)	**.007**
Stroke or TIA	43 (10.4)	36 (11.2)	**.73**	19 (15.2)	17 (8.7)	**.071**
CKD (eGFR< 60 ml/min)	258 (65.8)	176 (57.9)	**.032**	67 (59.3)	109 (57.1)	**.70**
CKD on HD	0 (0)	2 (0.6)	**.10**	1 (0.8)	1 (0.5)	**.74**
Peripheral artery disease	20 (4.9)	12 (3.7)	**.46**	3 (2.4)	9 (4.6)	**.31**
Coronary artery disease	66 (16.1)	34 (10.6)	**.033**	13 (10.4)	21 (10.7)	**.92**
Valve surgery	10 (2.4)	3 (0.9)	**.12**	2 (1.6)	1 (0.5)	**.33**
BNP, median, pg/ml (IQR)	122.7 (56.7-243.9)	91.6 (45.5-190.6)	**.010**	89.5 (46.5-185.0)	91.8 (43.0-192.5)	**.92**
CHADS2 score, mean (SD)	2.06 (1.24)	1.56 (1.23)	**<.001**	1.90 (1.37)	1.35 (1.09)	**<.001**
CHADS2-VASc score, mean (SD)	3.73 (1.42)	3.12 (1.50)	**<.001**	3.53 (1.69)	2.86 (1.31)	**.001**
HAS-BLED score, mean (SD)	2.65 (0.96)	2.50 (0.96)	**.052**	2.65 (0.97)	2.41 (0.94)	**.043**
LA diameter, median, cm (IQR)	4.2 (3.7-4.7)	4.0 (3.5-4.4)	**<.001**	4.0 (3.6-4.3)	3.9 (3.5-4.4)	**.33**
Type of AF						
Paroxysmal	233 (56.6)	230 (71.7)	**<.001**	87 (69.6)	143 (73.0)	**.51**
Persistent	179 (43.4)	91 (28.3)	**<.001**	38 (30.4)	53 (27.0)	**.51**
Current drug therapy						
β blockers	221 (53.6)	169 (52.6)	**.78**	66 (52.8)	103 (52.6)	**.96**
ACE inhibitors/ ARBs	174 (42.2)	115 (35.8)	**.078**	45 (36.0)	70 (35.7)	**.95**
Ca channel blockers	187 (45.4)	154 (48.0)	**.48**	54 (43.2)	100 (51.0)	**.17**
Digoxin	36 (8.7)	16 (5.0)	**.050**	7 (5.6)	9 (4.6)	**.68**
Currently using antiarrhythmic drug therapy						
Overall	0 (0)	159 (49.5)	**<.001**	95 (76.0)	64 (32.7)	**<.001**
Cibenzoline	0 (0)	16 (5.0)	**<.001**	13 (10.4)	3 (1.5)	**<.001**
Disopyramide	0 (0)	8 (2.5)	**.001**	4 (3.2)	4 (2.0)	**.51**
Pilsicainide	0 (0)	61 (19.0)	**<.001**	38 (30.4)	23 (11.7)	**<.001**
Flecainide	0 (0)	21 (6.5)	**<.001**	15 (12.0)	6 (3.1)	**.002**
Amiodarone	0 (0)	5 (1.6)	**.011**	2 (1.6)	3 (1.5)	**.96**
Bepridil	0 (0)	40 (12.5)	**<.001**	19 (15.2)	21 (10.7)	**.23**
Oral anticoagulation						
Overall	370 (89.8)	288 (89.7)	**.97**	105 (84.0)	183 (93.4)	**.007**
Warfarin	61 (14.8)	41 (12.8)	**.43**	14 (11.2)	27 (13.8)	**.50**
Direct oral coagulants						
Overall	309 (75.0)	247 (76.9)	**.54**	91 (72.8)	156 (79.6)	**.15**
Dabigatran	23 (5.6)	42 (13.1)	**<.001**	20 (16%)	22 (11.2)	**.21**
Rivaroxaban	78 (19.0)	82 (25.5)	**.033**	23 (18.4)	59 (30.1)	**.019**
Apixaban	167 (40.5)	95 (29.6)	**.002**	38 (30.4)	57 (29.1)	**.80**
Edoxaban	41 (10.0)	28 (8.7)	**.57**	10 (8.0)	18 (9.2)	**.71**
Antiplatelet therapy	7 (1.7)	9 (2.8)	**.31**	6 (4.8)	3 (1.5)	**.084**

Values are numbers (%), median (25th percentile, 75th percentile) or mean (SD).
AAD, antiarrhythmic drug; CA, catheter ablation; IQR, interquartile range; BMI, body mass index; TIA, transient ischemic attack; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HD, hemodialysis; BNP, brain natrium peptide; SD, standard deviation; LVEF, left ventricular ejection fraction; LA, left atrium; AF, atrial fibrillation; ACE, angiotensin converting enzyme.

In terms of the clinical effectiveness of rhythm-control therapy, follow-up electrocardiogram data were available for 81.6% (n = 262) of the patients in the rhythm-control group. In this sample, the percentages of successful rhythm-control, defined as maintenance of sinus rhythm at the 1-year follow-up regardless of antiarrhythmic drug

Figure 2



Overall distribution of each treatment strategies. AAD, antiarrhythmic drug; CA, catheter ablation.

use, were 62.9% (n = 66/105) and 94.3% (n = 148/157) in the AAD and CA groups, respectively. In the AAD group, the mean changes in AFEQT-OS score from baseline to 1-year follow-up were not significantly different between patients with and those without successful rhythm-control (**Supplemental Table II**). In the CA group, the mean changes in AFEQT-OS score were significantly higher in patients with successful rhythm-control than in those without successful rhythm-control (14.9 [95% CI 12.9-16.9] vs. 4.23 [95% CI -3.75-12.2]; P = .011; **Supplemental Table II**).

Predictors associated with meaningful improvement in QOL

The results of the multivariable analyses are shown in Table IV. Implementation of CA was associated with meaningful improvement in QOL among elderly patients with AF within the one-year study period (adjusted OR 2.75 [95% CI 1.78-4.25]). By contrast, use of AAD was not associated with meaningful improvement in QOL among elderly patients with AF within the one-year study period (adjusted OR 0.74 [95% CI 0.50-1.11]). Importantly, patients with higher AFEQT-OS score at baseline were inversely associated with meaningful improvement in QOL (adjusted OR for per 10-point increase 0.46 [95% CI 0.41-0.53]). These results persisted after excluding patients with preserved QOL at baseline (eg, patients with AFEQT-OS score ≥80); **Supplemental Table III**).

Discussion

The main findings of our study are as follows: first, slightly less than half of the registered elderly patients

Table II. QOL status at 1-year after registration among elder population.

	Baseline AFEQT score	AFEQT score at 1-year follow-up	Change from baseline	*P*-value
Rate-control (n = 412)				
Overall	80.0 (16.1)	82.5 (14.6)	2.56 (0.71)	<**0.001**
Symptom	84.3 (16.3)	88.2 (13.4)	3.87 (0.80)	<**0.001**
Daily Activities	76.9 (20.8)	77.9 (20.3)	1.05 (0.96)	**0.27**
Treatment Concern	81.2 (17.3)	84.9 (14.7)	3.65 (0.79)	<**0.001**
Treatment Satisfaction	72.1 (18.9)	74.4 (16.0)	2.33 (1.10)	**0.034**
Rhythm-control (n = 321)				
Overall	71.8 (20.3)	82.0 (17.7)	10.2 (1.10)	<**0.001**
Symptom	73.4 (22.7)	84.9 (19.4)	11.4 (1.32)	<**0.001**
Daily Activities	70.9 (24.8)	79.7 (22.0)	8.7 (1.39)	<**0.001**
Treatment Concern	71.5 (20.7)	83.3 (16.8)	11.8 (1.15)	<**0.001**
Treatment Satisfaction	66.5 (20.1)	79.3 (18.2)	12.7 (1.48)	<**0.001**
Antiarrhythmic drugs (n = 125)				
Overall	70.5 (19.9)	74.5 (18.9)	4.01 (1.62)	**0.014**
Symptom	72.7 (22.8)	80.5 (21.2)	7.78 (2.01)	<**0.001**
Daily Activities	68.7 (25.2)	70.3 (24.0)	1.61 (2.14)	**0.45**
Treatment Concern	71.5 (20.0)	76.7 (17.9)	5.17 (1.69)	**0.003**
Treatment Satisfaction	67.3 (19.4)	72.3 (17.2)	5.08 (2.21)	**0.024**
Catheter ablation (n = 196)				
Overall	72.7 (20.6)	86.3 (15.1)	14.1 (1.40)	<**0.001**
Symptom	73.9 (22.7)	87.7 (17.6)	13.8 (1.72)	<**0.001**
Daily Activities	72.3 (24.5)	85.7 (18.3)	13.4 (1.74)	<**0.001**
Treatment Concern	71.5 (21.2)	87.7 (14.6)	16.2 (1.47)	<**0.001**
Treatment Satisfaction	66.0 (20.6)	84.1 (17.4)	18.0 (1.86)	<**0.001**

Values are mean (SD), QOL, quality-of-life; AFEQT, Atrial Fibrillation Effect on Quality-of-Life; CI, confidence interval; SD, standard deviation.

with AF were managed with rhythm-control strategy, and 60% of the rhythm-control patients underwent CA; second, compared with the patients managed with rate-control strategy, the patients managed with rhythm-control strategy were younger and less likely to have comorbidities but had lower QOL scores at baseline; third, after a 1-year follow-up, patients had improved QOL scores regardless of treatment strategies, but the changes in QOL scores over 1 year among patients with AAD alone were not clinically meaningful; fourth, implementation of CA, along with lower AFEQT score at baseline, was associated with meaningful improvement in QOL. Our results suggest that rhythm-control strategy is widely implemented in elderly patients with AF, and CA, if selected in the appropriate patient population, can aid in improving QOL.

The incidence of AF increases rapidly with advancing age.[11] An estimated 700,000 people in Japan have AF, which is projected to increase to >1 million by 2050[12,13,14,15] Nevertheless, few studies have investigated AF in elderly patients. Previous trials compared the effectiveness of rate- and rhythm-control strategies on improvement in patient-reported QOL; however, elderly patients were excluded from the trials partly due to older age and comorbidities[3,4,16,17] Although a previous observational study showed that patients with AF treated with rhythm-control strategy were more likely to improve their QOL than those treated with rate-control strategy,[18] the registry included mainly younger patients with AF (ie, mean age was 67.6 years [SD 11.8]). These findings suggest that QOL evaluations focusing on elderly patients with AF are limited. Moreover, no study evaluating patient-reported QOL has been reported using a disease-specific questionnaire. For older patients with AF, symptoms could be somewhat atypical and often mixed up with those of other comorbidities. In this study, we used the AFEQT as a disease-specific questionnaire for evaluating patient-reported QOL; therefore, there are fewer concerns about the sensitivity and specificity required to observe the changes of QOL.

Our results also emphasize the importance of assessing patient-reported QOL and providing an appropriate therapeutic strategy according to its objective measurement. We found that elderly patients with AF with preserved QOL are expected to receive few benefits from rhythm- and rate-control strategies. Rate-control therapy is considered as a first-line therapy among elderly patients with AF[19] but not among patients with preserved QOL in our study. On the other hand, elderly patients with AF with impaired QOL improved their QOL score regardless of treatment strategies, but implementation of AAD was not associated with meaningful improvement in QOL. AADs can effectively maintain sinus rhythm for patients with AF; the restoration rate of sinus rhythm for one year is 88% for amiodarone, 81% for sotalol, and 79% for Class I agents.[20] However, elderly patients are known to be more prone to pharmacological intolerance and treatment discontinuation than younger patients,[21] and AADs might have a more substantial negative impact on their reported QOL than we expected.

Table III. Changes in AFEQT overall summary score within 1-year study period.

	Absolute changes (mean [SD])	*P*-value	Adjusted for baseline AFEQT scores*		*P*-value	Adjusted for selected factors **		*P*-value	Excluding patients with an overall AFEQT score ≧80 at baseline, and adjusted for selected factors***		*P*-value
			changes (mean [SE])	95%CI		changes (mean [SE])	95%CI		changes (mean [SE])	95% CI	
Rate-control	2.56 [14.3]	<**0.001**	4.49 [0.6]	3.15-5.84	**0.002**	5.05 [3.6]	3.68-6.42	**0.078**	12.3 [1.3]	9.78-15.0	**0.16**
Rhythm-control	10.2 [19.6]		7.73 [0.7]	6.2-9.2		7.02 [0.8]	5.45-8.60		15.1 [1.2]	12.5-17.6	
Antiarrhythmic drug	4.01 [18.0]	<**0.001**	3.22 [1.3]	0.65-5.79	<**0.001**	3.88 [1.3]	1.21-6.55	<**0.001**	8.8 [2.0]	4.75-12.8	<**0.001**
Catheter ablation	14.1 [19.6]		14.6 [1.0]	12.6-16.7		14.2 [1.0]	12.1-16.3		23.2 [1.6]	20.0-26.4	

AFEQT, Atrial Fibrillation Effect on Quality-of-Life; SD, standard deviation; SE, standard error; CI, confidence interval.
Covariates:
*; baseline AFEQT scores (per 1-point increase).
**; baseline AFEQT scores (per 1-point increase), age (per 1-year increase), gender, body mass index (per 1-point increase), prior heart failure, hypertension, diabetes mellitus, stroke (cerebral infarction or transient ischemic attack), paroxysmal AF, coronary artery disease.
***; Excluding patients with an overall AFEQT score ≧80 at baseline, covariates were same as an above model.

In our study, implementation of CA was a sole factor that was associated with meaningful improvement in patient-reported QOL within the 1-year study period. Importantly, the improvement in QOL was more pronounced in patients with successful rhythm control, in line with several prior observations[22,23,24,25] In the CABANA trial that enrolled 2204 symptomatic patients with AF, 308 patients (13.9%) older than 75 years. The trial compared CA and conventional drug therapy on patient-reported QOL using the AFEQT questionnaire and showed that CA led to clinically important and significant improvements in QOL at 12 months.[26] Although other studies indicated the benefits of CA, which maintain sinus rhythm with the improvement in QOL, CA carries a risk of complications and demands high medical cost. In fact, there is a growing concern since the annual case volume of CA procedures has increased to more than 6-fold over the past decade in relation to the growing number of elderly patients who relatively have mild to moderate symptoms as compared with younger patients with AF.[27] Because of the high proportion of older patients requiring rhythm-control therapy and the relatively high perceptions of frailty and comorbidities due to an aging society, further appropriate identification of elderly patients who may benefit from invasive therapy is important. The application of our study results in clinical practice may induce better selection of AF management and help clinicians to build a truly patient-centered health care system.

Limitations

For a thorough understanding of our results, several limitations should be acknowledged. First, nonrandomized observational research involves inherent limitations; nevertheless, it is the best way to describe the current treatment patterns and outcomes of care. It is likely that there are unmeasured confounders such as depression, frailty, and economic status that may explain some of the observed differences in QOL. There are also concerns about selection bias that more symptomatic patients were more likely to receive rhythm-control strategies and improve their QOL. Second, the patients who were initially treated with AADs but then converted to rate-control therapy because of poor treatment response or intolerance for AADs were included in the AAD group. As a result, the effectiveness of the rate-control strategy might have been overestimated. Finally, not all patients with AF in Japan participated in the KiCS-AF registry. Sampling bias and generalizability of the study results to Japan is a potential concern, although we included patients presenting with new-onset AF. Nevertheless, our registry is multicenter and includes a relatively large number of patients. We believe that this is one of the most representative Japanese databases of patients with AF, and our results comprise the most complete assessment of the current practice patterns in Japan.

Conclusions

In a contemporary Japanese practice, rhythm-control strategy is widely implemented in elderly patients with AF. Use of CA is associated with improvement in QOL in carefully selected patient population. Efforts on improving the communication between caregivers and patients to appropriately identify candidate patients for CA are warranted.

Table IV. Factors associated with meaningful improvement for QOL within 1-year.

variable	Multivariable analysis	
	OR (95% CI)	*P*-value
Age (per 1-y increase)	1.00 (0.96-1.03)	**0.84**
Female (vs male)	0.87 (0.61-1.25)	**0.46**
Congestive heart failure	0.97 (0.61-1.54)	**0.88**
Hypertension	1.14 (0.78-1.66)	**0.50**
Diabetes Mellitus	0.93 (0.59-1.48)	**0.76**
Stroke	0.88 (0.49-1.56)	**0.65**
Baseline AFEQT scores (per 10-point increase)	0.46 (0.41-0.53)	<**0.001**
OAC at baseline	1.10 (0.61-1.97)	**0.75**
Prescription of AAD	0.74 (0.50-1.11)	**0.15**
Implementation of Catheter ablation	2.75 (1.78-4.25)	<**0.001**

QOL; quality-of-life, CI; confidence interval, AFEQT; Atrial Fibrillation Effect on Quality-of-Life; OAC, oral anticoagulant; AAD, antiarrhythmic drug.

Acknowledgments

We would like to thank all the study coordinators, investigators, and patients who participated in the Keio Interhospital Cardiovascular Studies for Atrial Fibrillation registry.

Additional contributions

The site investigators were Yukihiko Momiyama, Munehisa Sakamoto, Jun Fuse, Kojiro Tanimoto, Yoko Tanimoto, Yukinori Ikegami, and Kohei Inagawa (National Hospital Organization Tokyo Medical Center); Iwao Nakamura, Jyunji Suzuki, Tomohiro Matsuhashi, and Hiroshi Shiga (Hino Municipal Hospital); Seiji Takatsuki, Yoshiyasu Aizawa, Nobuhiro Nishiyama, Takahiko Nishiyama, Yoshinori Katsumata, Shin Kashimura, Akira Kunitomi, Kazuaki Nakajima, and Taishi Fujisawa (Keio University School of Medicine); Masahiro Suzuki, Takaharu Katayama, Keisuke Matsumura, Tomohiko Ono, Hanako Tokuda, Ryutaro Yamaguchi, and Hiroaki Tanaka (National Hospital Organization Saitama National Hospital); Shigetaka Noma, Takashi Yagi, Kenichiro Shimoji, Koji Ueno, and Satoshi Mogi (Saiseikai Utsunomiya Hospital); Takashi Koyama, Shiro Ishikawa, Hideaki Kanki, Takashi Akima, Masahito Munakata, and Kazutaka Miyamoto (Saitama City Hospital); Hideo Mitamura, Kazunori Moritani, Masaru Shibata, and Toshimi Kageyama (Tachikawa Hospital); Takahiro Oki, Akiyasu Baba, Yoshinori Mano, and Hiroaki Sukegawa (Tokyo Dental College Ichikawa General Hospital); Kouji Negishi, Takahiro Koura, Daisuke Shinmura, Kotaro Fukumoto, and Hiroyuki Yamakawa (Yokohama Municipal Citizen's Hospital); Keiichi Nagami, Kazuhiro Oyamada, Kotaro Naitou, and Keijiro Chiba (Keiyu Hospital); Megumi Shimada (Tokai University Oiso Hospital); and Makoto Akaishi (Tokai University Tokyo Hospital). The clinical coordinators were Aki Kato, Ikumi Koishi, Miho Matsuoka, Takako Nozaki, Hiroaki Nagayama, Chieko Tamura, Reiko Tamura, Junko Susa, Miho Umemura, and Itsuka Saito. We are grateful to all study coordinators, investigators, and patients who participated in the Keio Interhospital Cardiovascular Studies-Atrial Fibrillation (KiCS-AF) registry. None of the additional contributors received compensation.

Sources of funding

This study was funded by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (Grant no. 16H05215, 16KK0186) and by an unrestricted research grant from Bayer Yakuhin Ltd.

Declarations of interest

Dr. Kohsaka received an unrestricted research grant for the Department of Cardiology at Keio University School of Medicine from Bayer Pharmaceutical and Daiichi Sankyo; grants from Bayer Yakuhin Ltd. and Daiichi Sankyo; and personal fees from Bristol-Myers Squibb. Dr. Kimura received grants from Bayer Yakuhin Ltd. Dr. Takatsuki received grants and personal fees from Bayer and personal fees from Daiichi Sankyo and Bristol-Myers Squibb. The authors report no other relationships that could be construed as a conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2020.01.011.

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