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ORIGINAL RESEARCH

Baseline and Postprocedural Health Status Outcomes in Contemporary Patients With Atrial Fibrillation Who Underwent Catheter Ablation: A Report from the Japanese Outpatient Registry

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BACKGROUND: Randomized clinical trials have demonstrated that catheter ablation (CA) for atrial fibrillation improves health-related quality of life (HRQoL). In daily practice, however, CA is performed on a wide range of patients, and outcomes may vary. We aimed to examine baseline and 1-year HRQoL outcomes of patients with atrial fibrillation after CA in daily practice.

METHODS AND RESULTS: Using a registry-based cohort study designed to recruit patients with atrial fibrillation newly referred to 11 hospitals, we extracted data from 1097 consecutive patients with atrial fibrillation who underwent CA between 2012 and 2019. The Atrial Fibrillation Effects on Quality of Life Overall Summary (AFEQT-OS) was assessed at registration and 1 year after, and a 5-point increase in AFEQT-OS score was considered a meaningful improvement. Overall, the median age was 64 (interquartile range, 56–70) years, 836 (76.2%) were men, and 93.0% (n=1021) of the patients answered the AFEQT questionnaire. The mean AFEQT-OS score was 74.9 (SD, 18.0) at registration and 88.8 (SD, 12.6) at 1 year after. Notably, the incidence of meaningful improvement in HRQoL after CA was 88.6% for the patients with impaired HRQoL (AFEQT-OS score <80), which was only 40.1% in those with preserved HRQoL (AFEQT-OS score ≥80). Female sex, left atrium diameter, and high baseline HRQoL were independently associated with nonimprovement after CA.

CONCLUSIONS: The improvement in HRQoL after CA was similar to that seen in clinical trials; however, one-third of patients did not show improvement. These results underscore the importance of quantitative evaluation of patients' HRQoL to maximize the effect of CA before its performance.

Key Words: atrial fibrillation ■ catheter ablation ■ gender differences ■ patient-reported outcome ■ quality of life

Atrial fibrillation (AF) is the most frequently encountered sustained arrhythmia and is associated with substantial morbidity and mortality and impaired quality of life worldwide.[1,2] The incidence of AF is known to increase rapidly with advancing age, and its burden is expected to continue to rise.[3] An estimated 700 000 people in Japan have AF, which is projected to increase to >1 million by 2050.[4,5]

Over the past decade, efficacy of new therapies for rhythm control has been demonstrated. The CABANA (Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation)[6] and several randomized controlled

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CLINICAL PERSPECTIVE

What Is New?

- Approximately one-third of patients failed to have a clinically meaningful improvement after catheter ablation in our registry of newly referred patients with atrial fibrillation.
- Along with female sex and left atrial dilatation, preserved quality-of-life status was an important predictor of nonimprovement after catheter ablation.

What Are the Clinical Implications?

- The clinical benefit of catheter ablation for atrial fibrillation has been demonstrated in carefully designed clinical trials.
- Caution is needed when extrapolating the results of these clinical trials to unselected atrial fibrillation populations in the real world.
- Careful clinical assessment, along with the objective and quantitative evaluation of quality of life may aid in improving and maximize the outcomes of catheter ablation for atrial fibrillation.

Nonstandard Abbreviations and Acronyms

AAD	antiarrhythmic drug
AFEQT	Atrial Fibrillation Effect on Quality of Life
AFEQT-OS	Atrial Fibrillation Effect on Quality of Life Overall Summary
CA	catheter ablation
CABANA	Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation
HRQoL	health-related quality of life
KiCS-AF	Keio Interhospital Cardiovascular Studies–Atrial Fibrillation

trials have demonstrated the quality-of-life benefits of catheter ablation (CA) for AF.[7–9] Consequently, the clinical guidelines have considered CA as an initial rhythm-control strategy for patients with refractory or recurrent symptomatic AF and highlighted the importance of evaluation of health-related quality of life (HRQoL).[7,10]

However, these pivotal trials were conducted with selected cohorts of patients and hospital centers,[6,9] and understanding how this expanding technology performs, outside the strict inclusion and exclusion criteria of clinical trials in Western countries, is of interest to international audiences. Patients with AF present with diverse symptoms and backgrounds, and the provided care and consequent outcomes vary worldwide.[1] In addition, 15% of patients reported impaired HRQoL 12 months after the procedure in the CABANA trial,[6] identification of patient subgroups that are less likely to benefit from AF ablation can highlight areas in which future research might lead to better AF ablation outcomes.

To date, the clinical utility of HRQoL assessment for identifying potential candidates likely to derive a robust benefit from CA has been scarcely studied. Given the rapid increase in the burden of AF,[5] a deeper understanding of the symptoms, HRQoL, and satisfaction with CA and appropriate identification of those who may benefit from CA in nonselected populations are particularly needed. Therefore, we examined the 1-year HRQoL outcomes of patients with AF after CA in the KiCS-AF (Keio Interhospital Cardiovascular Studies–Atrial Fibrillation) registry.

METHODS

The data and materials used to conduct this research are available to researchers, on request, for scientific projects aimed at identifying a novel clinical finding that may further improve patient outcome. Attempts to co-validate country-specific observations, risk stratification schemes, and outcomes are also welcome. The procedure does need to follow the Act on the Protection of Personal Information Law (as of May 2017) and the Ethical Guidelines for Medical and Health Research Involving Human Subjects (as of March 2015) in Japan.

Data Sources

The rationale and design of the KiCS-AF registry have been described previously.[11,12] Briefly, the KiCS-AF is a multicenter, registry-based retrospective cohort study designed to collect clinical variables and outcomes data from consecutive patients with AF who were newly diagnosed at, or referred to, an outpatient clinic at each of the 11 participating tertiary care hospitals within the Kanto area of Japan. To investigate the association between treatment intervention and HRQoL, the registry included patients with AF who were newly referred to the network hospitals within the previous 6 months. Approximately 150 variables regarding the patients' background, symptoms, prior and current drug use, including oral anticoagulants, electrocardiography and echocardiography results, and blood sampling test results were collected for each patient. Upon study entry, patients were classified by type of AF (first detected, paroxysmal, persistent, or permanent AF), according to the American College of Cardiology/American Heart Association/European Society of Cardiology 2006 guidelines for the management of patients with AF[13] and the 2007 Heart Rhythm Society/European Heart Rhythm Association/

European Cardiac Arrhythmia Society expert consensus statement on catheter and surgical ablation of AF,[14] as described in Data S1. Yearly follow-up examinations were performed for all patients by mail, phone interviews, and chart reviews. Dedicated study coordinators updated the status of major cardiovascular events, laboratory test results, performed procedures, and subsequent changes in the medications. Data quality assurance was achieved through systematic validation that highlighted outliers and data completeness, and the clinical research coordinators in each institution answered all inquiries regarding data entry. To ensure consecutive case enrollment, the senior study coordinator (I.U.) and investigator (S.K.) performed on-site auditing to ensure proper registration of each eligible patient. The protocol was approved by the respective ethical review board of each institution, and all participants provided written informed consent. Almost all of the approached patients agreed to participate in the present study.[12]

Assessment of Patients' Health Status

In addition to traditional data collected by healthcare providers, the KiCS-AF also collected patient-reported outcomes using the internationally validated Atrial Fibrillation Effect on Quality of Life (AFEQT; http://www.afeqt.org).[15] Patients were requested to complete the AFEQT questionnaire at registration and follow-up visit (eg, 1 year after registration) or by mail. The AFEQT is a 20-item questionnaire that quantifies 4 domains of AF-related HRQoL, including symptoms, daily activities, treatment concerns, and treatment satisfaction, using 7-point Likert response scales. An overall summary score can be calculated from the first 3 domains and ranges from 0 to 100 (100, best possible health status [no impairment]; 0, worst health status). A recent analysis has suggested that a 5-point change in the AFEQT Overall Summary (AFEQT-OS) score is observed among patients who change by one European Heart Rhythm Association functional status class and is a clinically meaningful difference.[16] Additionally, a previous study comparing the European Heart Rhythm Association symptom classification in AF and AFEQT showed that the mean AFEQT-OS score in patients classified as European Heart Rhythm Association class 1 (eg, no symptom) is 78.4 (SD, 19.0).[17] Thus, we regarded patients with AFEQT-OS scores ≥80 as those with preserved HRQoL and patients with AFEQT-OS scores <80 as those with impaired HRQoL. A culturally and linguistically translated version of the AFEQT for Japan was used.

Study Population

All data available up to the 1-year follow-up examination through December 2019 were included. At that time, 3166 consecutive AF outpatients were registered in the registry, of whom 1150 (36.3%) underwent CA. Among these patients, 1097 (95.3%) had 1-year follow-up data for major cardiovascular events, procedures, subsequent medication changes, and laboratory test values, and the rates of missing AFEQT data were 0.2% (n=3/1097) at registration and 6.7% (n=74/1097) at 1 year after registration; the change in AFEQT-OS scores after CA was available in 1021 patients (92.1%). During the follow-up, patients underwent CA for AF, on average, 105.5 (SD, 83.8) days after registration and answered the AFEQT questionnaire, on average, 305 (SD, 110) days after CA.

Statistical Analysis

Baseline characteristics for the analytic cohort are presented as medians with interquartile ranges (IQRs) for continuous variables and as numbers with percentages for categorical variables. To highlight variability in changes in patients' health status, AFEQT scores are reported as a mean (SD). Changes in AFEQT scores at 1 year from baseline were evaluated using paired *t*-tests. Additionally, to more completely define factors associated with HRQoL, mean AFEQT-OS scores at 1 year were compared among key subgroups using analysis of covariance; subgroups were selected on the basis of clinical experience and prior research.[18] These comparisons were adjusted for baseline AFEQT-OS scores except for the analysis that was stratified by baseline AFEQT-OS scores. The rates of patients whose HRQoL had not improve (changes in AFEQT-OS score <5) by 1 year were estimated for each subgroup and compared using χ^2 tests.

We defined change in AFEQT-OS scores after CA as the AFEQT-OS score at 1 year minus the AFEQT-OS score at registration, and a change in AFEQT-OS score <5 was considered a nonimprovement in patient-reported HRQoL. A positive change represents improved HRQoL, and a negative change implies worsening HRQoL. We then constructed a logistic regression model with generalized estimating equations to account for clustering of patients within sites, and whether patients had a non-improvement in their HRQoL (changes in AFEQT-OS score <5) or not was entered as a dependent variable. The model was adjusted for clinically relevant factors, and the full list of covariates is presented in Data S2. We examined factors associated with changes in AFEQT-OS scores after CA using multivariable linear regression with generalized estimating equations to account for clustering of patients within sites and adjusted for the aforementioned clinically relevant variables. Additionally, to investigate the association between patients with preserved HRQoL (eg, those with AFEQT-OS score ≥80) at registration and both the changes in AFEQT-OS scores after CA and the odds for

nonimprovement in their HRQoL, baseline AFEQT-OS score was entered as a dichotomous variable (eg, AFEQT-OS score <80 or ≥80) in the above models not as continuous variables. A sensitivity analysis was performed to exclude patients with AFEQT-OS score ≥80 at registration, as these patients might not be able to experience improvement, making the interpretation of changes in AFEQT-OS scores difficult. Furthermore, we performed a subgroup analysis for distance between registration and CA procedure (eg, less than or more than the average days from registration to procedure). Although patients who underwent CA in a delayed fashion can change their HRQoL by other provided care, the associations between HRQoL and CA procedure might differ in those patients.

Further, the association between successful CA and patient-reported HRQoL were analyzed among a subgroup of patients with follow-up ECG (93.0%; 1021/1097); a successful CA was defined as patients with maintenance of sinus rhythm in a single 12-lead ECG at 1-year follow-up without the use of antiarrhythmic drugs (AADs), and who was not aware of having an episode of AF within 1 month when answering the AFEQT questionnaire at follow-up. Additionally, the above models were applied for patients with clinical success of CA to investigate associations between the factors associated with a nonimprovement in their HRQoL and clinical success of CA.

To ensure that we examined a representative cohort of patients, we examined differences in baseline characteristics between patients with and without available AFEQT data. There were no missing data for covariates, except for left atrial diameter (8.7%; 89/1021), who did not undergo echocardiogram within 6 months before registration. To account for missing data, a single median imputation was used. SPSS version 24.0 (IBM Corp., Armonk, NY) was used for all analyses. All reported *P* values were 2-sided, with $P<0.05$ being considered statistically significant.

RESULTS

Study Sample

Overall, the median age was 64 (IQR, 56–70) years, 836 (76.2%) were men, and the calculated median CHA_2DS_2-VASc score was 2 (IQR, 1–3) in the analytic cohort (Table 1). As for the details on the AF phenotype, 662 (60.3%) had paroxysmal AF, 52 (4.7%) had undergone catheter ablation at least once before registration, and 337 (30.7%) were treated with AADs at the time of registration. Only a minority of the patients had a history of congestive heart failure (n=78, 7.1%); the median brain natriuretic peptide level was 70.5 (IQR, 29.9–147.2) pg/mL, and the median left atrial diameter was 4.0 (IQR, 3.5–4.4) cm.

Table 1. Baseline Characteristics of the Analytic Cohort

Characteristics	Patients who underwent catheter ablation within 1 year after registration n=1097 no. (%)
Age, y, median (IQR)	64 (56–70)
Men	836 (76.2)
Women	261 (23.8)
Family history of atrial fibrillation	283 (25.8)
Education level	
High school graduate or less	315 (28.7)
Junior college diploma	143 (13.0)
Bachelor's degree or more	614 (56.0)
BMI, median, kg/m^2 (IQR)	23.6 (21.5–26.0)
Heart rate, median, bpm (IQR)	75 (65–88)
Blood pressure, median, mm Hg (IQR)	
Systolic	139 (118–141)
Diastolic	78 (70–88)
Medical history	
Smoking	186 (17.0)
Hypertension	566 (51.6)
Diabetes	132 (12.0)
Dyslipidemia	377 (34.4)
Heart failure	78 (7.1)
Sick sinus syndrome	41 (3.7)
Obstructive sleep apnea	40 (3.6)
Stroke or TIA	79 (7.2)
Gastrointestinal bleeding	12 (1.1)
CKD (eGFR<60 mL/min)	88 (8.0)
CKD on HD	5 (.5)
Peripheral artery disease	25 (2.3)
Coronary artery disease	50 (4.6)
Prior valve surgery	6 (0.6)
BNP, median, pg/mL, (IQR)	70.5 (29.9–147.2)
CHA_2DS_2-VASc score, median (IQR)	2 (1–3)
LVEF <50%	79 (7.2)
LA diameter, median, cm (IQR)	4.0 (3.5–4.4)
Type of visit	
Diagnosed at health screening	322 (30.3)
Referral from emergency department	66 (6.0)
Type of AF	
First detected	21 (1.9)
Paroxysmal	662 (60.3)
Persistent	309 (28.2)
Permanent	97 (8.8)
Current drug therapy	
β-blockers	562 (51.2)
ACE inhibitors/ARBs	352 (32.1)

(*Continued*)

Table 1. Continued

Characteristics	Patients who underwent catheter ablation within 1 year after registration n=1097 no. (%)
Calcium-channel blockers	422 (38.5)
Digoxin	45 (4.1)
Diuretics	105 (9.6)
Currently using antiarrhythmic drugs	
Overall	337 (30.7)
Cibenzoline	41 (3.7)
Disopyramide	19 (1.7)
Pilsicainide	117 (10.7)
Flecainide	46 (4.2)
Amiodarone	17 (1.5)
Bepridil	93 (8.5)
Oral anticoagulants	
None	147 (13.4)
Warfarin	138 (12.6)
Direct oral anticoagulants	812 (74.0)
Antiplatelet therapy	83 (7.6)
Prior interventional therapy for AF	
Catheter ablation of AF	52 (4.7)
Surgical maze	2 (0.2)

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; AV node, atrioventricular node; BMI, body mass index; BNP, brain natriuretic peptide; CKD, chronic kidney disease; HD, hemodialysis; IQR, interquartile range; KiCS-AF, the Keio Interhospital Cardiovascular Studies–Atrial Fibrillation; LVEF, left ventricular ejection fraction; LA, left atrium; and TIA, transient ischemic attack.

Patients without AFEQT data (n=76, 6.9%) were largely comparable to those in the analytic cohort; however, patients with missing data were less likely to be old and have a family history of AF and comorbidities and, therefore, were more likely to have a lower CHA_2DS_2-VASc score (Table S1).

During follow-up, 277 patients (25.2%) were initiated on AADs before CA for AF, and the remaining 483 patients (44.0%) were never treated with AADs. Regarding poor clinical outcomes, 4 patients (0.4%) were dead, 6 patients (0.5%) had an ischemic stroke, 10 patients (0.9%) had major bleeding event, and 7 patients (0.6%) had heart failure hospitalization within 1 year after registration. Patients experienced these poor clinical outcomes, on average, 109 (SD, 96.5) days after CA for AF, and there are 5 procedure-related events within 2 weeks after CA for AF (2 cases of vascular access site bleedings, 1 case of procedure-related ischemic stroke, and 2 cases of heart failure hospitalization after CA).

Quality-of-Life Outcomes

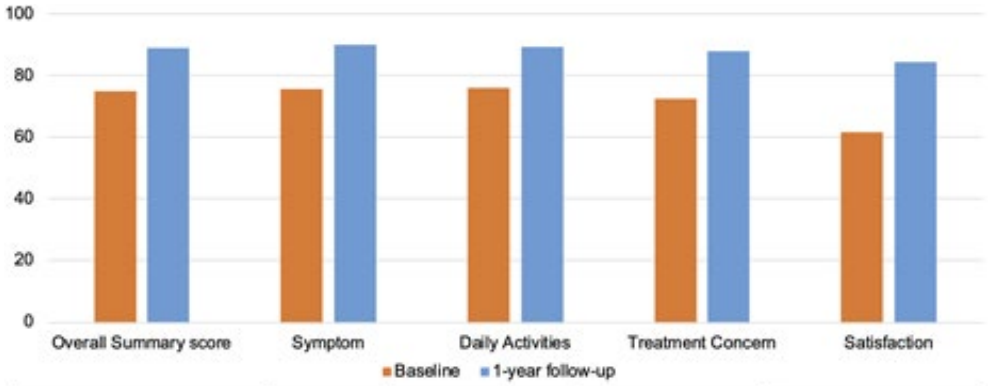
The mean baseline AFEQT-OS score was 74.9 (SD, 18.0), and 466 patients (45.6%) had preserved HRQoL at registration (eg, patients with AFEQT-OS score ≥80). The average scores for each of the individual domains are described in Figure 1. Notably, the average score for the satisfaction domain was particularly low (61.7; SD, 20.7). Among the components of AFEQT-OS scores (eg, the first 3 domains), the absolute value was lowest in the treatment concern domain (72.5; SD, 18.7) and highest in the daily activities domain (76.0; SD, 22.3).

Figure 2 describes the distribution of AFEQT-OS scores at registration and at 1-year follow-up. At 1-year follow-up (ie, 1 year after registration), AFEQT-OS scores improved by a mean of 13.9 points (95% CI, 12.8–15.0; $P<0.001$) to a mean score of 88.8 (SD, 12.6). A scatterplot of AFEQT-OS scores at registration and 1-year follow-up in the analytic cohort is presented in Figure S1. Overall, 832 patients (81.5%) had preserved HRQoL at 1-year follow-up, and the difference in the proportion of patients with preserved HRQoL at registration was statistically significant (McNemar test, P value <0.001). When each of the domains were examined individually, the absolute improvement from baseline to 1-year follow-up was the highest in the scores of treatment concerns domain (22.4; 95% CI, 20.6–24.2), although all scores are improved uniformly, and there were no significant visual differences in the distribution of each score (Figure 2).

Factors Associated With Nonimprovement of HRQoL After Catheter Ablation

Despite the overall improvement in the average AFEQT-OS score, 345 patients (31.4%) did not show clinically meaningful improvements in their HRQoL (ie, changes in AFEQT-OS score ≥5) after CA. Notably, the incidence of meaningful improvement in HRQoL after CA was 88.6% for the patients with impaired HRQoL (AFEQT-OS score <80), which was only 40.1% in those with preserved HRQoL (AFEQT-OS score ≥80). Furthermore, a scatterplot of changes in AFEQT-OS scores within 1 year and AFEQT-OS scores at registration in the analytic cohort is presented in Figure S1, indicating that patients with preserved HRQoL (ie, a higher AFEQT-OS score) at registration were less likely to improve their HRQoL after CA (Figure 3).

There were notable differences in mean AFEQT-OS scores and the proportion of patients with a nonimprovement of HRQoL after CA across key subgroups of patients (Table 2). Type of AF (ie, those with first detected AF or permanent AF), preserved baseline HRQoL, female sex, low education level (ie, high school graduate or less), and use of digitalis at registration were associated with worse HRQoL after CA. Patients who had either of the following variables; diagnosis at medical screening, prior history of stroke or transient ischemic attack, left atrial dilatation (≥4.0 cm) were associated with higher rates of nonimprovement in HRQoL at 1-year follow-up. In contrast, a family



AFEQT Measure	No. of Patients	Baseline Score, Mean (SD)	Follow-up Score, Mean (SD)	Changes From Baseline (95% CI)
Overall summary	1,021	74.9 (18.0)	88.8 (12.6)	13.9 (12.8-15.0)
Symptom	1,014	75.7 (20.0)	89.9 (14.5)	14.2 (12.8-15.5)
Daily activities	1,015	76.0 (22.3)	88.9 (15.5)	12.9 (11.6-14.2)
Treatment concerns	1,010	72.5 (18.7)	87.8 (13.2)	15.3 (14.1-16.4)
Treatment satisfaction	799	61.7 (20.7)	84.1 (18.7)	22.4 (20.6-24.2)

Figure 1. AFEQT survey among patients with newly referred AF who underwent catheter ablation
Each bar indicates the average scores for AFEQT Overall Summary score and each of the individual domains. *All changes from baseline are significant (P<0.001) based on the paired t-test. **Scores range from 0 to 100, with higher scores indicating less symptom burden and better quality of life. AF indicates atrial fibrillation; and AFEQT indicates Atrial Fibrillation Effect on Quality of Life.

history of AF or use of AAD at registration were associated with lower rates of nonimprovement in HRQoL at the 1-year follow-up.

In the multivariable linear regression analyses, patients who had better HRQoL at registration were associated with a lower improvement of 1-year AFEQT-OS scores, with every 1-point increase in baseline AFEQT-OS score being associated with a 0.74-point reduction in 1-year AFEQT-OS score (95% CI, −0.79 to −0.68 point; P<0.001, Table 3). Additionally, when baseline AFEQT-OS scores were entered as a dichotomous variable (eg, AFEQT-OS score <80 or ≥80), the patients with preserved HRQoL (eg, AFEQT-OS score ≥80) at registration was associated with a 19.8-point reduction in 1-year AFEQT-OS score (95% CI, −21.4 to −18.1point; P<0.001, Table S2). Other notable variables associated with lower AFEQT-OS scores at the 1-year follow-up were female sex, low education level (ie, high school graduate or less), and left atrial diameter.

A similar trend was seen in the multivariable logistic regression model; patients with higher AFEQT-OS score at registration were associated with nonimprovement of their HRQoL (changes in AFEQT-OS score <5) at the 1-year follow-up (adjusted odds ratio, 1.12 [per 1-point increase]; 95% CI, 1.09–1.14; P<0.001, Table 4). Furthermore, when baseline AFEQT-OS scores were entered as a dichotomous variable, the odds ratio for nonimprovement of patients' HRQoL among those with preserved HRQoL at registration was 12.6 (95% CI, 8.77–18.1, P<0.001, Table S3). Female sex (odds ratio, 1.80; 95% CI, 1.23–2.88; P<0.001) and left atrial diameter (odds ratio, 1.60 [per 1-cm increase]; 95% CI, 1.23–2.08; P<0.001) were also associated with nonimprovement of HRQoL, but the education level was not.

Sensitivity Analyses

The above clinical variables (eg, female sex, left atrial diameter) and higher baseline AFEQT-OS score were predictors of nonimprovements of HRQoL after excluding patients with preserved HRQoL at registration (eg, patients with AFEQT-OS score ≥80) (Tables S4 and S5). As for the subgroup analysis for distance between registration and CA procedure, patients had significantly improved AFEQT-OS scores regardless of distance, and a similar trend was observed in each of the individual domains (Table S6).

Within the subgroup of patients with follow-up ECG data (93.0%; 1021/1097), the mean changes in AFEQT-OS score within 1 year were 15.6 (95% CI,

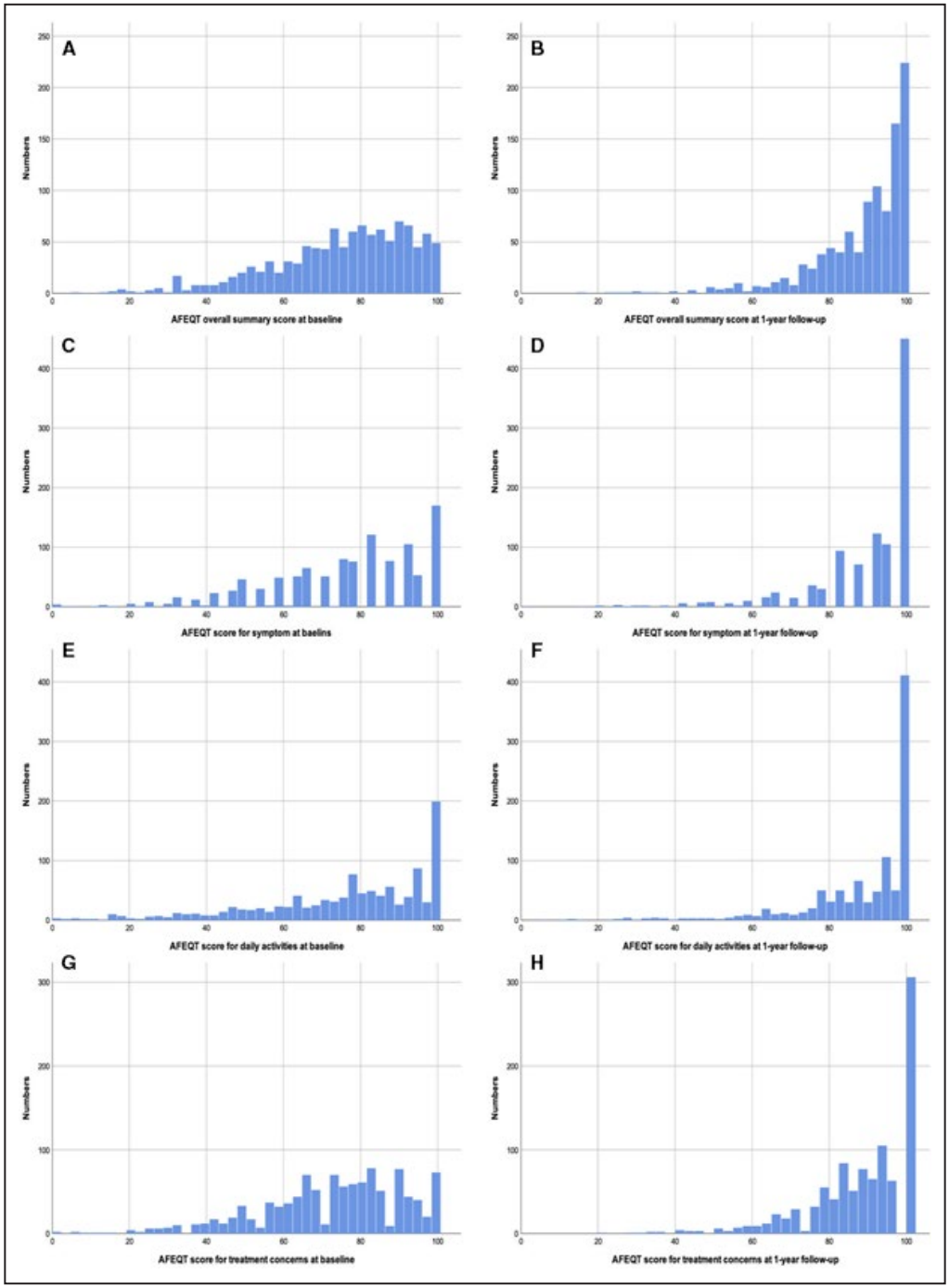


Figure 2. AFEQT Overall Summary score and each individual domain at registration and the 1-year follow-up

A, Distribution of AFEQT-overall summary scores at registration. **B**, Distribution of AFEQT Overall Summary scores at the 1-year follow-up. **C**, Distribution of AFEQT score for symptom at registration. **D**, Distribution of AFEQT score for symptom at the 1-year follow-up. **E**, Distribution of AFEQT score for daily activities at registration. **F**, Distribution of AFEQT score for daily activities at the 1-year follow-up. **G**, Distribution of AFEQT score for treatment concerns at registration. **H**, Distribution of AFEQT score for treatment concerns at the 1-year follow-up. AFEQT indicates Atrial Fibrillation Effect on Quality of Life Overall Summary.

14.3–16.7; *P*<0.001) in patients with a successful CA and 8.8 (95% CI, 6.7–10.9; *P*<0.001) in those without a successful CA (Table S7). The factors associated with a nonimprovement in patient' reported HRQoL in the overall model, such as female sex, left atrial diameter, and higher baseline AFEQT-OS score were significant

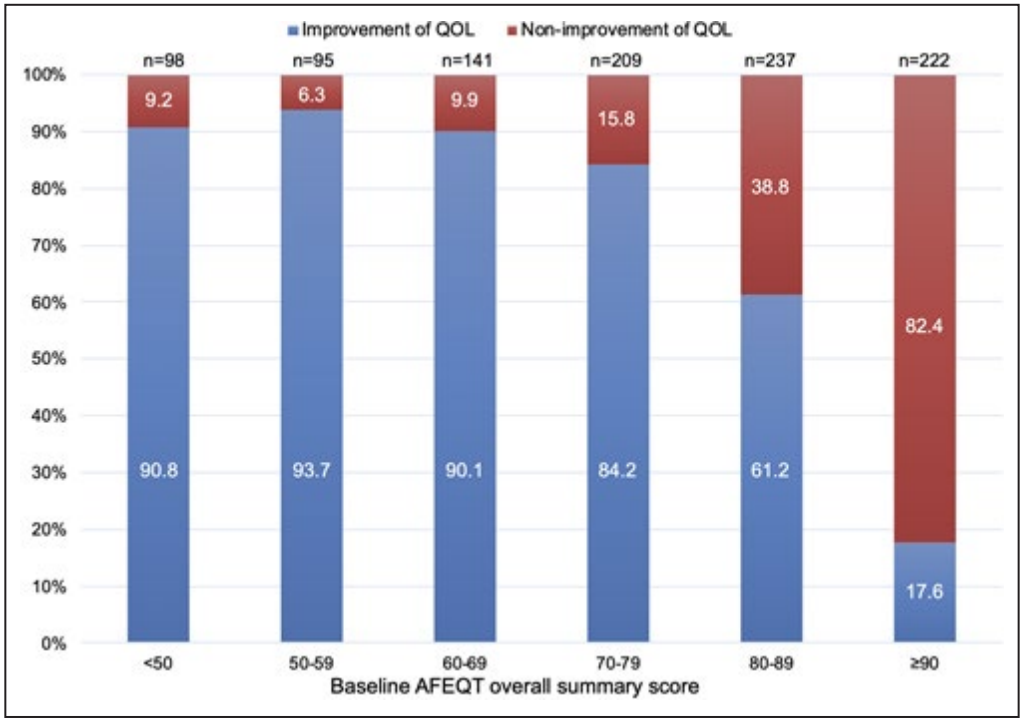


Figure 3. Changes in AFEQT-OS scores within 1-year and AFEQT-OS scores at registration in the analytic cohort

Overall distributions of patients with and without clinically meaningful improvement of HRQoL after CA according to baseline AFEQT-OS scores. *A nonimprovement of HRQoL was defined as an AFEQT-OS score at 1 year minus an AFEQT-OS score at registration was <5. AFEQT-OS indicates Atrial Fibrillation Effect on Quality of Life Overall Summary score; CA, catheter ablation; HRQoL, health-related quality of life.

predictors of HRQoL nonimprovement despite successful CA (restored sinus rhythm; Table S8).

DISCUSSION

In a large, 11-center Japanese registry of newly recognized AF, we found that almost half of the patients who underwent CA had some impairment in HRQoL at registration and showed large improvements in their reported HRQoL after 1 year, irrespective of the presence or absence of important clinical characteristics including age and comorbidities. Despite overall improvement in the average HRQoL score, approximately one-third of the patients failed to have a clinically meaningful improvement of their HRQoL after CA; notably, the trend was obvious for patients with preserved HRQoL at registration. Furthermore, female sex and left atrial diameter were predictors of patients whose HRQoL would not improve after CA.

In this study, we used data from patients with newly referred AF among an unselected population and identified potential factors for intervention to improve patient selection, and HRQoL outcomes of CA for AF should be underscored. For example, left atrial diameter is associated with atrial remodeling as well as AF recurrence after CA,[19] and this study extended the notion that left atrial diameter is also a risk factor for poor HRQoL outcomes after CA. We also found that women with AF were less likely to show improvements in HRQoL after CA. Previously, we reported that women experienced more AF-related symptoms and had worse HRQoL at registration; they were less likely to receive rhythm control treatment compared with men, and the gender gap in HRQoL tended to grow.[11] The greater HRQoL impact of AF for women may be attributed to increased sensitivity to disease and symptoms of disease manifestation, differences in the perception of illness, or lower thresholds for reporting illness burden.[20] It remains unclear what accounts for these large sex differences among patients with AF, and future studies ascertaining the psychological and physical effects and factors underlying these differences will inform clinicians in AF practice to further optimize the treatment of AF to minimize sex disparities.

HRQoL results after CA for AF in routine clinical practice is not well documented in the literature. Our HRQoL results are comparable to those observed in the CABANA trial regardless of differences in patients'

Table 2. AFEQT Outcomes at 1 Year Follow-up in Key Subgroups

Subgroup	No. of patients	1-y AFEQT Score (95% CI)*	*P* value	Patients with nonimprovement, %**	*P* value
Sex					
Male	773	89.9 (89.0–90.7)	<0.001	34.5	0.29
Female	248	86.0 (84.6–87.4)		30.9	
Age, y					
<75	899	89.2 (88.4–89.9)	0.078	33.2	0.45
≥75	122	87.2 (85.1–89.2)		36.7	
Family history of AF					
Yes	275	88.0 (86.6–89.4)	0.14	27.9	0.020
No	746	89.2 (88.4–90.1)		35.7	
Education level					
High school graduate or less	295	87.1 (85.8–88.4)	0.002	35.7	0.18
Junior college diploma	131	89.1 (87.1–91.0)		26.9	
Bachelor degree or higher	573	90.0 (89.1–90.0)		34.6	
Diagnosed at medical screening					
Yes	203	89.0 (87.7–90.4)	0.82	44.6	<0.001
No	718	88.9 (88.0–89.7)		29	
Initial visit					
Emergency department	60	89.5 (86.6–92.5)	0.67	22	0.052
Outpatient clinic	961	88.9 (88.1–89.6)		34.4	
Type of AF at registration					
First detected	19	81.8 (76.5–87.1)	0.003	66.7	<0.001
Paroxysmal	613	89.6 (88.7–90.5)		27.9	
Persistent	292	88.9 (87.5–90.2)		38.7	
Permanent	89	86.5 (73.3–89.1)		50	
Prior congestive heart failure					
Yes	76	86.3 (83.6–89.0)	0.050	25.7	0.14
No	945	89.1 (88.4–89.8)		34.2	
Prior stroke or TIA					
Yes	72	88.2 (85.4–90.9)	0.58	44.8	0.046
No	949	89.0 (88.2–89.7)		32.8	
Renal function					
eGFR ≥ 60	928	88.9 (88.2–89.7)	0.89	34.2	0.25
eGFR < 60	82	88.8 (86.2–91.3)		27.8	
Ejection fraction, %					
≤50	76	89.4 (84.3–94.6)	0.89	22.2	0.27
>50	828	89.1 (88.3–89.9)		34.5	
Left atrial size, cm					
≥4.0	609	88.3 (87.4–89.3)	0.060	39.3	<0.001
<4.0	412	89.7 (88.6–90.9)		27.8	
Use of antiarrhythmic drugs at registration					
Yes	313	89.2 (87.9–90.5)	0.61	22.1	<0.001
No	708	88.8 (87.9–89.7)		38.8	
Type of oral anticoagulants					

(*Continued*)

Table 2. Continued

Subgroup	No. of patients	1-y AFEQT Score (95% CI)*	*P* value	Patients with nonimprovement, %**	*P* value
None	137	89.2 (87.3–91.2)	0.53	38.2	0.33
Warfarin	130	87.9 (85.8–89.9)		29.7	
NOACs	754	89.0 (88.2–89.9)		33.5	
Use of diuretics at registration					
Yes	101	87.9 (85.5–90.2)	0.33	27.7	0.19
No	920	89.0 (88.3–89.8)		34.3	
Use of digitalis at registration					
Yes	44	84.8 (81.4–88.3)	0.019	38.1	0.53
No	977	89.1 (88.4–89.8)		33.4	
Presence of sick sinus syndrome					
Yes	39	85.5 (81.8–89.2)	0.063	21.1	0.094
No	982	89.0 (88.3–89.8)		34.1	
Prior catheter ablation for AF					
Yes	49	89.4 (86.1–92.6)	0.77	36.7	0.63
No	972	88.9 (88.2–89.6)		33.5	
AFEQT overall summary score at registration					
≥80	466	93.0 (91.9–94.1)	<0.001	59.9	<0.001
<80	555	85.5 (84.5–86.5)		11.4	

*Mean AFEQT-OS scores at 1 y were compared using analysis of covariance that adjusted for baseline AFEQT-OS scores except for the analysis that was stratified by baseline AFEQT-OS scores. **A nonimprovement of HRQoL was defined as AFEQT-OS score at 1-year minus AFEQT-OS score at registration was <5. AF indicates atrial fibrillation; AFEQT, Atrial Fibrillation Effect on Quality of Life; eGFR, estimated glomerular filtration rate; NOAC, non–vitamin K antagonist oral anticoagulants; and TIA, transient ischemic attack.

backgrounds.[6] Nonetheless, several subtle differences in HRQoL outcomes between the CABANA trial and the present study should be mentioned. For example, the baseline AFEQT-OS score in the KiCS-AF registry is 74.9 (SD, 18.0), approximately 10 points greater than that in the CABANA trial, but the AFEQT-OS scores

Table 3. Factors Independently Associated With Changes in AFEQT-OS Scores Within 1 Year

Factor	Result of a linear regression model*			
	Estimated change from baseline	95% CI		*P* value
		Lower limit	Upper limit	
Female sex (vs male sex)	3.72	−5.67	−1.78	<0.001
Age, y, >75	−1.29	−3.58	1.01	0.27
Family history of AF	−1.13	−2.79	0.53	0.18
Education level (high school graduate or less vs or higher)	−1.77	−3.46	−0.07	0.04
Diagnosed at medical screening	0.13	−1.31	1.56	0.86
Initial visit at emergency department (vs outpatient clinic)	−0.86	−3.93	2.20	0.58
Paroxysmal AF (vs others)	1.05	−0.58	2.67	0.21
Prior congestive heart failure	−2.04	−5.18	1.10	0.20
Prior stroke or TIA	−0.32	−3.07	2.42	0.82
Sick sinus syndrome	−3.21	−7.60	1.18	0.15
Use of AADs at registration	−0.06	−1.84	1.72	0.95
Use of digitalis at registration	−3.27	−7.79	1.24	0.16
Left atrial size (per 1-cm increase)	−1.39	−2.58	−0.21	0.02
Baseline AFEQT-OS score (per 1-point increase)	−0.74	−0.79	−0.68	<0.001

AAD indicates antiarrhythmic drug; AF, atrial fibrillation; AFEQT-OS, Atrial Fibrillation Effect on Quality of Life Overall Summary score; and TIA, transient ischemic attack.

*Dependent variable; changes in AFEQT-OS score (continuous variable) defined as AFEQT-OS score at 1 year minus AFEQT-OS score at registration.

Table 4. Factors Independently Associated With Nonimprovement in HRQoL After Catheter Ablation

Factor	Odds ratio	95% CI		*P* value
		Lower limit	Upper limit	
Female sex (vs male sex)	1.89	1.23	2.88	<0.001
Age, y, >75	1.53	0.95	2.47	0.08
Family history of AF	0.96	0.66	1.39	0.82
Education level (high school graduate or less vs or higher)	1.29	0.90	1.85	0.17
Diagnosed at medical screening	0.83	0.58	1.19	0.32
Initial visit at emergency department (vs outpatient clinic)	1.43	0.69	2.99	0.34
Paroxysmal AF (vs others)	0.94	0.65	1.36	0.76
Prior congestive heart failure	0.75	0.40	1.42	0.38
Prior stroke or TIA	1.79	1.00	3.20	0.05
Sick sinus syndrome	0.58	0.24	1.41	0.23
Use of AADs at registration	0.92	0.61	1.37	0.67
Use of digitalis at registration	1.89	0.79	4.53	0.15
Left atrial size (per 1-cm increase)	1.60	1.23	2.08	<0.001
Baseline AFEQT-OS score (per 1-point increase)	1.12	1.09	1.14	<0.001

AAD indicates anti-arrhythmic drug; AF, atrial fibrillation; AFEQT-OS, Atrial Fibrillation Effect on Quality Of Life Overall Summary score; and TIA, transient ischemic attack.

*Dependent variable; patients without a clinically meaningful improvement of HRQoL (categorical variable); defined as change in AFEQT-OS score within 1 year, AFEQT-OS score at 1 year minus AFEQT-OS score at registration is <5 point.

at the 1-year follow-up in both studies were comparable. The underlying reasons for these discrepancies are not wholly clear, yet may relate to differences between patients treated in routine clinical practice and those in the randomized control trials. In our study, only one-third of the patients were treated using AADs at registration, which is lower than the proportion in the CABANA trial,[6] and almost half of the patients had no AADs before the CA procedures. Japanese medical care is universally covered under social health insurance to ensure easy access to health care including visits to secondary or tertiary referral hospitals based on patients' request.[21] In addition, in Japan, employers have a legal obligation to provide annual health examinations that include a 12-lead ECG to employees and their families.[22] For nonemployed or retired residents, the government provides access to annual health examinations, although attendance is optional. Therefore, patients diagnosed at medical screening would be less likely to be symptomatic, have a severe substrate, and have impaired HRQoL, than those diagnosed at the clinic or emergency room. These differences in healthcare systems might have led to differences in the range of patients with AF that underwent CA. Although, undoubtedly, a few patients in the KiCS-AF registry were at an even higher risk than those included in the pivotal trials (eg, undergoing dialysis or surgical maze procedure), the typical patient treated in routine clinical practice appears to be at a somewhat lower risk than the trial participants and had fewer comorbidities that might hinder improvement of HRQoL after the procedure. Additionally, ongoing improvements in patient selection, procedural techniques, and postprocedural care are likely to have contributed to an advanced health status improvement after CA.

A substantial number of patients in the KiCS-AF registry and CABANA trial did not have an HRQoL improvement after CA. For example, consistent with the present study's findings, sensitivity analyses in the CABANA trial showed that 15% of the patients in the CA group had AFEQT-OS scores <70 points (eg, severely symptomatic) at the 12-month follow-up, and patients with higher AFEQT-OS score at registration were less likely to have improved HRQoL.[6] These observations, including ours, suggested discordance in the recognition of AF symptom burdens by physicians. We previously reported that discordance in the recognition of AF symptom burden by physicians was frequent, and treatment in an ablation facility was an independent predictor for physicians' apparent overrecognition.[23] Although AF-related symptoms were likely to be initially perceived in an ablation facility, a considerable number of patients have experienced symptoms that could be somewhat atypical and often mixed up with other comorbidities. Use of objective assessments (eg, AFEQT) may be essential in tailoring management for patients with AF to further improve the selection of patients for CA and their HRQoL.[15]

Limitations

Several limitations should be acknowledged. First, nonrandomized observational research involves inherent limitations, but it is the best way to describe the current treatment patterns and outcomes of care. There is likely to be unmeasured confounding variables, such as depression, frailty, or economic status, that may have had an impact on patient-reported HRQoL. Second, long-term HRQoL outcomes were not included in the KiCS-AF registry data; thus, their associations with long-term HRQoL could not be examined. Although the CABANA trial examined annual patient-reported HRQoL up to 5 years, patient-reported HRQoL changed dramatically within the first year and then remained virtually unchanged after the 1-year follow-up. Therefore, our 1-year follow-up might have been a sufficient period of time for examining the HRQoL benefits of CA. Third, the electrocardiography data were obtained only once at the 1-year follow-up visit; thus, we were not able to capture a recurrence of AF completely, and the definition of successful CA in our study might not reflect the clinical success of the procedure. Fourth, our numbers were relatively small, particularly for analyses of clinical outcomes. Finally, not all AF patients in Japan participated in the KiCS-AF registry, and the sampling bias and the generalizability of the study results to Japan is a potential concern, but we were very inclusive of those patients presenting to participating centers with new-onset AF. Regardless, we believe this is one of the most representative Japanese databases of AF patients, and our results comprise the most complete assessment of current practice patterns and HRQoL outcomes in Japan.

CONCLUSIONS

Our findings are encouraging and suggest that the HRQoL benefits of CA for AF that have been previously demonstrated within carefully designed and conducted clinical trials can be extended to unselected AF populations. Previous observations, including ours, highlight the need for objective and quantitative evaluation of patients' HRQoL in the clinical field to further improve patient selection and maximize the HRQoL outcomes of CA for AF. Additionally, future investigation focusing on the causal factors underlying patients of the female sex or with left atrial diameter may aid in improving the treatment of these patients.

ARTICLE INFORMATION

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Supplementary Material

Data S1–S3
Tables S1–S8
Figure S1

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Supplemental Material

Data S1. The classification and definition for type of AF in the KiCS-AF study.

First detected AF: patients with new symptoms attributable to AF.

Paroxysmal AF: patients with recurrent AF (≥ 2 episodes) that terminated spontaneously or with intervention within 7 days of onset.

Persistent AF: patients with AF sustained beyond 7 days, necessitating pharmacological or electrical cardioversion.

Permanent AF: patients with continuous AF of greater than one year duration, in which cardioversion has either failed or not been attempted.

Data S2. List of covariates for the multivariable models.

sex, age, family history, low education level (e.g., high school graduate or less; patients with junior college diploma or high degree as reference), diagnosed at medical screening, initial visit at emergency department (patients visited the outpatient clinic as reference), type of AF, prior congestive heart failure, prior stroke or transient ischemic attack, sick sinus syndrome, use of AADs at registration, use of digitalis at registration, left atrium diameter (as a continuous variable), and baseline AFEQT-OS score (as a continuous variable).

Data S3. KiCS-AF registry.

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Table S1. Baseline Characteristics of Patients with and without AFEQT Data.

Characteristics	Patients with AFEQT data n=1,021, no. (%)	Patient without AFEQT data n=76, no.(%)	P value
Age, median (IQR), years	64 (56-70)	60 (49-68)	.001
Men	757(75.4)	57(85.1)	.073
Family history of atrial fibrillation	269(26.8)	7(10.6)	.004
Education level			
High school graduate or less	287(29.2)	17(26.6)	.82
Junior college diploma	131(13.3)	10(15.6)	
Bachelor degree or more	564(57.4)	37(57.8)	
BMI, median, kg/m^2 (IQR)	23.6 (21.5-26.1)	23.6 (21.5-25.1)	.47
Medical history			
Smoking	167(16.6)	13(19.4)	.55
Hypertension	525(52.3)	25(37.3)	.018
Diabetes mellitus	121(12.1)	5(7.5)	.25
Dyslipidemia	354(35.3)	13(19.4)	.008
Heart failure	70(7.0)	1(1.5)	.081
Sick sinus syndrome	38(3.8)	0(.0)	.10
Obstructive sleep apnea	38(3.8)	2(3.0)	.73
Stroke or TIA	67(6.7)	6(9.0)	.47
Gastrointestinal bleeding	12(1.2)	0(.0)	.66
CKD (eGFR<60 ml/min)	79(8.0)	4(6.2)	.60
CKD on HD	5(.5)	0(.0)	.56
Peripheral artery disease	24(2.4)	0(.0)	.20
Coronary artery disease	45(4.5)	2(3.0)	.56
Prior valve surgery	6(0.6)	0(.0)	.81
BNP, median, pg/ml, (IQR)	71.6 (30.6-147.4)	36.0 (15.9-86.2)	.001
CHA_2DS_2-VASc score, median (IQR)	2 (1-3)	1 (0-2)	<0.001
LVEF, median, % (IQR)	60 (60-60)	60 (60-60)	.93
LA diameter, median, cm (IQR)	4.0 (3.5-4.4)	3.9 (3.3-4.3)	.084
Type of visit			

Diagnosed at health screening	296(29.5)	26(38.8)	.10
Referral from emergency department	59(5.9)	5(7.5)	.59
Type of AF			
First detected/new onset	18(1.8)	1(1.5)	.76
Paroxysmal	607(60.5)	45(67.2)	
Persistent	284(28.3)	15(22.4)	
Permanent	87(8.7)	6(9.0)	
Current drug therapy			
β-blockers	511(50.9)	33(49.3)	.79
ACE inhibitors/ARBs	323(32.2)	15(22.4)	.095
Calcium-channel blockers	402(40.0)	12(17.9)	<0.001
Digoxin	42(4.2)	1(1.5)	.27
Diuretics	94(9.4)	3(4.5)	.17
Currently using antiarrhythmic drugs			
Oral anticoagulants			
None	136(13.5)	10(14.9)	.83
Warfarin	128(12.7)	7(10.4)	
Direct oral anticoagulants	740(73.7)	50(74.6)	
Antiplatelet therapy	78(7.8)	4(6.0)	.59
Prior interventional therapy for AF			
Catheter ablation of AF	49(4.9)	3(4.5)	.88
Surgical maze	2(.2)	0(.0)	.71

KiCS-AF, the Keio interhospital Cardiovascular Studies-atrial fibrillation; IQR, interquartile range; SD, standard deviation; BMI, body mass index; TIA, transient ischemic attack; CKD, chronic kidney disease; HD, hemodialysis; coronary artery bypass grafting; BNP, brain natriuretic peptide; LVEF, left ventricular ejection fraction; LA, left atrium; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

Table S2. Factors Independently Associated with Changes in AFEQT-OS Scores Within 1 Year (when baseline AFEQT-OS score was entered as dichotomous variable [<80 or ≥80])

Factor	Estimated change from baseline	95% confidence interval		
		Lower limit	Upper limit	P Value
Female (vs male)	-2.26	-4.55	0.03	.054
Age (more than 75 years old)	-0.36	-3.64	2.91	.82
Family history of AF	-0.53	-2.47	1.41	.59
Education level (High school graduate or less vs or high)	-3.34	-5.33	-1.36	.001
Diagnosed at medical screening	-1.72	-3.27	-0.16	.030
Initial visit at emergency department (vs outpatient clinic)	-2.62	-6.57	1.31	.19
Paroxysmal AF (vs others)	1.23	-0.68	3.14	.20
Prior congestive heart failure	-3.04	-6.86	0.77	.11
Prior stroke or TIA	-0.08	-3.39	3.22	.95
Sick sinus syndrome	-1.39	-5.91	3.12	.54
Use of AADs at registration	1.96	-0.20	4.13	.076
Use of digitalis at registration	-4.14	-9.59	1.30	.13
LA size (per 1 cm increase)	-1.43	-2.80	-0.05	.041
Patients with preserved HRQoL (AFEQT-OS score ≥80 vs <80)	-19.8	-21.4	-18.1	<0.001

*Dependent variable; changes in AFEQT-OS score (continuous variable) defined as AFEQT-OS score at 1-year minus AFEQT-OS score at registration

AF, atrial fibrillation; TIA, transient ischemic attack: AAD, anti-arrhythmic drug: LA, left atrium: HRQoL, health-related quality of life: AFEQT-OS, Atrial Fibrillation Effect on Quality of Life Overall Summary score.

Table S3. **Factors Independently Associated with Non-Improvement in HRQoL After Catheter Ablation (when baseline AFEQT-OS score was entered as dichotomous variable [<80 or ≥80]).**

Factor	Odds ratio	95% confidence interval		P Value
		Lower limit	Upper limit	
Female (vs male)	1.57	1.05	2.33	.026
Age (more than 75 years old)	1.62	1.03	2.53	.034
Family history of AF	0.89	0.62	1.28	.54
Education level (High school graduate or less vs or high)	1.43	1.01	2.03	.044
Diagnosed at medical screening	0.95	0.66	1.36	.80
Initial visit at emergency department (vs outpatient clinic)	1.34	0.65	2.75	.41
Paroxysmal AF (vs others)	0.87	0.61	1.25	.47
Prior congestive heart failure	0.66	0.35	1.23	.19
Prior stroke or TIA	1.59	0.91	2.76	.097
Sick sinus syndrome	0.48	0.20	1.15	.10
Use of AADs at registration	0.79	0.54	1.16	.24
Use of digitalis at registration	2.03	0.90	4.58	.088
LA size (per 1 cm increase)	1.59	1.23	2.04	<0.001
Patients with preserved HRQoL (AFEQT-OS score ≥80 vs <80)	12.6	8.77	18.1	<0.001

*Dependent variable; patients without a clinically meaningful improvement of QOL (categorical variable); defined as change in AFEQT-OS score within 1 year, AFEQT-OS score at 1-year minus AFEQT-OS score at registration is less than 5 point.

AF, atrial fibrillation; TIA, transient ischemic attack: AAD, anti-arrhythmic drug: LA, left atrium: HRQoL, health-related quality of life: AFEQT-OS, Atrial Fibrillation Effect on Quality of Life Overall Summary score.

Table S4. Sensitivity Analysis Excluding Patients with Preserved HRQoL at Registration (e.g., patients with AFEQT-OS score ≥80) for a Multivariable Linear Regression Analysis

Factor	Estimated change from baseline	95% confidence interval		
		Lower limit	Upper limit	P Value
Female (vs male)	-3.71	-6.45	-0.98	.008
Age (more than 75 years old)	-0.04	-3.29	3.20	.97
Family history of AF	-1.23	-3.66	1.20	.32
Education level (High school graduate or less vs or high)	-1.52	-4.19	1.14	.26
Diagnosed at medical screening	0.14	-2.51	2.79	.91
Initial visit at emergency department (vs outpatient clinic)	-0.30	-4.67	4.06	.89
Paroxysmal AF (vs others)	1.19	-1.60	3.99	.40
Prior congestive heart failure	-2.43	-7.12	2.25	.31
Prior stroke or TIA	1.13	-3.56	5.83	.63
Sick sinus syndrome	-4.26	-10.35	1.84	.17
Use of AADs at registration	-0.18	-2.71	2.33	.88
Use of digitalis at registration	-5.30	-11.94	1.33	.11
LA size (per 1 cm increase)	-2.10	-4.03	-0.17	.03
Baseline AFEQT-OS score (per 1-point increase)	-0.71	-0.81	-0.60	<0.001

*dependent variable; changes in AFEQT-OS score (continuous variable) defined as AFEQT-OS score at 1-year minus AFEQT-OS score at registration

AF, atrial fibrillation; TIA, transient ischemic attack: AAD, anti-arrhythmic drug: LA, left atrium: AFEQT-OS, Atrial Fibrillation Effect on Quality of Life Overall Summary score.

Table S5. Sensitivity Analysis Excluding Patients with Preserved HRQoL at registration (e.g., patients with AFEQT-OS score ≥80) for the Multivariable Logistic Regression Analysis.

Factor	Odds ratio	95% confidence interval		
		Lower limit	Upper limit	P Value
Female (vs male)	1.96	1.08	3.58	.03
Age (more than 75 years old)	0.64	0.26	1.60	.34
Family history of AF	0.74	0.40	1.38	.34
Education level (High school graduate or less vs or high)	1.10	0.60	2.04	.75
Diagnosed at medical screening	1.09	0.54	2.22	.81
Initial visit at emergency department (vs outpatient clinic)	1.25	0.38	4.09	.72
Paroxysmal AF (vs others)	1.71	0.82	3.56	.15
Prior congestive heart failure	0.46	0.17	1.20	.11
Prior stroke or TIA	0.86	0.25	2.96	.81
Sick sinus syndrome	0.69	0.14	3.32	.64
Use of AADs at registration	0.83	0.45	1.56	.57
Use of digitalis at registration	2.65	0.95	7.40	.06
LA size (per 1 cm increase)	2.57	1.64	4.03	<0.001
Baseline AFEQT-OS score (per 1-point increase)	1.03	1.00	1.06	.03

*dependent variable; patients without a clinically meaningful improvement of QOL (categorical variable); defined as change in AFEQT-OS score within 1 year, AFEQT-OS score at 1-year minus AFEQT-OS score at registration is less than 5 point. AF, atrial fibrillation; TIA, transient ischemic attack: AAD, anti-arrhythmic drug: LA, left atrium: AFEQT-OS, Atrial Fibrillation Effect on Quality of Life Overall Summary score.

Table S6. AFEQT Outcomes at 1 Year After Catheter Ablation Across Patients in Earlier or Delayed Fashion.

AFEQT Measure	No. of Patients	Baseline Score, Mean (SD)	Follow-up Score, Mean (SD)	Changes From Baseline (95% CI)
Patients underwent CA in an earlier fashion				
Overall summary	537	74.5 (17.9)	88.7 (13.2)	14.2 (12.6-15.6)
Symptom	533	74.9 (20.4)	89.3 (15.3)	14.4 (12.4-16.2)
Daily activities	533	75.1 (21.7)	88.4 (16.2)	13.3 (11.4-15.1)
Treatment concerns	527	73.2 (18.5)	88.4 (13.5)	15.2 (13.6-16.7)
Treatment satisfaction	421	62.9 (20.7)	84.8 (18.7)	21.9 (19.5-24.2)
Patients underwent CA in a delayed fashion				
Overall summary	480	75.3 (18.1)	89.0 (11.8)	13.7 (12.1-15.2)
Symptom	477	76.5 (19.5)	90.6 (13.6)	14.1 (12.2-15.9)
Daily activities	478	76.9 (23.0)	89.6 (14.6)	12.7 (10.7-14.5)
Treatment concerns	479	71.8 (18.9)	87.3 (12.9)	15.5 (13.7-17.2)
Treatment satisfaction	374	60.3 (20.7)	83.2 (18.7)	22.9 (20.2-25.6)

AFEQT, Atrial Fibrillation Effect on Quality of Life.

* All changes from baseline were significant ($P < .001$) based on paired t test.

** Scores range from 0 to 100, with higher scores indicating less symptom burden and better quality of life.

Table S7. AFEQT Outcomes at 1 Year After Catheter Ablation Across Patients with and without a Successful Catheter Ablation.

AFEQT Measure	No. of Patients	Baseline Score, Mean (SD)	Follow-up Score, Mean (SD)	Changes From Baseline (95% CI)
Patients with a successful catheter ablation				
Overall summary	771	75.5 (17.8)	91.1 (10.5)	15.6 (14.3-16.7)
Symptom	766	75.8 (20.0)	92.0 (13.0)	16.2 (14.6-17.7)
Daily activities	766	76.8 (22.2)	91.3 (13.1)	14.5 (12.9-16.0)
Treatment concerns	764	73.2 (18.3)	90.1 (11.6)	16.9 (15.6-18.1)
Treatment satisfaction	602	62.2 (20.9)	88.7 (14.7)	26.5 (24.5-28.4)
Patients without a successful catheter ablation				
Overall summary	250	73.0 (18.5)	81.8 (15.6)	8.8 (6.7-10.9)
Symptom	248	75.3 (20.0)	83.2 (16.8)	7.9 (5.4-10.4)
Daily activities	249	73.4 (22.5)	81.5 (19.5)	8.1 (5.4-10.7)
Treatment concerns	246	70.5 (19.6)	80.9 (15.4)	10.4 (7.9-12.8)
Treatment satisfaction	197	60.0 (19.9)	70.0 (22.3)	10.0 (6.2-13.7)

AFEQT, Atrial Fibrillation Effect on Quality of Life.

* All changes from baseline were significant ($P < .001$) based on paired t test.

** Scores range from 0 to 100, with higher scores indicating less symptom burden and better quality of life.

*** A successful CA was defined as patients with maintenance of sinus rhythm at 1-year follow-up without the use of anti-arrhythmic drugs, and who did not aware of having an episode of AF within 1 month when answering the AFEQT questionnaire at follow-up.

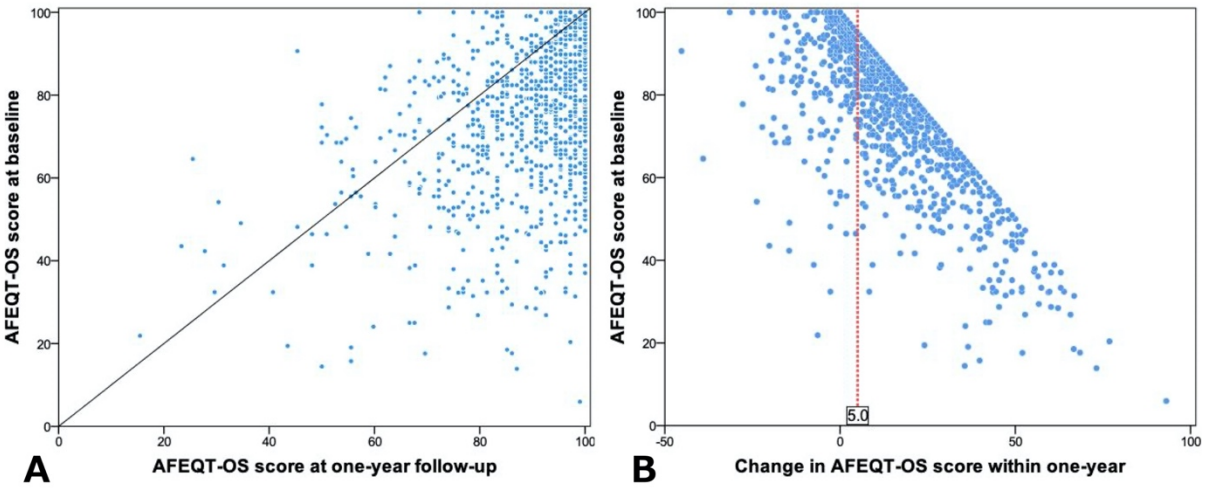
Table S8. A Sub-group analysis for Patients with a Successful Catheter Ablation for a Multivariable Logistic Regression model.

Factor	Odds ratio	95% confidence interval		
		Lower limit	Upper limit	P Value
Female (vs male)	2.04	1.19	3.52	.010
Age (more than 75 years old)	2.43	1.29	4.57	.006
Family history	0.96	0.59	1.56	.89
Education level (High school graduate or less vs or high)	1.72	1.07	2.75	.023
Diagnosed at medical screening	0.83	0.54	1.26	.38
Initial visit at emergency department (vs outpatient clinic)	1.54	0.62	3.85	.34
Paroxysmal AF (vs others)	1.10	0.71	1.72	.65
Prior congestive heart failure	0.84	0.35	2.01	.70
Prior stroke or TIA	1.60	0.85	3.03	.14
Sick sinus syndrome	1.18	0.42	3.25	.74
Use of AADs at registration	0.80	0.48	1.35	.41
Use of digitalis at registration	1.17	0.46	2.95	.73
LA size (per 1 cm increase)	1.47	1.06	2.05	.020
Baseline AFEQT-OS score (per 1-point increase)	1.16	1.12	1.20	<0.001

*dependent variable; patients without a clinically meaningful improvement of QOL (categorical variable); defined as change in AFEQT-OS score within 1 year, AFEQT-OS score at 1-year minus AFEQT-OS score at registration is less than 5 point.

** A successful CA was defined as patients with maintenance of sinus rhythm at 1-year follow-up without the use of anti-arrhythmic drugs, and who did not aware of having an episode of AF within 1 month when answering the AFEQT questionnaire at follow-up. AF, atrial fibrillation; TIA, transient ischemic attack: AAD, anti-arrhythmic drug: LA, left atrium: AFEQT-OS, Atrial Fibrillation Effect on Quality of Life Overall Summary score.

Figure S1. A Scatterplot of AFEQT-OS Scores at Registration and 1-year Follow-up.



A. Relationship between the baseline and 1-year follow-up AFEQT-overall summary scores.

B. Relationship between the baseline AFEQT-OS scores and changes in AFEQT-OS scores within 1-year.*A non-improvement of HRQOL was defined as an AFEQT-OS score at 1-year minus an AFEQT-OS score at registration, which was <5 (the threshold is indicated by the red dotted line).

AFEQT-OS, Atrial Fibrillation Effect on Quality of Life-overall summary.