

Differences in Quality of Life Between Atrial Fibrillation Patients with Low Stroke Risk Treated With and Without Catheter Ablation

Ying Bai, MD; Rong Bai, MD, PhD; Jia-Hui Wu, MD, PhD; Ting Zhang, MD, PhD; Nian Liu, MD, PhD; Xu-Bo Shi, MD, PhD; Xin-Yao Liu, MD; Xiao-Hui Liu, MD, PhD; Xin Du, MD, PhD; Jian-Zeng Dong, MD; Chang-Sheng Ma, MD, PhD

Background—Impacts of a single radiofrequency ablation (RFA) on quality of life (QoL) were not well investigated in atrial fibrillation (AF) patients with low stroke risk.

Methods and Results—Nine hundred AF patients with low CHADS₂ score (ie, CHADS₂ ≤1) who completed both a baseline and 6-month Atrial Fibrillation Effect on Quality-of-life (AFEQT) questionnaire were selected from The Chinese Atrial Fibrillation Registry between 2011 and 2013. A final cohort of 222 patients was constructed after a propensity score matching with 74 in the RFA group and 148 in the non-RFA group. Domains of AFEQT were balanced at baseline between the 2 groups. No statistically significant differences were noted in QoL (all $P>0.05$) when AFEQT at 6 months was compared between groups, except for the symptoms domain (83.07 ± 12.37 units in the RFA group vs. 77.68 ± 17.14 units in the non-RFA group; $P=0.008$) and treatment satisfaction domain (76.34 ± 14.92 units in the RFA group vs. 70.38 ± 16.81 units in the non-RFA group; $P=0.01$). Within-group changes in all domains and the global score of the questionnaire were moderate to large, whereas between-group comparisons in baseline to 6-month changes and QoL at 6 months were small to moderate according to Cohen effect sizes.

Conclusions—QoL was balanced at baseline and improved at 6 months in both groups from this observational propensity-matched cohort based on the AFEQT questionnaire. However, RFA treatment was only associated with small-to-moderate superiorities over non-RFA treatment. The role of RFA in QoL improvement among AF patients with low stroke risk requires further research. (*J Am Heart Assoc.* 2015;4:e002130 doi: 10.1161/JAHA.115.002130)

Key Words: atrial fibrillation effect on quality-of-life questionnaire • atrial fibrillation • CHADS₂ score • quality of life

Atrial fibrillation (AF) is a common cardiac arrhythmia associated with a broad range of symptoms and quality-of-life (QoL) impairment.¹ It can also lead to some vital complications, such as stroke,² which can boost a great reduction of QoL on patients. Some studies have shown that a reduced incidence of stroke was observed in patients treated with radiofrequency ablation (RFA),^{3,4} which may bring

benefits for AF patients, especially for those with high stroke risk (ie, high CHADS₂ score).

Currently, RFA, as an effective AF treatment, becomes the most robust method for symptoms relief and QoL improvement, which are the main treatment objectives for AF ablation.^{5–7} Therefore, the clinical relevance of AF management with RFA is increasingly highlighted, as reflected in recent AF guidelines.⁸ Postablation QoL improvement has been demonstrated in several previous studies.^{6,9,10} However, most of the studied population were composed of AF patients with both low and high risk of stroke. To our knowledge, no reports were found to assess the effects of RFA on the changes of symptoms and QoL in AF patients with low stroke risk (ie, low CHADS₂ score) so far, though there is still a residual stroke rate of 1.9% (CHADS₂=0) and 2.8% (CHADS₂=1) every year.⁵ We hypothesized that AF patients with low stroke risk could benefit from RFA treatment as well compared to non-RFA treatment. To address these questions, we evaluated the impacts of ablation on patients with low stroke risk by comparing the results of Atrial Fibrillation Effect on Quality-of-life (AFEQT) questionnaire¹¹ in its Chinese version at 6 months based on a propensity-score matching cohort. We also conducted within- and between-group

From the Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, National Clinical Research Center for Cardiovascular Diseases (Y.B., R.B., J.-H.W., T.Z., N.L., X.-H.L., X.D., J.-Z.D., C.-S.M.) and Cardiovascular Center, Beijing Tongren Hospital, Capital Medical University (X.-B.S., X.-Y.L.), Beijing, China.

Accompanying Appendix S1, Tables S1 through S3 and Figures S1 through S3 are available at <http://jaha.ahajournals.org/content/4/9/e002130/suppl/DC1>

Correspondence to: Chang-Sheng Ma, MD, PhD, Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, National Clinical Research Center for Cardiovascular Diseases, No. 2, Anzhen Road, Chaoyang District, Beijing 100029, China. E-mail: chshma@vip.sina.com

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comparisons about changes in domains and the global score of AFEQT for further confirmation.

Methods

The Chinese Atrial Fibrillation Registry (CAFR) prospectively enrolled consecutive AF patients from multiple centers, confirmed by objective tests such as 12-lead electrocardiograms (ECGs) or 24-hour Holter monitorings before registration. Data collected were reported as baseline characteristics in Table 1. All patients provided written consent to participate in the registry. The protocol was approved by the institutional ethics committee first in Beijing Anzhen Hospital and then in each participating hospital.

Studied Population and Comparison Groups

Because only tertiary hospitals provided catheter ablation facilities, data of CAFR from 4 tertiary hospitals in Beijing, China, between April 2011 and February 2013 were selected to reduce confounders caused by different centers (Beijing Anzhen Hospital, Beijing Tongren Hospital, Beijing Chaoyang Hospital, and Peking University Third Hospital). Patients with baseline CHADS₂ scores (congestive heart failure [CHF]: 1 score, hypertension [HTN]: 1 score, age ≥ 75 years: 1 score, diabetes mellitus [DM]: 1 score, previous stroke or transient ischemic attack [TIA]: 2 scores) ≤ 1 were considered eligible for the study regardless of their AF types.

AFEQT questionnaires with at least 50% of responses finished for each domain were used for final analyses. Patients who completed both baseline and 6-month AFEQT questionnaires met the inclusion criteria. Those who received RFA other than circumferential pulmonary vein isolation, which was described precisely before, were excluded.¹² To minimize the variation of the length of the follow-up, the date of baseline was defined as the index date. Patients who underwent RFA more than 5 days before or after the index date were excluded. The follow-up started from the index date to 6 months ± 5 days through outpatient, telephone, visiting at home every month, or admission into hospital whenever necessary. Patients were advised to record any possible symptomatic episodes of AF by doing 12-lead ECGs in the nearest clinics. Furthermore they were routinely scheduled to do 12-lead ECGs or 24-hour Holter monitorings at every follow-up regardless of AF-related symptoms.

Patients in the following cases were excluded: patients with AF of rheumatoid valvular diseases; age younger than 18 years; previous ablation for AF; life expectancy of less than 6 months; patients who switched to ablation therapy when they refused the procedure at inclusion; and patients who received a second ablation during the 6-month follow-up. The full cohort was then divided into those who received a single RFA (RFA group) and those who did not (non-RFA group).

Propensity Score Adjustment

To reduce the impact of selection bias on the estimation of treatment effects, baseline differences in AF patients with low CHADS₂ score were adjusted by propensity score matching, which was based on 1:2 matching within a prespecified caliper width and without replacement. We estimated the propensity score by regressing treatment status based on the covariates using a multinomial logistic regression model. The matched samples were obtained by matching subjects on the logit of the propensity score by nearest neighbor matching, with caliper of 0.6 of the pooled standard deviations of the logit of the propensity score.¹³

Covariates for propensity score matching were baseline characteristics of getting AF and adjustment confounders and biases according to previous literature¹⁴ and earlier knowledge. They included age, sex, type of AF, admission type, educational status, insurance plan type, European Heart Rhythm Association (EHRA) classification, New York Heart Association (NYHA) stratification, clinical history (history of HTN, DM, myocardial infarction, coronary heart diseases, hypertrophic cardiomyopathy, dilated cardiomyopathy, thyroid disease, and lung diseases), echocardiographic parameters (left atrial diameter, left ventricular [LV] end-diastolic diameter, and LVEF), and successive medications for rate or rhythm control, as well as anticoagulant drugs.

Outcomes and AFEQT Questionnaire

The primary outcome was the comparison of each domain and the global score of AFEQT questionnaire at 6 months between groups based on the propensity score matched cohorts. Secondary outcomes were: (1) changes from baseline to 6 months within groups and the between-group differences of changes in each domain and the global score of AFEQT questionnaire based on the propensity score matched cohorts. (2) AF recurrence rate in RFA group and rate of treatment failure in the non-RFA group. AF recurrence was defined as documented AF/atrial flutter/atrial tachycardia (AT) ≥ 30 seconds by 24-hour Holter monitorings or 12-lead ECGs beyond 3-month blanking period and within 6-month follow-up postablation.¹⁵ Documented AF of at least twice in the non-RFA group was considered as treatment failure during the 6-month period.¹⁶ (3) Complications or adverse effects related to the procedure or medicines used during the 6-month follow-up.

The AFEQT questionnaire (see Appendix S1) is an AF-specific QoL evaluation according to its authors' descriptions,¹¹ which adequately correlates with other commonly used, well-established questionnaires. The impact of AF on their QoL during the previous 4 weeks are indicated with 20 items from 4 individual domains, including symptoms

Table 1. Baseline Characteristics of Patients Before and After Matching

	Before Matching		P Value	After Matching		P Value
	RFA N=144	Non-RFA N=722		RFA N=74	Non-RFA N=148	
Sex			0.37			0.92
Male	91 (63.19%)	427 (59.14%)		47 (63.51%)	93 (62.84%)	
Female	53 (36.81%)	295 (40.86%)		27 (36.49%)	55 (37.16%)	
Age, y	61.20±10.12	64.46±9.79	<0.001	61.82±8.90	62.42±10.52	0.66
Insurance plan type			<0.001			0.15
Socialized	105 (72.92%)	534 (73.96%)		55 (74.32%)	108 (72.97%)	
Self-paying	18 (12.5%)	169 (23.41%)		10 (13.51%)	31 (20.95%)	
Other	21 (14.58%)	19 (2.63%)		9 (12.16%)	9 (6.08%)	
Education ratings			0.76			0.99
High school or below	88 (61.11%)	473 (65.51%)		45 (60.81%)	92 (62.16%)	
Undergraduate	35 (24.31%)	160 (22.16%)		15 (20.27%)	28 (18.92%)	
Graduate or above	3 (2.08%)	15 (2.08%)		2 (2.7%)	5 (3.38%)	
Unknown	18 (12.5%)	74 (10.25%)		12 (16.22%)	23 (15.54%)	
Admission type			<0.001			0.14
Inpatient	129 (89.58%)	301 (41.69%)		62 (83.78%)	111 (75%)	
Outpatient	15 (10.42%)	421 (58.31%)		12 (16.22%)	37 (25%)	
AF type			<0.001			0.03
Paroxysmal	95 (65.97%)	338 (46.81%)		52 (70.27%)	81 (54.73%)	
Nonparoxysmal	49 (34.03%)	384 (53.19%)		22 (29.73%)	67 (45.27%)	
Comorbidities*						
HTN	72 (50%)	361 (50%)	1.00	38 (51.35%)	82 (55.41%)	0.57
DM	5 (3.47%)	33 (4.57%)	0.56	4 (5.41%)	5 (3.38%)	0.72
MI	6 (4.17%)	45 (6.23%)	0.34	5 (6.76%)	7 (4.73%)	0.75
CAD	12 (8.33%)	91 (12.6%)	0.15	6 (8.11%)	15 (10.14%)	0.63
COPD	5 (3.47%)	75 (10.39%)	0.009	3 (4.05%)	6 (4.05%)	1.00
EHRA stratification			0.01			0.32
EHRA I	17 (11.81%)	105 (14.54%)		11 (14.86%)	13 (8.78%)	
EHRA II	67 (46.53%)	416 (57.62%)		30 (40.54%)	77 (52.03%)	
EHRA III	57 (39.58%)	187 (25.9%)		30 (40.54%)	54 (36.49%)	
EHRA IV	3 (2.08%)	14 (1.94%)		3 (4.05%)	4 (2.7%)	
NYHA stratification			<0.001			0.71
NYHA I	128 (88.89%)	403 (55.82%)		59 (79.73%)	113 (76.35%)	
NYHA II	15 (10.42%)	238 (32.96%)		14 (18.92%)	34 (22.97%)	
NYHA III or IV	1 (0.69%)	81 (11.22%)		1 (1.35%)	1 (0.68%)	
Echocardiographic parameters						
LAD	38.77±5.20	40.69±6.76	<0.001	39.09±6.94	38.84±6.23	0.79
LVDD	47.24±5.69	48.66±6.57	0.008	46.93±8.16	47.78±7.68	0.46
LVEF	65.32±9.11	62.38±8.73	<0.001	64.21±9.66	63.63±9.31	0.67
CHADS ₂ scores			0.03			0.84
CHADS ₂ =0	62 (43.06%)	241 (33.38%)		28 (37.84%)	54 (36.49%)	
CHADS ₂ =1	82 (56.94%)	481 (66.62%)		46 (62.16%)	94 (63.51%)	

Continued

Table 1. Continued

	Before Matching		P Value	After Matching		P Value
	RFA N=144	Non-RFA N=722		RFA N=74	Non-RFA N=148	
Medication						
Antiarrhythmic drugs						
Rate control	57 (39.58%)	474 (65.65%)	<0.001	33 (44.59%)	69 (46.62%)	0.78
Rhythm control	96 (66.67%)	229 (31.72%)	<0.001	42 (56.76%)	89 (60.14%)	0.63
Baseline anticoagulant drugs			<0.001			0.29
No antithrombotic drugs	93 (64.58%)	246 (34.07%)		41 (55.41%)	67 (45.27%)	
Monoantiplatelet	24 (16.67%)	302 (41.83%)		18 (24.32%)	57 (38.51%)	
Double antiplatelet	3 (2.08%)	33 (4.57%)		2 (2.7%)	5 (3.38%)	
Warfarin	20 (13.89%)	87 (12.05%)		9 (12.16%)	13 (8.78%)	
Warfarin combined with antiplatelet	4 (2.78%)	54 (7.48%)		4 (5.41%)	6 (4.05%)	

Values are given as mean±SD or numbers (percentages). CHADS₂ scores, congestive heart failure: 1 score, hypertension: 1 score, age ≥75 years: 1 score, diabetes mellitus: 1 score, previous stroke or transient ischemic attack: 2 score. AF indicates atrial fibrillation; CAD, coronary artery diseases; COPD, chronic obstructive pulmonary diseases; DM, diabetes mellitus; EHRA, European Heart Rhythm Association; HTN, hypertension; LAD, left atrium diameter; LVDD, left ventricular diastolic diameter; LVEF, left ventricular ejection fraction; MI, myocardial infarction; non-RFA, non radiofrequency ablation; NYHA, New York Heart Association; RFA, radiofrequency ablation.

*History of hypertrophic cardiomyopathy, dilated cardiomyopathy and thyroid disease were not listed because no cases matched based on propensity score matching.

(4 items), daily activities (8 items), treatment concern (6 items), and treatment satisfaction (2 items). The AFEQT questionnaire can be divided into 2 parts: evaluation of health status and treatment satisfaction. Global health status is determined based on the sum of scores of the first 3 domains. Each item is presented with a 7-point Likert response. Raw scores within each domain are transformed to a 0 to 100 scale, where a score of 0 indicates the most severe symptoms or disability and a score of 100 indicates no limitation or disability. Each domain contributes to an insight into a different aspect of patients' QoL, with higher scores representing a better life and less mental burden.

Statistical Analyses

Both in unadjusted and adjusted cohorts, descriptive variables were expressed as mean±SD or median (range), and categorical variables were given as numbers (percentages). Baseline characteristics, including baseline AFEQT domains and global score, were compared between the 2 groups using the Student *t* test or chi-squared test or Fisher's exact analysis, as appropriate.

A series of paired *t* tests were conducted to compare scores between baseline and 6 months and thus changes from baseline to 6 months of each domain and the global score within each group. Scores of all AFEQT domains and the global score at 6 months and their changes during the 6-month follow-up between the 2 propensity-matched groups were compared using an independent *t* test. The Cohen

approach of defining effect sizes of 0.2, 0.5, and 0.8 were used as indication of small, moderate, and large clinical changes for interpretation.¹⁷

The study provided at least 90% power at a 2-sided alpha level of 0.05 for a difference of a 20% score increase for the health status domains and treatment satisfaction domains of the AFEQT at 6 months.

Exploratory subgroup analyses stratified by AF type and age strata of 65 years were conducted in fear that QoL may be affected by these factors and to minimize the modification. To further confirm our findings, baseline and 6-month score of each domain and the global score of AFEQT questionnaire in AF patients with low CHA₂DS₂-VASc score (CHF: 1 score, HTN: 1 score, age ≥75 years: 2 scores, DM: 1 score, previous stroke or TIA: 2 scores, vascular disease: 1 score, age 65 to 74 years: 1 score, sex category of female: 1 score) were also compared between groups.

All tests were 2-tailed and *P*<0.05 was considered to be statistically significant. We performed all analyses using the SAS statistical package (version 9.1; SAS Institute Inc., Cary, NC) and SPSS 18.0 for Windows (SPSS, Inc., Chicago, IL).

Results

Patient Characteristics

During 2011 to 2013, 2178 patients with AF were enrolled in the CAFR from 4 tertiary hospitals. A total of 1196 (54.9%) of them were excluded for their CHADS₂ score ≥2. Another 39 (1.8%) were also excluded because their AFEQT

questionnaires were not filled either at baseline (n=11) or 6 months (n=28: 2 died, 12 were lost, and 14 failed to complete the AFEQT questionnaire at 6 months). Of the remaining patients, 43 (2.0%) were excluded because of other exclusion criteria (4 second RFA during 6-month follow-up, 21 previous ablation, and 18 switched from non-RFA to RFA during 6-month follow-up). Of 900 eligible patients, 34 (1.6%) were excluded because they did not meet the requirement that at least 50% of responses of each domain should be completed. No significant difference was noted in baseline characteristics between eligible and ineligible patients, except that eligible patients were older (Table S1).

To report this observational study transparently, a selection flow diagram consistent with the best-practice guidelines (STROBE statement) for cohort studies is listed in Figure 1. For current analysis, 866 subjects with CHADS₂ scores of 0 and 1 were included with 144 (mean age: 64.46±9.79 years; 59.14% male) in the RFA group and 722 (mean age: 61.20±12.63 years; 63.19% male) in the non-RFA group. The baseline characteristics of the 2 groups were summarized and many of them were different before adjustment (Table 1, left column). From this sample, 74 patients in the RFA group and 148 in the non-RFA group were selected based on a 1:2 matching within a prespecified caliper width. Characteristics of the final propensity-matched cohorts (RFA vs. non-RFA) are also listed in Table 1, as shown in the right column. After matching, it seemed that the characteristics were well balanced, with the only significant difference in the proportions of AF type (paroxysmal AF: 70.3% in the RFA group vs. 55.4% in the non-RFA group; $P=0.03$).

Primary Outcome

The first 3 domains and the global score of the baseline AFEQT questionnaire between groups were different before matching (Table 2, left), whereas differences disappeared after matching (Table 2, right and Figure 2A). When domains and the global score at 6 months were compared between the 2 groups (Figure 2A), the statistically significant differences were noted in the symptoms domain (83.07 ± 12.37 units in the RFA group vs. 77.68 ± 17.14 units in the non-RFA group; $P=0.008$) and the treatment satisfaction domain (76.34 ± 14.92 units in the RFA group vs. 70.38 ± 16.81 units in the non-RFA group; $P=0.01$). Differences of QoL at 6 months were small (daily activities: 0.2, treatment concern: 0.2) or moderate (symptoms: 0.4, global score: 0.35 and treatment satisfaction: 0.4) in between-group analyses using Cohen effect sizes.

QoL Changes From Baseline to 6 Months

When scores between baseline and 6 months of each domain and the global score were compared, statistically significant within-group changes were observed in each domain and the global score in both groups (all $P<0.001$), except for the treatment satisfaction domain in the non-RFA group ($P=0.10$; Figure 2A). Using the Cohen effect size to evaluate clinical importance, mean changes of treatment satisfaction in the non-RFA group was 0.3 (moderate) whereas the other domains and the global score were more than 0.8 (large), which were considered to be clinically meaningful.

The differences between the RFA and non-RFA groups in score changes from baseline to 6 months are presented in

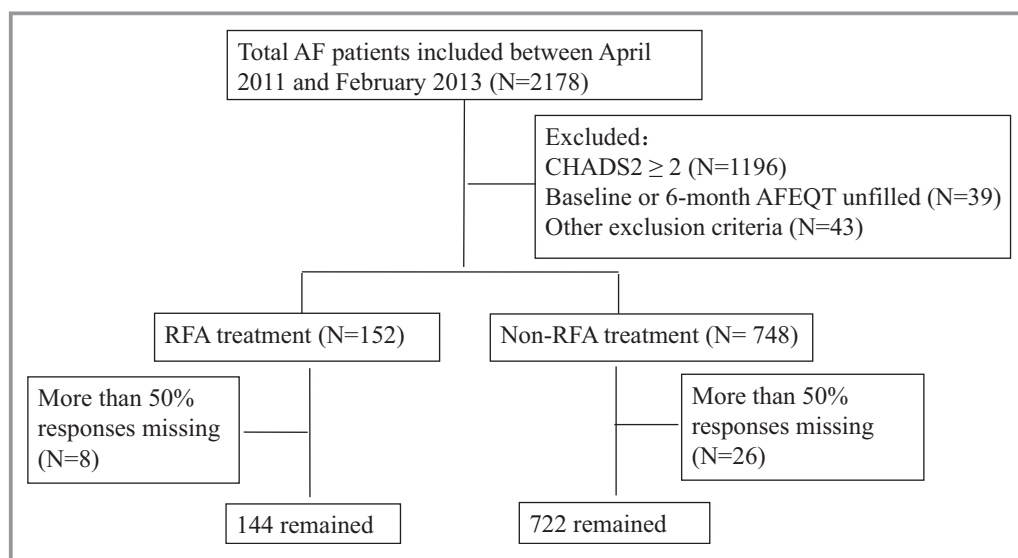


Figure 1. Selection flowchart according to STROBE. AFEQT indicates atrial fibrillation effect on quality of life; non-RFA, nonradiofrequency ablation; RFA, radiofrequency ablation.

Table 2. Baseline AFEQT of Patients Before and After Matching

Baseline AFEQT	Before Matching		P Value	After Matching		P Value
	RFA N=144	Non-RFA N=722		RFA N=74	Non-RFA N=148	
Symptoms	57.49±22.59	69.90±20.09	<0.001	58.28±22.12	59.86±22.94	0.62
DA	53.30±23.97	65.05±21.19	<0.001	58.68±25.24	58.31±22.91	0.92
TC	50.06±20.93	67.62±18.07	<0.001	55.96±20.98	57.28±25.24	0.65
GS	53.23±19.28	66.99±17.20	<0.001	57.86±19.32	58.41±18.89	0.84
TS	69.79±24.10	67.39±19.0	0.19	63.18±26.82	67.45±18.01	0.16

Values are given as mean±SD. AFEQT indicates atrial fibrillation effect on quality of life; DA, daily activities; GS, global score; non-RFA, nonradiofrequency ablation; RFA, radiofrequency ablation; TC, treatment concern; TS, treatment satisfaction.

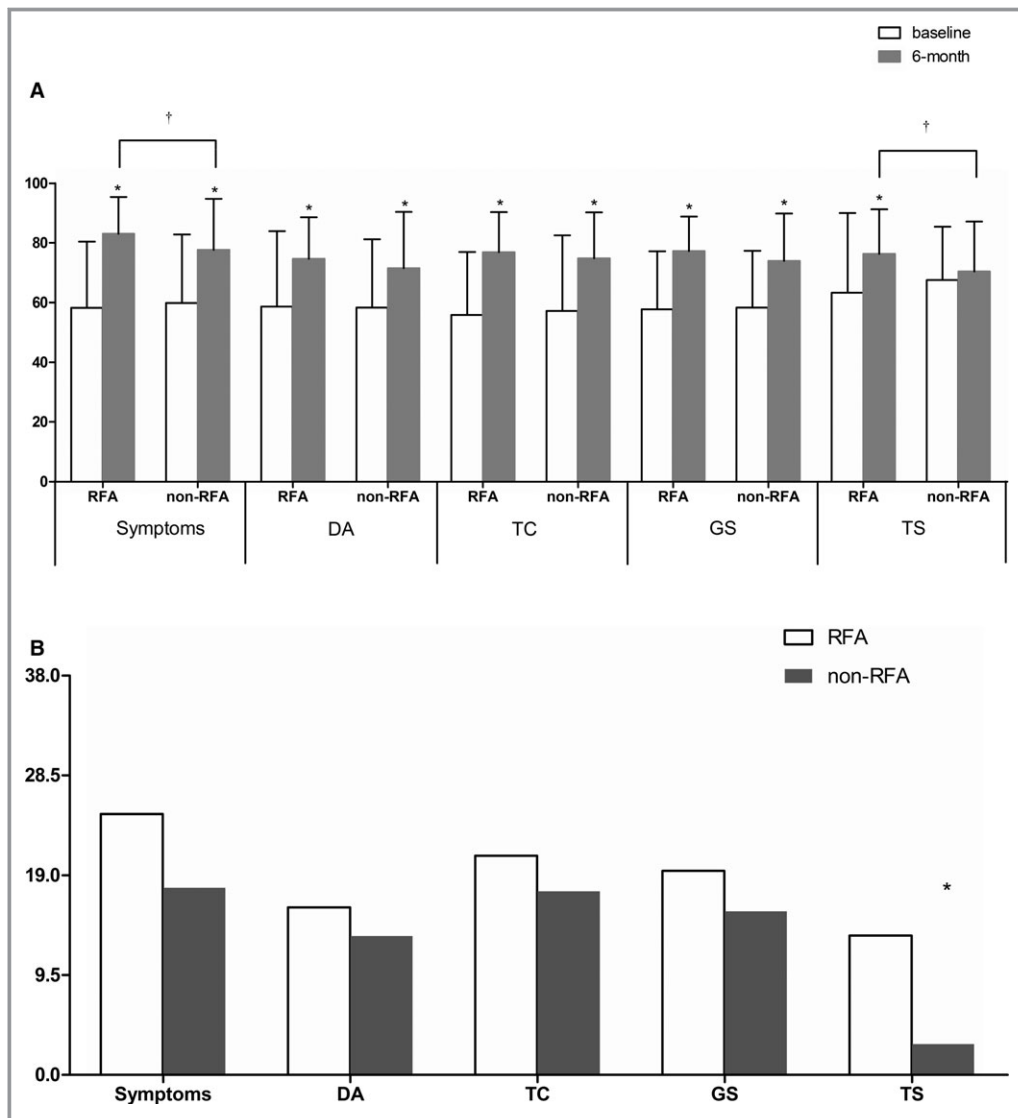


Figure 2. A, Domains and the global score of AFEQT questionnaire at baseline and 6 months in RFA and non-RFA groups. * $P < 0.001$ vs baseline; † $P < 0.05$ RFA versus non-RFA group at 6 months. B, Changes of domains and the global score of AFEQT questionnaire from baseline to 6 months. * $P < 0.05$ versus RFA group. AFEQT indicates atrial fibrillation effect on quality of life; DA, daily activities; GS, global score; non-RFA, nonradiofrequency ablation; RFA, radiofrequency ablation; TC, treatment concern; TS, treatment satisfaction.

Figure 2B. However, no significant difference was noted, except for the treatment satisfaction domain (13.17 ± 28.33 units in the RFA group vs. 2.92 ± 21.81 units in the non-RFA group; $P=0.007$). The Cohen effect sizes of differences in symptoms change and treatment satisfaction change were 0.3 and 0.4, respectively, which can be considered as moderate effect size.

QoL changes in 644 patients (RFA: 70 and non-RFA: 574) excluded after propensity matching are presented in Figure S1.

Subgroup Analysis

Results of the health status of the primary endpoint for subgroup analysis are shown in Table 3. In subgroup analysis classified by AF type, the global score at 6 months was higher in the RFA group compared to the non-RFA group in paroxysmal AF (79.31 ± 10.89 units in the RFA group vs. 72.40 ± 15.74 units in the non-RFA group; $P=0.003$) whereas no significant difference was found in nonparoxysmal AF from the matched cohort. In patients stratified by age strata of 65 years, no significant differences were noted in the global score of the AFEQT questionnaire between the RFA and non-RFA groups among the 127 AF patients with age <65 years. Nonetheless, the global scores of the AFEQT questionnaire achieved a significantly higher improvement after RFA in 95 patients with age ≥ 65 years (79.29 ± 11.16 units in the RFA group vs. 67.96 ± 16.04 units in the non-RFA group; $P<0.001$).

Table 3. Health Status of Primary Outcome in Subgroup Analysis

Subgroup	Category	No. of Patients	The Global Score (Units)	P Value	
AF type	PAF			0.003	
		RFA	52		79.31 ± 10.89
	Non-PAF			0.359	
		RFA	22		72.48 ± 11.71
Age, y	<65			0.221	
		RFA	47		76.12 ± 11.65
		Non-RFA	80		79.09 ± 13.89
	≥ 65			<0.001	
		RFA	27		79.29 ± 11.16
		Non-RFA	68		67.96 ± 16.04

AF indicates atrial fibrillation; non-PAF, nonparoxysmal atrial fibrillation; non-RFA, nonradiofrequency ablation; PAF, paroxysmal atrial fibrillation; RFA, radiofrequency ablation.

Detailed subgroup analyses of the primary outcome in the domains of AFEQT can be seen in Table S2.

CHA₂DS₂-VASc Scores=0 or 1

Cohorts of patients with low baseline CHA₂DS₂-VASc score (ie, CHA₂DS₂-VASc ≤ 1) were also constructed based on 1:2 propensity score matching. Of the 105 AF patients with low CHA₂DS₂-VASc score, 44 were from the RFA group and 61 were from the non-RFA group. No significant differences were observed in any domain and the global score of AFEQT questionnaire at 6 months between the 2 groups (see Table S3).

Efficacy and Safety

During 6-month follow-up, AF recurrence rate was 28.3% (21 of 74), with 9 paroxysmal AF and 12 nonparoxysmal AF. Treatment failure in the non-RFA group was 48.6% (72 of 148), with occurrence of AF more than twice in 31 paroxysmal AF and failing to restore sinus rhythm in 41 nonparoxysmal AF. Detailed changes in domains and the global score of the AFEQT questionnaire of patients with and without AF recurrence in both groups are listed in Figure S2.

Stroke occurred in 1 (0.96%) patient in the RFA group, 3 in the RFA group, and 2 in the non-RFA group were reported to have minor bleedings, respectively. No complications of clinical importance associated with RFA and medicines used were reported (see changes of medicine use in the non-RFA group in Figure S3).

Discussion

In the present study, 6-month QoL in AF patients with low stroke risk after RFA versus non-RFA were retrospectively evaluated using the AFEQT questionnaire based on data from a multicenter registry. Surprisingly, no significant superiorities of QoL were noted when RFA was compared to non-RFA treatment at 6 months from the propensity-matched cohorts, except for domains of symptoms and treatment satisfaction.

Changes of health status in the RFA group were more than 19 units, which were considered to be clinically meaningful.¹⁸ However, their score changes in the non-RFA group were near the cut-off point of 19 units. Although QoL improvement was observed in patients post-RFA, a similar degree of improvement could also be observed in patients from the non-RFA group. Several possible explanations were established assuming to be partially responsible for these findings. First, significant QoL increase within groups may be the results of increasing frequency of regular visits to the physicians and receiving more clinical care from cardiologists after recruitment. Given that medical resources might be relatively limited

in China, a country with a huge population, patients were often restricted from seeking for professional cardiologists' directions before they were enrolled in the registry. In our study, patients both in the RFA and non-RFA groups had similar experiences with respect to convenient access to AF clinics. The second possible reason was that complications and adverse effects associated with the procedure and medicines were uncommon owing to a relatively short follow-up period.

RFA treatment is perceived to be effective in improving QoL in the study population, but it seems to have only small or moderate superiorities to non-RFA treatment according to the ratings of differences in 6-month QoL assessed by Cohen effect size. A recently published randomized study¹⁹ also suggested a negative impact of ablation using the EuroQol-five dimensions (EQ-5D), with similar results with our study. No significant difference in 1-year QoL improvement was noted between patients receiving ablation treatment and antiarrhythmic drugs, although a lower rate of recurrent atrial tachyarrhythmias was achieved in the ablation group. However, in previous studies using Short Form 36 score or EQ-5D comparing symptomatic²⁰ or paroxysmal^{10,21} AF patients receiving RFA versus antiarrhythmic drugs, a higher rate of successful rhythm control was achieved and QoL improved and was maintained much better after ablation during follow-up. The varying range of QoL improvements may reflect differences in study design, patient selection, baseline QoL impairment, questionnaires used for QoL measures, procedural techniques, and period of follow-up. The results from our study mainly reflect QoL outcome regardless of AF type after a single RFA, different from some,^{10,19} but not all,^{20,21} previous trials. Another possible reason, at least as a partial explanation for the similar QoL at 6 months, was that most previous studies comparing QoL in AF patients treated with RFA were not conducted based on analysis stratified by low and high stroke risk.^{10,19–22} CHADS₂ and CHA₂DS₂-VASc scores are widely used for evaluating risk stratification of stroke in nonvalvular AF patients¹ and the former is more popular in China.²³ Concerns of stroke in low-risk patients are much weaker before RFA, but may increase owing to an at least 3-month anticoagulation period after the procedure,⁵ which can lead to psychological pressure that offsets the minimal benefits of RFA from rhythm control.¹⁴

Though differences of health status at 6 months were small, a significant difference in 6-month symptoms was demonstrated to be in favor of patients treated with RFA. The influence of symptoms relief and treatment effect on QoL were investigated in several ablation studies.^{19,24} Studies conducted by Savelieva et al.^{25,26} found that symptoms and QoL in AF patients were not necessarily correlated because they were partially overlapped. Symptomatic AF may become asymptomatic AF after RFA treatment, but the risk of stroke

was not reduced accordingly. Additionally, positive results concerning significant differences in symptoms domain should be interpreted with caution owing to risk of false-positive results originating from multiple comparisons.

The findings in our report should be interpreted with several potential concerns. Selection bias was of the most important limitations in this retrospective observational study. Patients who moved from the non-RFA group to the RFA group had to be excluded in order to maintain the consistency of the length of 6-month follow-up, though these patients might have high symptoms load. Although propensity matching was performed to minimize or avoid confoundings and ensure the balance of the baseline characteristics between the 2 groups, the existence of residual bias could not be neglected because of other unmeasured characteristics. Subgroup analyses stratified by AF type were further performed to adjust the imbalance of AF type, which still existed after propensity score matching. RFA treatment was found to be significantly superior to non-RFA with respect to health status in paroxysmal AF patients. The results that higher QoL improvement was observed in older patients after RFA, compared to non-RFA, based on subgroup analyses stratified by age provided evidence for the assumption that patients eligible in the study would more likely benefit from RFA treatment than ineligible patients because they are relatively older. Nonetheless, subgroups in this study were formed after propensity matching and baseline measures made it very difficult to determine whether a statistically significant improvement was the result of AF type, age category, or other factors. No significant improvement of QoL in the RFA group was noted when based on the more efficient CHA₂DS₂-VASc score stroke stratification.

The result of higher treatment satisfaction at 6 months in the RFA group was speculated to be partially attributable to a placebo effect of RFA, which was assumed to be a defect of the study similar to previous studies.²² AF patients were instructed to fill in the AFEQT questionnaires by trained nurses under conditions that patients completely understood the questions. The main differences of between-group settings in this study were whether patients were treated with RFA. There were still no significant superiorities in QoL improvement compared to the non-RFA group, though several factors in favor of AF patients with RFA treatment were adopted. First, a short-term follow-up of 6 months was considered to be beyond the duration of the anticoagulation period⁵ and with an acceptable AF recurrence rate (28.38%).²⁷ Second, exclusion of AF recurrent patients receiving a second RFA during the 6-month follow-up were probably in favor of AF patients in the RFA group¹⁹ because they usually had symptoms leading to impairment of well-being after a single RFA. Third, the fact that a higher proportion of patients in paroxysmal AF after propensity matching is favorable for the

RFA group according to the results of the subgroup analysis in paroxysmal AF, in keeping with previous studies,^{19,20,28} given that patients with paroxysmal AF often have larger QoL improvement. Nonetheless, it is hard to draw conclusions because no sufficient evidence was obtained for lacking an efficiently constructed placebo model for control of RFA. In spite of 6-month improvement of QoL post-RFA, the absence of a statistically significant difference between RFA and non-RFA treatment in health status were to be taken seriously before making a clinical decision whether AF patients with low stroke risk should be treated with RFA. We suggested that our study provided a basis for prospective, randomized design evaluating outcomes on QoL in low-stroke-risk patients by RFA versus non-RFA.

Conclusions

In this retrospective, observational study of a propensity-matched cohort, improvement of QoL was observed from baseline to 6 months both in RFA and non-RFA groups using the AFEQT questionnaire. Health status at 6 months in patients treated with RFA was small-to-moderately superior to those without. It is discreetly supposed that RFA has not lived up to the high expectations for improvement of QoL in AF patients with low stroke risk during a 6-month follow-up.

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References

- Ahmed S, Ranchar AV, Crijns HJ, Van Veldhuisen DJ, Van Gelder IC; CONVERT investigators. Effect of continuous versus episodic amiodarone treatment on quality of life in persistent atrial fibrillation. *Europace*. 2010;12:785–791.
- Ansari JG, Garcha GS, Lakkis N. Oral anticoagulation in atrial fibrillation. *Cardiovasc Hematol Agents Med Chem*. 2014;12:34–41.
- Reynolds MR, Gunnarsson CL, Hunter TD, Ladapo JA, March JL, Zhang M, Hao SC. Health outcomes with catheter ablation or antiarrhythmic drug therapy in atrial fibrillation: results of a propensity-matched analysis. *Circ Cardiovasc Qual Outcomes*. 2012;5:171–181.
- Bunch TJ, Crandall BG, Weiss JP, May HT, Bair TL, Osborn JS, Anderson JL, Muhlestein JB, Horne BD, Lappe DL, Day JD. Patients treated with catheter ablation for atrial fibrillation have long-term rates of death, stroke, and dementia similar to patients without atrial fibrillation. *J Cardiovasc Electro-physiol*. 2011;22:839–845.
- European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery, Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kohl P, Le Heuzey JY, Ponikowski P, Rutten FH. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010;31:2369–2429.
- Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ Jr, Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Ilesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Heart Rhythm*. 2012;9:632–696.
- Bulková V, Fiala M, Havránek S, Simek J, Skňouřil L, Januška J, Spinar J, Wichterle D. Improvement in quality of life after catheter ablation for paroxysmal versus long-standing persistent atrial fibrillation: prospective study with 3-year follow-up. *J Am Heart Assoc*. 2014;3:e000881 doi: 10.1161/JAHA.114.000881.
- January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2014;64:e1–e76.
- Carnlöf C, Insulander P, Pettersson PH, Jensen-Urstad M, Fossum B. Health-related quality of life in patients with atrial fibrillation undergoing pulmonary vein isolation, before and after treatment. *Eur J Cardiovasc Nurs*. 2010;9:45–49.
- Walfridsson H, Walfridsson U, Nielsen JC, Johannessen A, Raatikainen P, Janzon M, Levin LA, Aronsson M, Hindricks G, Kongstad O, Pehrson S, Englund A, Hartikainen J, Mortensen LS, Hansen PS. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation: results on health-related quality of life and symptom burden. The MANTRA-PAF trial. *Europace*. 2015;17:215–221.
- Spertus J, Dorian P, Buben R, Lewis S, Godejohn D, Reynolds MR, Lakkireddy DR, Wimmer AP, Bhandari A, Burk C. Development and validation of the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) Questionnaire in patients with atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2011;4:15–25.
- Dong J, Liu X, Long D, Yu R, Tang R, Lu F, Ma C. Single-catheter technique for pulmonary vein antrum isolation: is it sufficient to identify and close the residual gaps without a circular mapping catheter? *J Cardiovasc Electro-physiol*. 2009;20:273–279.
- Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. *Pharm Stat*. 2011;10:150–161.
- Ha AC, Breithardt G, Camm AJ, Crijns HJ, Fitzmaurice GM, Kowey PR, Le Heuzey JY, Naditch-Brulé L, Prystowsky EN, Schwartz PJ, Torp-Pedersen C, Weintraub WS, Dorian P. Health-related quality of life in patients with atrial fibrillation treated with rhythm control versus rate control: insights from a prospective international registry (Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation: RECORD-AF). *Circ Cardiovasc Qual Outcomes*. 2014;7:896–904.
- Letsas KP, Efremidis M, Giannopoulos G, Dettores S, Lioni L, Korantzopoulos P, Vlachos K, Xydonas S, Kossyvakis C, Sideris A. CHADS₂ and CHA₂DS₂-VASc scores as predictors of left atrial ablation outcomes for paroxysmal atrial fibrillation. *Europace*. 2014;16:202–207.
- Guédon-Moreau L, Capucci A, Denjoy I, Morgan CC, Périer A, Leplège A, Kacet S. Impact of the control of symptomatic paroxysmal atrial fibrillation on health-related quality of life. *Europace*. 2010;12:634–642.
- Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.

18. Dorian P, Burk C, Mullin CM, Bubien R, Godejohn D, Reynolds MR, Lakkireddy DR, Wimmer AP, Bhandari A, Spertus J. Interpreting changes in quality of life in atrial fibrillation: how much change is meaningful? *Am Heart J*. 2013;166:381–387.e8.
19. Morillo CA, Verma A, Connolly SJ, Kuck KH, Nair GM, Champagne J, Sterns LD, Beresh H, Healey JS, Natale A; RAAFT-2 Investigators. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAFT-2): a randomized trial. *JAMA*. 2014;311:692–700.
20. Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, Bash D, Schweikert R, Brachmann J, Gunther J, Gutleben K, Pisano E, Potenza D, Fanelli R, Raviele A, Themistoclakis S, Rossillo A, Bonso A, Natale A. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA*. 2005;293:2634–2640.
21. Wilber DJ, Pappone C, Neuzil P, De Paola A, Marchlinski F, Natale A, Macle L, Daoud EG, Calkins H, Hall B, Reddy V, Augello G, Reynolds MR, Vinekar C, Liu CY, Berry SM, Berry DA, ThermoCool AF; Trial Investigators. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. *JAMA*. 2010;303:333–340.
22. Chang CH, Lin JW, Chiu FC, Caffrey JL, Wu LC, Lai MS. Effect of radiofrequency catheter ablation for atrial fibrillation on morbidity and mortality: a nationwide cohort study and propensity score analysis. *Circ Arrhythm Electrophysiol*. 2014;7:76–82.
23. Chen T, Yang YM, Tan HQ, Liang Y, Zhu J. Baseline characteristics and 1-year follow-up of Chinese atrial fibrillation patients according to age: a registry study. *Pacing Clin Electrophysiol*. 2014;37:1392–1403.
24. Camm AJ, Reiffel JA. Defining endpoints in clinical trials on atrial fibrillation. *Eur Heart J Suppl*. 2008;10(suppl H):H55–H78.
25. Savelieva I, Paquette M, Dorian P, Luˆderitz B, Camm AJ. Quality of life in patients with silent atrial fibrillation. *Heart*. 2001;85:216–217.
26. Savelieva I, Camm AJ. Clinical relevance of silent atrial fibrillation: prevalence, prognosis, quality of life, and management. *J Interv Card Electrophysiol*. 2000;4:369–382.
27. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ Jr, Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace*. 2012;14:528–606.
28. Pappone C, Augello G, Sala S, Gugliotta F, Vicedomini G, Gulletta S, Paglino G, Mazzone P, Sora N, Greiss I, Santagostino A, LiVolsi L, Pappone N, Radinovic A, Manguso F, Santinelli V. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. *J Am Coll Cardiol*. 2006;48:2340–2347.