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Assessment of Atrial Fibrillation–Specific Symptoms Before and 2 Years After Atrial Fibrillation Ablation

Do Patients and Physicians Differ in Their Perception of Symptom Relief?

Anna Björkenheim, MD,[a] Axel Brandes, MD, DMSc,[b] Anders Magnuson, BSc,[c] Alexander Chemnitz, BSc,[b] Lena Svedberg, RN,[a] Nils Edvardsson, MD, PhD,[d] Dritan Poçi, MD, PhD[a]

ABSTRACT

OBJECTIVES The aim of this study was to evaluate patient-reported and physician-assessed atrial fibrillation (AF)–related symptoms after AF ablation.

BACKGROUND Success of AF ablation is usually defined as freedom from AF, although symptom relief is often patients' desire.

METHODS Symptom relief was assessed as perceived by patients using the short, validated, AF-specific symptom questionnaire AF6 and as classified by physicians using the European Heart Rhythm Association (EHRA) classification at baseline and 6, 12, and 24 months after AF ablation. Recurrence of arrhythmia was documented by continuous electrocardiographic monitoring.

RESULTS In total, 54 patients completed the 24-month follow-up. All 6 items on the AF6, AF6 sum score, and EHRA class improved significantly over time. The greatest improvement was seen during the first 6 months after ablation, but AF6 scores showed continued improvement up to 12 months, in contrast to EHRA class. There was a low correlation between AF6 score and EHRA class, but the predictive ability was low. Both AF6 scores and EHRA class were significantly correlated with AF burden at all times after ablation. A change of >9 points in AF6 sum score corresponded to a meaningful reduction in symptom severity.

CONCLUSION Patient-reported and physician-assessed outcomes were both useful in assessing symptom relief after AF ablation, although patient-reported outcomes were more sensitive tools. There was also a discrepancy between patient-reported and physician-assessed outcomes after ablation. Freedom from AF and a low AF burden most often resulted in a reduction of symptoms, but symptom relief also occurred despite little effect on the arrhythmia. (J Am Coll Cardiol EP 2017;3:1168–76) © 2017 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Catheter ablation has become a cornerstone in the management of atrial fibrillation (AF) (1,2). Impressive long-term success rates have been presented in terms of freedom from recurrence, but differences in patient selection, ablation techniques, and follow-up often make results difficult to compare. The typical candidate for AF ablation has symptomatic paroxysmal or persistent

From the [a]Department of Cardiology, School of Medical Sciences, Örebro University, Örebro, Sweden; [b]Department of Cardiology, Odense University Hospital, Odense, Denmark; [c]Clinical Epidemiology and Biostatistics, School of Medical Sciences, Örebro University, Örebro, Sweden; and the [d]Sahlgrenska Academy at Sahlgrenska University Hospital, Göteborg, Sweden.
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AF with minimal or no structural heart or other serious disease. The most common success criterion has been freedom from documented recurrence of AF or other atrial tachyarrhythmias of more than 30 s in duration (1–3). In determining the impact before and after ablation on symptoms and health-related quality of life, generic rather than AF-specific questionnaires have often been used (4). However, although the main purpose and indication for AF ablation is to reduce symptoms, the absence or reduction of AF recurrence, regardless of the definition and mode of follow-up, may not be an optimal success criterion alone, because it does not reflect what symptomatic patients experience.

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Electrocardiographic recordings are reliable in detecting AF, but symptoms are not, even if the patient suspects or believes that the symptoms are caused by the arrhythmia (5). In addition, AF ablation may also change the perception of AF so that a patient may experience diminished symptoms despite recurring episodes of arrhythmia (6,7). Studies also suggest that physicians may underestimate patient symptoms, especially when they are mild (8,9).

We hypothesized that patients and physicians may rate the change in symptoms after ablation differently. The aim of this study was to evaluate patient-reported and physician-assessed AF-related symptoms up to 2 years after AF ablation and to identify whether they were correlated, in relation to the AF burden continuously measured by an implantable loop recorder (ILR).

METHODS

PATIENTS. Patients were enrolled at 2 Scandinavian university hospitals and were eligible if they had: 1) documented symptomatic paroxysmal or persistent AF (<3 months) and were planned for catheter ablation; and 2) were 30 to 70 years of age. Important exclusion criteria were: 1) left atrial diameter >60 mm; 2) left ventricular ejection fraction <40%; 3) significant structural heart disease; and 4) contraindication to oral anticoagulation. All patients gave their written informed consent before enrollment in the study. The study protocol was approved by the appropriate ethical boards and was in compliance with the Declaration of Helsinki.

The baseline evaluation included a physical examination, laboratory tests, 12-lead electrocardiography, echocardiography, and the completion of a formally validated patient-related outcome form: the AF-specific symptoms form AF6. All patients were on long-term warfarin treatment with a target international normalized ratio between 2 and 3 for at least 4 weeks prior to ablation. Patients remained on their latest rhythm control medications during and up to 3 months after ablation, when the indication for rhythm control medication was reassessed.

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

EHRA = European Heart Rhythm Association

ILR = implantable loop recorder

IQR = interquartile range

DEVICE CHARACTERISTICS AND IMPLANT PROCEDURE. Patients were implanted with an ILR (Reveal XT, Medtronic, Minneapolis, Minnesota) in the left parasternal area at least 2 weeks before the ablation that remained for a minimum of 24 months after ablation. The autoactivation and the AF detection algorithm were programmed to ON, which classifies the heart rhythm as AF when the R-R intervals within a 2-min period show a certain pattern of uncorrelated irregularity (10). Patients were also encouraged to start manually triggered 30-s rhythm recordings during perceived arrhythmia symptoms using the patient activator. The ILR was programmed to provide, over time, the number of arrhythmia episodes, their duration, and, when all durations of AF episodes were added, the AF burden.

CATHETER ABLATION PROCEDURE. The catheter ablation procedure has been reported previously (11) and consisted of circumferential radiofrequency lines around each pair of pulmonary vein ostia in the left atrium. Reablation was permitted at the investigator's discretion without excluding the patient from the study.

PATIENT-REPORTED OUTCOMES. Symptoms were assessed using the AF-specific questionnaire AF6, which has undergone thorough validation (12) and testing of clinical responsiveness (13) and includes a recall period of the most recent 7 days. This 6-item questionnaire includes patient-reported AF-related symptoms: item 1, "breathing difficulties at rest"; item 2, "breathing difficulties upon exertion"; item 3, "limitations in day-to-day life due to AF"; item 4, "feeling of discomfort due to AF"; item 5, "tiredness due to AF"; and item 6, "worry/anxiety due to AF." A score of 0 (no symptoms) to 10 (severe symptoms) is reported for each item, and all scores are added into a single sum score. Sum scores range from 0 to 60, with higher values reflecting more severe AF-related symptoms. After initial instruction, the questionnaire was completed by the patient without interaction from physicians or nurses and before the electrocardiogram was recorded to document the actual cardiac rhythm. The AF6 questionnaire was completed before and 6, 12, and 24 months after ablation.

TABLE 1 Baseline Patient Characteristics (N = 57)

Male	34 (60.0)
Age, yrs	57 ± 9
BMI (kg/m^2)	29 ± 5
Paroxysmal AF	50 (88.0)
Months from first AF episode	57 (36-120)
Concomitant cardiovascular disease	
Heart failure	2 (4.0)
Hypertension	24 (42.0)
Diabetes	2 (4.0)
Coronary artery disease	1 (2.0)
Valvular heart disease	1 (2.0)
Stroke/TIA	8 (14.0)
CHA_2DS_2-VASc scores	
0	15 (26.0)
1	20 (35.0)
≥2	22 (39.0)
Medications	
Beta-blockers	37 (65.0)
Class I AADs	16 (28.0)
Class III AADs	16 (28.0)
Warfarin	42 (74.0)

Values are n (%), mean ± SD, or median (interquartile range).

AAD = antiarrhythmic drug; AF = atrial fibrillation; BMI = body mass index; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥65 or 75 yrs, diabetes, prior stroke or transient ischemic attack, vascular disease, female sex; TIA = transient ischemic attack.

PHYSICIANS' SYMPTOM EVALUATION. The physician categorized the patient's condition according to the European Heart Rhythm Association (EHRA) classification into class I (no symptoms), II (mild symptoms: normal daily activity not affected), III (severe symptoms: normal daily activity affected), or IV (disabling symptoms: normal daily activity discontinued) during presumed arrhythmia episodes depending on symptoms of palpitations, fatigue, dizziness, dyspnea, chest pain, and anxiety (14). EHRA class was noted before and 6, 12, and 24 months after ablation.

AF BURDEN. The AF burden composed of adjudicated AF episodes was calculated from the ILR data as the percentage of time in AF between each follow-up visit, as previously described. In addition to correlating the AF burden with symptom scores, we applied a previously suggested AF burden cutoff limit of 0.5% at each scheduled visit to define success of AF ablation (11,15).

STATISTICAL ANALYSIS. Categorical variables are presented as percentages and continuous variables as mean ± SD or median (interquartile range [IQR]), as appropriate. Friedman's test was applied to evaluate differences between time intervals for AF6 scores and EHRA class. The McNemar test was used for binary variables, and the Mann-Whitney *U* test was used when comparing subgroups. The chi-square test or Fisher exact test was used as appropriate. We assessed the correlation of AF6 score before and after ablation using the Pearson correlation coefficient (r) and all correlations involving AF burden, because of non-normality, and EHRA class, because of the ordinal scale, using the Spearman rank correlation coefficient (r). We also estimated the predictive ability by calculating the correlation coefficient squared (r^2) as a measure of the proportion of variance accounted for by the correlation. The distribution-based Cohen effect size was used to estimate a clinically important difference. The effect size was interpreted according to standard criteria with trivial (<0.20), small (0.20 to 0.49), moderate (0.50 to 0.79), and large (≥0.80) changes of baseline scores (16).

A p value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed using SPSS version 22 (IBM, Armonk, New York).

RESULTS

BASELINE DEMOGRAPHICS. Fifty-nine patients were screened, 1 withdrew consent, and 1 patient was excluded because of a lack of a correlation between AF and symptoms. Fifty-seven patients underwent AF ablation and constituted the study population. Their mean age was 57 ± 9 years, and 40% were women. The most common comorbidities were hypertension (42%) and previous stroke or transient ischemic attack (14%) (Table 1). Fifty-four patients completed the 24-month follow-up. Twenty-three patients (43%) underwent reablation during follow-up.

PATIENTS' ASSESSMENT OF AF-SPECIFIC SYMPTOMS BEFORE AND AFTER ABLATION. Before ablation, AF6 items 1 to 6 scored ≥1 point in 54%, 83%, 83%, 91%, 85%, and 89% of the patients, respectively, and in 30%, 59%, 54%, 52%, 54%, and 54% of the patients at 24 months. The most severe symptom before ablation was tiredness due to AF, which scored a median of 7 of a maximum of 10 points (Table 2). When symptoms persisted at 24 months, the most important item was the same but showed statistically significantly reduced scores. All items on the AF6 and the sum score decreased statistically significantly over the 24-month follow-up period. The median AF6 scores improved from before ablation to 6 months after ablation and further to 12 months for all items and the sum score, except for item 1, and remained at this level at 24 months after ablation. The AF6 sum score at all times after ablation correlated significantly with the AF6 sum score before

ablation (Figures 1A to 1C) ($r = 0.50$ [$p < 0.001$], $r = 0.38$ [$p = 0.008$], and $r = 0.28$ [$p = 0.04$], 6, 12, and 24 months after ablation, respectively).

There were 11 (20%), 12 (22%), and 16 (30%) patients, respectively, who reported no symptoms at all (AF6 score 0) at 6, 12, and 24 months after ablation. Five patients (9%) did not report any symptoms at any time after ablation.

The mean AF6 sum score was 29.5 ± 13.9 before ablation. The mean difference in the AF6 sum score from before ablation was 9.3 (95% confidence interval: 5.2 to 13.4; $p < 0.001$) at 6 months after ablation, 16.6 (95% confidence interval: 12.2 to 20.9; $p < 0.001$) at 12 months, and 13.6 (95% confidence interval: 9.0 to 18.3 ($p < 0.001$) 24 months after ablation, corresponding to Cohen effect sizes of 0.67, 1.2, and 0.98, respectively. Thus, effect sizes were moderate to large after ablation. An improvement of more than 9 points was therefore considered clinically meaningful and was seen in 25 patients (50%) at 6 months, 33 patients (75%) at 12 months, and 30 patients (61%) at 24 months after ablation.

TABLE 2 Patient and Physician Assessment of Atrial Fibrillation–Specific Symptoms Before and After Ablation Using the AF6 and European Heart Rhythm Association Classification, Respectively

	Before Ablation	6 Months*	12 Months†	24 Months‡	p Value, Friedman Test
AF6 item 1	1 (0–3)	0 (0–2)	1 (0–4)	0 (0–1)	0.001§
AF6 item 2	5 (2–8)	3 (0–7)	1 (0–4)	2 (0–6)	0.004§
AF6 item 3	5 (2–8)	2 (0–5)	1 (0–3)	1 (0–5)	0.001§
AF6 item 4	6 (3–8)	3 (0–6)	1 (0–3)	1 (0–6)	<0.001§
AF6 item 5	7 (4–8)	5 (0–8)	2 (0–6)	2 (0–7)	<0.001§
AF6 item 6	4 (2–6)	2 (0–5)	0 (0–3)	1 (0–3)	<0.001§
AF6 sum	30 (17–38)	17 (2–30)	7 (0–19)	9 (0–27)	<0.001§
EHRA class I	19 (35.0)	41 (76.0)	38 (70.0)	44 (82.0)	<0.001§
EHRA class II	22 (41.0)	10 (19.0)	14 (26.0)	7 (13.0)	<0.001§
EHRA class III	12 (22.0)	3 (6.0)	2 (4%)	3 (6.0)	<0.001
EHRA class IV	1 (2.0)	0	0	0	<0.001

Values are median (interquartile range) or n (%). All 6 items in the AF6, the AF6 sum score, and EHRA class improved significantly over time. AF6 item 1, "breathing difficulties at rest"; item 2, "breathing difficulties upon exertion"; item 3, "limitations in day-to-day life due to AF"; item 4, "feeling of discomfort due to AF"; item 5, "tiredness due to AF"; and item 6, "worry/anxiety due to AF." A score of 0 (no symptoms) to 10 (severe symptoms) is reported for each item, and all scores are added to give a single sum score of 0 to 60. EHRA class I (no symptoms), II (mild symptoms), III (severe symptoms), or IV (disabling symptoms). *1 patient missing. †5 patients missing. ‡1 patient missing. §Statistically significant ($p < 0.05$).

AF = atrial fibrillation; EHRA = European Heart Rhythm Association.

PHYSICIANS' EVALUATION OF SYMPTOMS BEFORE AND AFTER ABLATION: EHRA CLASSIFICATION. EHRA class improved statistically significantly over the 2-year follow-up period, and at 6, 12, and 24 months after ablation, 76%, 70%, and 82% of patients, respectively, were in EHRA class I (Table 2). The greatest improvement was seen during the first 6 months after ablation, with no further improvement beyond that period. EHRA class most often improved by 1 class (from II to I, n = 20; from III to II, n = 1) and less often by 2 or 3 classes (from III to I, n = 10; from IV to I, n = 1).

Nineteen patients (35%) were already categorized in EHRA class I before ablation, and 9 of them were also considered to be in EHRA class I at all times after the ablation. The remaining 10 patients varied from EHRA class I to III after ablation; at 24 months, 4 patients were in EHRA class I, 4 in EHRA class II, and 2 in EHRA class III.

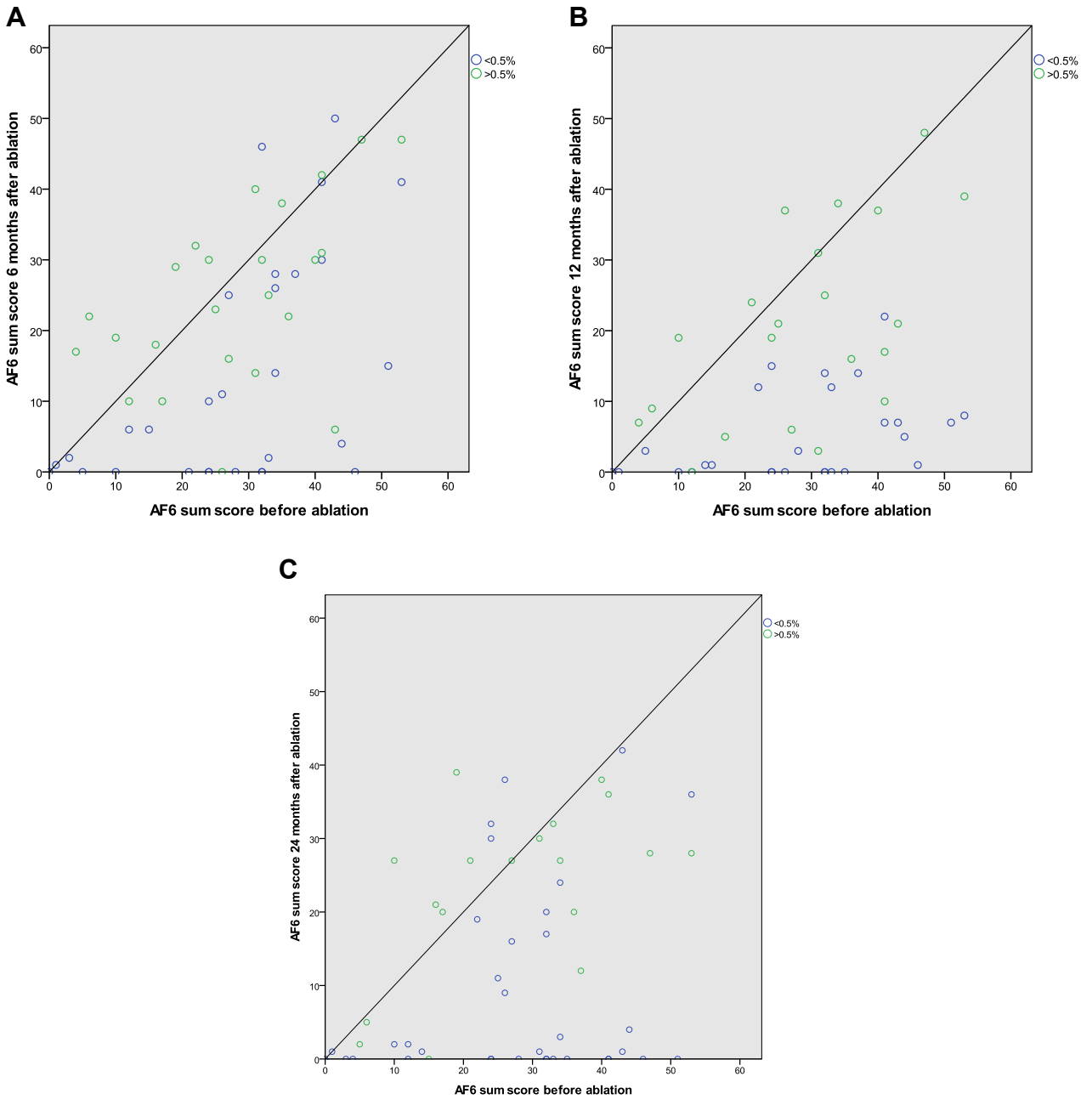
PATIENTS' VERSUS PHYSICIANS' EVALUATION OF SYMPTOMS. The AF6 sum score decreased with improving EHRA class, showing a significant correlation at 6 months ($r = 0.48$, $r^2 = 0.23$; $p < 0.001$), 12 months ($r = 0.58$, $r^2 = 0.34$; $p < 0.001$), and 24 months after ablation ($r = 0.27$, $r^2 = 0.07$; $p = 0.049$).

The changes in AF6 sum score and EHRA class from before ablation were visualized with scatterplots at 6 ($r = 0.31$, $r^2 = 0.10$; $p = 0.02$), 12 ($r = 0.32$, $r^2 = 0.10$; $p = 0.03$), and 24 months ($r = 0.22$, $r^2 = 0.05$; $p = 0.12$) after ablation (Figures 2A to 2C). In Figure 2A, 25 patients decreased in AF6 sum score by more than 9 points, and nearly two-thirds of them also had a 1- or 2-class change in EHRA score. However, 12 patients had smaller changes in AF6 sum score, and one-third of them still had 1- or 2-class EHRA score changes, implying that physicians had a more positive interpretation of symptom improvement than patients. Patients considered to be improved in EHRA class had statistically significantly lower median AF6 sum scores of 1 (IQR: 0 to 4), 6 (IQR: 0 to 13), and 5 (IQR: 0 to 28) at 6, 12, and 24 months after ablation, respectively, compared with patients with unchanged or worse EHRA class with median AF6 sum scores of 40 (IQR: 27 to 46; $p = 0.003$), 31 (IQR: 12 to 39; $p = 0.001$), and 36 (IQR: 28 to 36; $p = 0.02$).

The 19 patients (paroxysmal AF, n = 15; persistent AF, n = 4) considered to be in EHRA class I before ablation had a median AF6 sum score of 24 (IQR: 14 to 34) before ablation. The most common AF6 items were limitations in day-to-day life due to AF and worry/anxiety due to AF, while the highest scoring item was tiredness due to AF.

EFFECT OF ABLATION ON AF OVER TIME IN RELATION TO SYMPTOMS. The proportion of patients with AF burden of 0% during the past 6-month period was 26%, 43%, and 43% at 6, 12, and 24 months after ablation, increasing to 46%, 56%, and 65% if an AF burden cutoff of ≤0.5% was applied. The proportion of patients with AF burden ≤0.5% increased from before ablation to 6 ($p = 0.01$), 12 ($p = 0.01$), and

FIGURE 1 Scatterplot Comparing the AF6 Sum Score Before and After Ablation

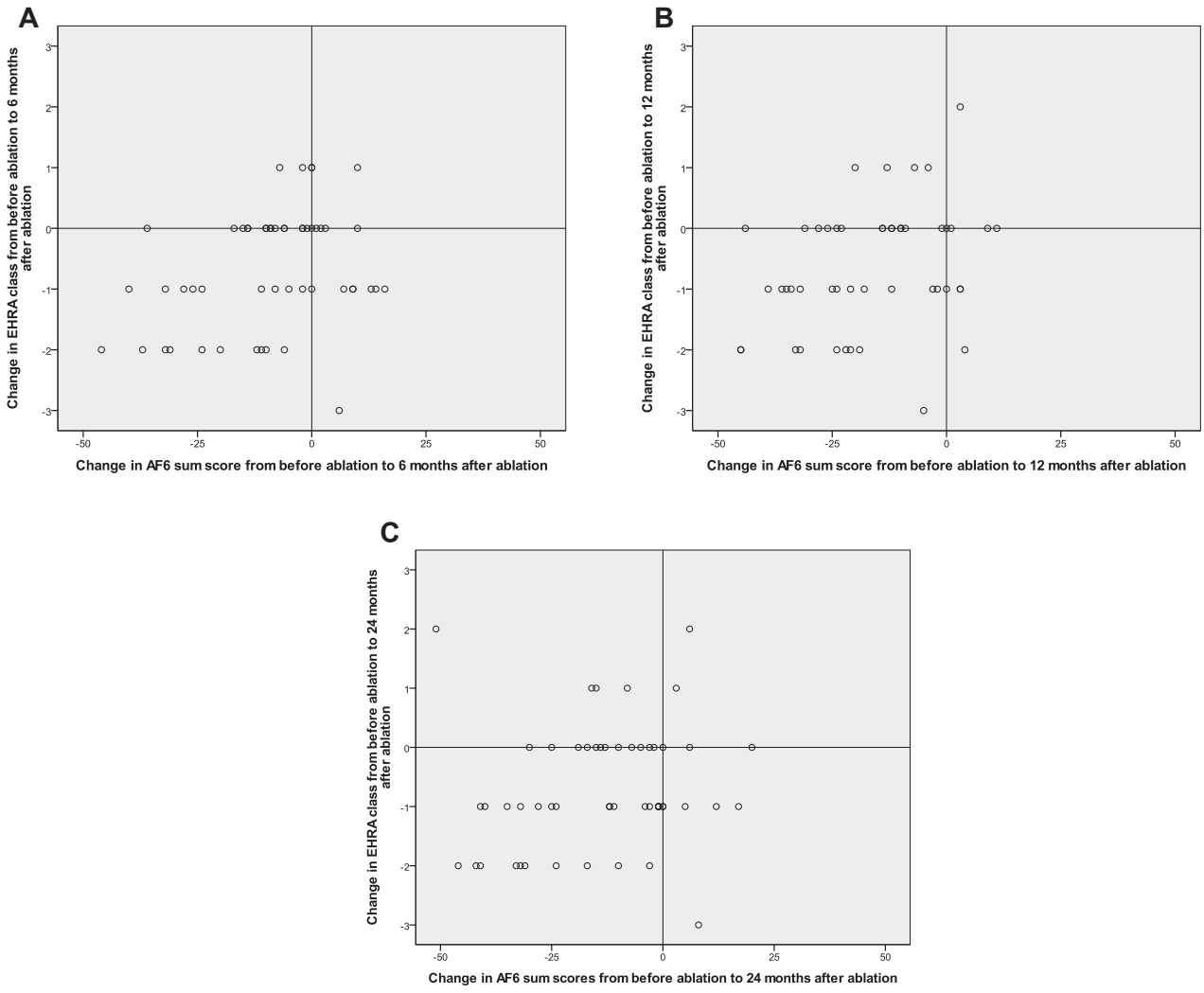


(A) 6 months ($r = 0.50$; $p < 0.001$, $n = 50$), **(B)** 12 months ($r = 0.38$; $p = 0.008$, $n = 44$), and **(C)** 24 months ($r = 0.28$; $p = 0.04$, $n = 49$) after ablation. Patients above the line of identity had worsened and patients below the line improved scores following ablation. Atrial fibrillation burden is defined as <0.5% **(blue circles)** or >0.5% **(green circles)**.

24 ($p = 0.004$) months after ablation. There was a small but not significant decrease in median AF burden over time (11).

The AF6 sum score was significantly correlated with AF burden at 6 ($r = 0.37$; $p < 0.01$), 12 ($r = 0.62$; $p < 0.01$), and 24 ($r = 0.52$; $p < 0.01$) months after ablation. When the AF burden cutoff of >0.5% was applied, there was also a significant association with higher AF6 sum scores at all times after ablation (Figure 3). EHRA class and AF burden were significantly correlated at

FIGURE 2 Scatterplot Comparing Changes in AF6 Sum Score and European Heart Rhythm Association Class Before and After Ablation



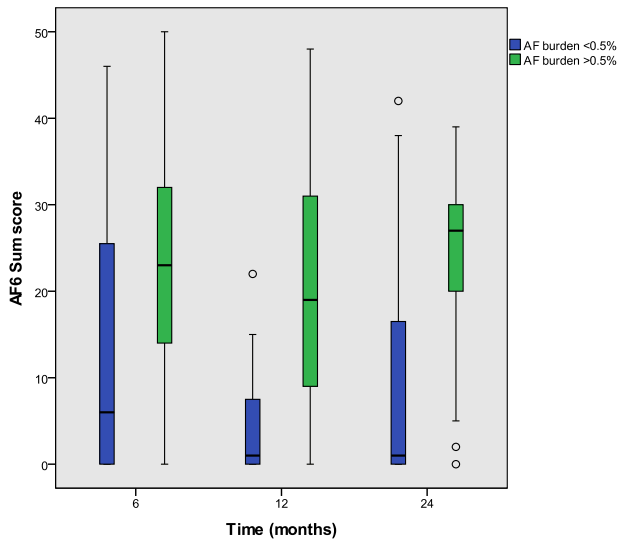
(A) 6 months ($r = 0.31$, $r^2 = 0.10$; $p = 0.02$), **(B)** 12 months ($r = 0.32$, $r^2 = 0.10$; $p = 0.03$), and **(C)** 24 months ($r = 0.22$, $r2 = 0.05$; $p = 0.12$) after ablation. Negative values indicate improvement and positive values deterioration. Patients in the lower left quadrant show improvement and in the upper right quadrant worsening in both AF6 score and European Heart Rhythm Association (EHRA) class, while patients with discordant results are found in the upper left and lower right quadrants.

6 ($r = 0.35$; $p = 0.01$), 12 ($r = 0.42$; $p = 0.002$), and 24 ($r = 0.44$; $p = 0.001$) months after ablation.

The actual AF burden in the subgroup of patients with AF burden >0.5% during the period 18 to 24 months after ablation ($n = 19$) varied between 0.53% and 100%. All patients with an AF burden up to 9% improved in EHRA class ($n = 7$) compared with before ablation or remained in EHRA class I ($n = 4$) (Table 3). Six patients improved more than 9 points in the AF6 sum score from baseline, compared with 25 patients with AF burden ≤0.5% at 24 months.

When examining the 14, 23, and 23 patients with AF burden of 0% at 6, 12, and 24 months after ablation, the median AF6 sum score was low, and the IQR showed a relatively wide range (6-month median, 0 [IQR: 0 to 27]; 12-month median, 0.5 [IQR: 0 to 7]; 24-month median, 0 [IQR: 0 to 11]). The most common AF6 item was worry/anxiety due to AF, and the highest ranking item was tiredness due to AF. Patients without any AF at any time after ablation were categorized into EHRA class I in 100%, 91%, and 96% at 6, 12, and 24 months after ablation, respectively.

FIGURE 3 Boxplot Showing a Significant Difference Versus Baseline in the AF6 Sum Score at 6, 12, and 24 Months Between Patients With Atrial Fibrillation Burden ≤0.5% and >0.5% ($p = 0.005$; $p < 0.001$; and $p < 0.001$)



Boxes show the 25th and 75th percentiles. **Horizontal lines** within **boxes** show the median; **whiskers** indicate minimum and maximum, and outliers are plotted as **circles**.

TABLE 3 Patients With an Atrial Fibrillation Burden >0.5% 18 to 24 Months After Atrial Fibrillation Ablation

Patient #	AF Burden	EHRA Class Before Ablation	EHRA Class, 24 Months	AF6 Sum Before Ablation (Median)	AF6 Sum, 24 Months (Median)
1	0.53%	I	I	37	12
2	0.55%	II	I	2	2
3	0.8%	II	I	10	27
4	1%	I	I	34	27
5	1%	III	II	33	32
6	2%	II	I	16	5
7	2%	II	II	41	36
8	3%	I	I	15	0
9	5%	I	I	19	39
10	5%	II	I	27	27
11	9%	II	I	16	21
12	9%	II	I	53	28
13	18%	I	I	41	-
14	27%	I	III	21	26
15	71%	III	III	40	38
16	100%	I	II	36	20
17	100%	II	I	31	30
18	100%	II	II	47	28
19	100%	I	II	17	20

AF = atrial fibrillation; EHRA = European Heart Rhythm Association.

PAROXYSMAL VERSUS PERSISTENT AF. When comparing the 7 patients with persistent AF before ablation with the 47 with paroxysmal AF, we detected no significant difference in AF6 sum scores before or after ablation and no difference in the proportion of patients considered to be in EHRA class ≥II between the groups.

DISCUSSION

In the present study, patients were followed by patient-reported symptoms using the AF6 and physician-assessed EHRA class for 2 years after AF ablation with complete knowledge of the underlying rhythm. AF ablation led to long-lasting symptom relief as perceived both by patients and by physicians, and AF burden correlated with both AF6 sum score and EHRA class, especially when AF burden was low. However, there was often a discrepancy between AF6 sum score and EHRA class, implying that physicians were more likely to indicate improvement in terms of a better EHRA class, while the AF6 appeared to be a more sensitive tool. Complete freedom from AF did not preclude that patients felt some symptoms, while patients with AF burden up to 10% at 24 months indicated symptomatic reduction after ablation.

PATIENT-REPORTED OUTCOMES USING THE AF6. Disease-specific questionnaires have been developed for AF but have not often been used after ablation. We used the AF-specific AF6 and demonstrated significantly lower AF6 scores 24 months after ablation compared with before, which is in line with previous studies using disease-specific assessment tools (17,18). The AF6 sum scores before and after ablation were correlated; that is, the patients with the highest scores before ablation also had the highest scores after ablation, which still allowed considerable reductions in the scores. Using the Cohen effect size, we found a reduction of more than 9 points to represent a moderate effect size, which we accepted as a clinically meaningful change and was observed in more than one-half of the patients during follow-up. In patients with AF recruited from tertiary care facilities, Dorian et al. (19) found the minimal clinically important difference of the Atrial Fibrillation Effect on Quality of Life questionnaire score to be 19 points after 3-month follow-up.

PATIENT-REPORTED OUTCOMES VERSUS AF BURDEN. AF burden was low at all times after AF ablation, while symptomatic relief improved over time. The AF6 sum score had improved considerably at 6 months and

improved further at 12 months, remaining at that level during the rest of the follow-up period. Because the continued improvement was not caused by a further reduction of AF burden, an adaptation seems to have occurred, possibly partly because patients needed time to get used to fewer symptoms and less worry and anxiety because of a lower risk for recurrent AF episodes. AF6 scores were correlated with AF burden after ablation. This finding contrasts with studies using the Arrhythmia-Specific Questionnaire in Tachycardia and Arrhythmia (18) and the AF Symptom Severity Scale (20), in which no correlation was found between AF burden and symptoms, possibly because of the intermittent rhythm follow-up using electrocardiography and Holter monitoring as opposed to our continuous rhythm monitoring during the entire follow-up period. Although patients with AF burden >0.5% had higher AF6 scores, symptom relief occurred in this group as well, either as judged by the physician or as felt by the patient, but not often by both at the same time. One-third of patients with AF burden >0.5% at 24 months after ablation had a clinically meaningful improvement in decreasing their AF6 sum score by more than 9 points, but the proportion was more than twice as high in patients with AF burden ≤0.5%. Even patients with AF burden of 0% after ablation had some AF6 sum scores, although low, despite the theoretical impossibility of having AF-specific symptoms without AF. The most probable reason is that few, if any, symptoms are unique in patients with AF. Interestingly, the most common AF6 item in completely AF-free patients was worry/anxiety due to AF.

PHYSICIAN ASSESSMENT: EHRA CLASS. Physician-assessed EHRA class improved in the first 6 months, but not thereafter. A large study on the EHRA classification and the AF-specific Atrial Fibrillation Effect on Quality of Life questionnaire in patients with AF, although not ablation patients (9), found that patients assessed as asymptomatic by physicians reported AF-specific symptoms. This suggests that physicians may underestimate symptoms when they are mild, which is in line with the results of our study. In another study, EHRA class correlated well with Atrial Fibrillation Effect on Quality of Life score but did not discriminate sufficiently in patients with low-level symptoms in terms of health-related utility (21). The investigators recommended that EHRA class II should be divided into 2 subgroups on the basis of whether the patient is troubled by symptoms of AF (class IIb) or not (class IIa). Thus, our and other studies suggest a difference between what patients might perceive and what physicians can detect. However, to our knowledge, our study is the only to correlate these findings with complete knowledge of the underlying cardiac rhythm.

PHYSICIAN-ASSESSED OUTCOMES VERSUS AF BURDEN. When the AF burden was ≤0.5% at 24 months, EHRA class was always improved, while the results were less consistent in patients with AF burden >0.5%. In the 19 patients with AF burden >0.5%, 42% were reported to be improved by 1 EHRA class. Thus, the physician-assessed EHRA class correlated well with AF burden when the burden was very low but not when AF burden was higher.

PATIENT-REPORTED VERSUS PHYSICIAN-ASSESSED OUTCOMES. In contrast to the physician-assessed EHRA class, the patient-reported AF6 scores showed continued improvement up to 12 months after ablation, indicating that AF6 is a more sensitive tool for measuring symptoms. Despite a low correlation between EHRA class and AF6 sum score, the predictive ability was low, and the change in EHRA class was not concordant with the change in the AF6 sum score in nearly one-half of the patients, demonstrating a discrepancy between physicians' and patients' assessments of AF-specific symptoms.

HOW CAN PATIENTS BEST BE INVOLVED IN DECISIONS ABOUT TREATMENT? Recently updated guidelines advocate more patient involvement in decisions about how to treat AF, both when selecting drugs for rhythm and/or rate control and when deciding for or against AF ablation (2). Decisions regarding rhythm (and/or rate) control, including ablation, are based on symptomatology in relation to the type of AF and its duration as well as benefits and risks in individual patients. Symptoms are most often what bring patients to their doctors, and the way they verbally express and explain their symptoms may differ a great deal. A short, informative, and validated symptom score may add significant information and be of help in the selection of treatment.

STUDY LIMITATIONS. The study population was small, but all patients were followed in great detail for a minimum of 2 years, and our conclusions should be considered hypothesis generating. The ILR was implanted only a few weeks before ablation, and the AF burden before ablation may therefore not be entirely reliable. The AF6 was formally validated using a recall period of 7 days, while no such period has been indicated for EHRA class, meaning that any

comparison or correlation of such results must be made with caution.

CONCLUSIONS

Patient-reported and physician-assessed outcomes both correlated with AF burden after AF ablation, but there were frequent discrepancies between patients and the physicians, especially at higher AF burdens. Freedom from AF and a low AF burden resulted most often in a reduction of symptoms, but symptom relief also occurred despite little effect on the arrhythmia. A short, validated AF-specific symptom score such as the AF6 may provide greater patient input to the evaluation of treatment for AF.

ADDRESS FOR CORRESPONDENCE: Dr. Anna Björkenheim, Department of Cardiology, Örebro University Hospital, Södra Grev Rosengatan, 701 85 Örebro, Sweden. E-mail: anna.bjorkenheim@regionorebrolan.se.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The perception of outcomes after AF ablation differs a great deal between patients and their physicians, which emphasizes that patient-reported outcomes should be a primary aim of AF ablation done in order to evaluate symptom relief and improve health-related quality of life. A short, validated AF-specific symptom score such as the AF6 provides greater patient input to the evaluation of the results of AF ablation.

TRANSLATIONAL OUTLOOK: Routine use of an AF-specific instrument may help provide optimal individualized treatment from the patient's point of view. Additional studies may also show the value of such an instrument in other AF patient populations and/or after other interventions than AF ablation.

REFERENCES

1. January CT, Wann LS, Alpert JS, et al. 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:e1–76.

2. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS: the Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC endorsed by the European Stroke Organisation (ESO). Eur Heart J 2016;50:e1–88.

3. Calkins H, Kuck KH, Cappato R, et al. 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.

4. Aliot E, Botto GL, Crijns HJ, Kirchhof P. Quality of life in patients with atrial fibrillation: how to assess it and how to improve it. Europace 2014;16:787–96.

5. Garimella RS, Chung EH, Mounsey JP, Schwartz JD, Pursell I, Gehi AK. Accuracy of patient perception of their prevailing rhythm: a comparative analysis of monitor data and questionnaire responses in patients with atrial fibrillation. Heart Rhythm 2015;12:658–65.

6. Verma A, Champagne J, Sapp J, et al. Discerning the incidence of symptomatic and asymptomatic episodes of atrial fibrillation before and after catheter ablation (DISCERN AF): a prospective, multicenter study. JAMA Intern Med 2013;173:149–56.

7. Hindricks G, Piorkowski C, Tanner H, et al. Perception of atrial fibrillation before and after radiofrequency catheter ablation: relevance of asymptomatic arrhythmia recurrence. Circulation 2005;112:307–13.

8. Vermond RA, Crijns HJ, Tijssen JG, et al. Symptom severity is associated with cardiovascular outcome in patients with permanent atrial fibrillation in the RACE II study. Europace 2014;16:1417–25.

9. Freeman JV, Simon DN, Go AS, et al. Association between atrial fibrillation symptoms, quality of life, and patient outcomes: results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). Circ Cardiovasc Qual Outcomes 2015;8:393–402.

10. Hindricks G, Pokushalov E, Urban L, et al. Performance of a new leadless implantable cardiac monitor in detecting and quantifying atrial fibrillation: results of the XPECT trial. Circ Arrhythm Electrophysiol 2010;3:141–7.

11. Bjorkenheim A, Brandes A, Chemnitz A, Magnuson A, Edvardsson N, Poci D. Rhythm control and its relation to symptoms during the first two years after radiofrequency ablation for atrial fibrillation. Pacing Clin Electrophysiol 2016;39:914–25.

12. Harden M, Nystrom B, Kulich K, Carlsson J, Bengtson A, Edvardsson N. Validity and reliability of a new, short symptom rating scale in patients with persistent atrial fibrillation. Health Qual Life Outcomes 2009;7:65.

13. Harden M, Nystrom B, Bengtson A, Medin J, Frison L, Edvardsson N. Responsiveness of AF6, a new, short, validated, atrial fibrillation-specific questionnaire—symptomatic benefit of direct current cardioversion. J Interv Card Electrophysiol 2010;28:185–91.

14. Kirchhof P, Auricchio A, Bax J, et al. Outcome parameters for trials in atrial fibrillation: executive summary. Eur Heart J 2007;28:2803–17.

15. Pokushalov E, Romanov A, Corbucci G, et al. Ablation of paroxysmal and persistent atrial fibrillation: 1-year follow-up through continuous subcutaneous monitoring. J Cardiovasc Electrophysiol 2011;22:369–75.

16. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd edition. Hillsdale, NJ: Lawrence Erlbaum, 1988.

17. Fichtner S, Deisenhofer I, Kindsmuller S, et al. Prospective assessment of short- and long-term quality of life after ablation for atrial fibrillation. J Cardiovasc Electrophysiol 2012;23:121–7.

18. Walfridsson H, Walfridsson U, Nielsen JC, et al. 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;17:215–21.

19. Dorian P, Burk C, Mullin CM, et al. Interpreting changes in quality of life in atrial fibrillation: how much change is meaningful? Am Heart J 2013;166:381–7.

20. Patel N, Chung EH, Mounsey JP, Schwartz JD, Pursell I, Gehi AK. Effectiveness of atrial fibrillation monitor characteristics to predict severity of symptoms of atrial fibrillation. Am J Cardiol 2014;113:1674–8.

21. Wynn GJ, Todd DM, Webber M, et al. The European Heart Rhythm Association symptom classification for atrial fibrillation: validation and improvement through a simple modification. Europace 2014;16:965–72.

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