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Gender and age differences in symptoms and health-related quality of life in patients with atrial fibrillation referred for catheter ablation

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Abstract

Background: Primary indication for catheter ablation of atrial fibrillation (AF) is to reduce symptoms and improve health-related quality of life (HRQoL). There are data showing differences between the genders and between younger and older patients. To evaluate this, we studied a large Scandinavian cohort of patients referred for catheter ablation of AF.

Methods: Consecutive patients filled out the ASTA questionnaire, assessing symptoms, HRQoL, and perception of arrhythmia, prior to ablation. Patients were recruited from four Swedish and one Danish tertiary center.

Results: A total of 2493 patients (72% men) filled out the ASTA questionnaire. Women experienced eight of the nine ASTA scale symptoms more often than men. Patients <65 years reported four symptoms more often, only tiredness was more frequent in those ≥65 years ($P = .007$). Women and patients <65 years experienced more often palpitations and regarding close to fainting and this was more common among women, no age differences were seen. Women and men scored differently in 10 of the 13 HRQoL items. Only negative impact on sexual life was more common in men ($P < .001$). Older patients reported more negative influence in four of the HRQoL items and the younger in one; ability to concentrate.

Conclusions: Women experienced a more pronounced symptom burden and were more negatively affected in all HRQoL concerns, except for the negative impact on sexual life, where men reported more influence of AF. Differences between age groups were less pronounced. Disease-specific patient-reported outcomes measures (PROMs) add important information where gender differences should be considered in the care.

KEYWORDS

age, atrial fibrillation, disease-specific questionnaire, gender, health-related quality of life, symptoms

1 | INTRODUCTION

In accordance with current guidelines, the primary indication for catheter ablation in patients with atrial fibrillation (AF) is to reduce symptoms and improve health-related quality of life (HRQoL).[1] AF might affect patients in many ways and, therefore, it is crucial in patient-centered care to have an understanding and a comprehensive insight into the patients' own experiences.[2] Hence, patient-reported outcomes measures (PROMs) should be a part of the clinical routine.[2]

Studies exploring patients' experiences from a gender and age perspective have shown considerable differences between women and men, as well as an impact of age in regard to the effect of arrhythmia on symptoms and HRQoL. There are studies with data from AF-specific questionnaires, those who have made use of generic

and domain-specific questionnaires and those using a combination of questionnaires.[3–6] Generic and domain-specific questionnaires allow for comparisons between patients with different diagnoses while the advantage with a disease-specific is that it adds specific, disease-related information.[7–9]

The importance of identifying valid disease-specific questionnaires to assess HRQoL is highlighted in the guideline document from 2015 and if not available, it is recommended to develop and validate such a questionnaire.[2] The Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia (ASTA) was developed in collaboration with patients suffering from arrhythmias and healthcare professionals working with the targeted patient population. The ASTA questionnaire was validated in patients with AF, supraventricular, and ventricular arrhythmias and assesses not only symptoms and HRQoL, but also how palpitations are perceived.[10,11]

The aim of this article is to present the impact of AF on perceived palpitations, symptoms, and HRQoL, from a gender and age perspective, using disease-specific PROMs in a clinical setting in a large Scandinavian cohort of patients prior to a catheter ablation procedure.

2 | METHODS

2.1 | Design

The present study was an observational, cross-sectional study in patients referred for catheter ablation of AF.

2.2 | Patients

Consecutive patients referred for catheter ablation of AF were asked to complete the ASTA questionnaire before catheter ablation, as part of the clinical routine. The data collection period was from November 2011 until January 2017. Inclusion criteria were age ≥18 years, sufficient knowledge of the Swedish or Danish language, capability to independently fill out the questionnaire, and willingness to participate.

Patients were recruited from five tertiary centers; four in Sweden: the Department of Cardiology, University Hospital in Linköping (892 patients); the Department of Cardiology, University Hospital in Örebro (196 patients); the Department of Cardiology, Skaraborgs sjukhus Skövde (158 patients); and the Department of Cardiology, Skåne University Hospital in Lund (189 patients). Participating center in Denmark was Heart Center Molholm, Private Hospital Molholm, Vejle (1058 patients).

2.3 | Patient-reported outcome measures with the arrhythmia-specific ASTA questionnaire

The disease-specific questionnaire ASTA is divided into three separate parts: Part I evaluates the patient's latest episode of arrhythmia and current medication. Part II assesses symptom burden, including a nine-item symptom scale with a four-point response scale (ASTA symptom scale), with response alternatives from: "No (0), Yes, to a certain extent

(1), Yes, quite a lot (2), or Yes, a lot (3)" where higher scores imply a higher symptom burden. Outside the symptom scale, questions are put on the following: the frequency of arrhythmia occasions during the last 3 months and the average and the longest duration of an arrhythmia episode, how the arrhythmia is experienced (palpitations), what factors might influence arrhythmia occurrence (special occasions) and the experience of coming close to fainting, or fainting in connection with arrhythmia.

Part III assesses HRQoL with a 13-item scale, with the same four-point response scale (ASTA HRQoL scale) as for the symptom scale where higher scores imply a more negative influence on daily life concerns. The ASTA HRQoL scale is further divided into a seven-item physical subscale and a six-item mental subscale.

Scale scores are calculated for the symptom scale and for the HRQoL scales. Scores can be calculated for the symptom scale if at least eight of the nine items are filled out and for the HRQoL scale if 11 of the 13 items are completed. Values range from 0 to 100, where higher scores reflect a higher symptom burden and a worse effect on HRQoL, due to arrhythmia.[10–12]

The majority of patients filled out the questionnaire in its electronic version, 1944 (78%) while 549 (22%) used the paper version.

2.4 | Ethical considerations

The Regional Ethical Review Board at the Faculty of Health Sciences, Linköping, Sweden approved the extraction and publication of the clinical data (DNR 2016-349-31). The study complies with the Declaration of Helsinki.[13] Since this evaluation was part of the clinical routine, oral informed consent was considered adequate.

2.5 | Statistical analysis

Continuous variables were expressed as means ± standard deviation (±SD). Categorical data were presented as counts and percentages. Variables not normally distributed as medians with 25th and 75th percentiles within brackets. The students' t-test was used for comparisons between women and men and patients <65 years and ≥65 years concerning symptom and HRQoL scale scores and χ^2 was used for categorical data. We have chosen a cut-off point of 65 years to compare the situation in younger patients, for example, those expected to still be working, in comparison with patients who might have retired and were older. The internal consistency, that is, homogeneity, indicating the degree of intercorrelation of the items in the four scales (the symptom scale, the HRQoL total scale, and the HRQoL physical and mental subscales) was assessed by Cronbach's α values, and considered satisfactory when exceeding the recommended limit of 0.7.[14,15]

Univariate and multivariate linear regression analyses were performed to determine the correlation of gender and age with symptoms and HRQoL as expressed by the ASTA questionnaire. The ASTA symptom scale score and HRQoL scores were used as dependent variables. Gender and patients ≥65 years were used as independent factors. The analyses were corrected for obesity (BMI≥30 kg/m^2), hypertension, diabetes mellitus, ischemic heart disease, previous stroke, or transient

ischemic attack (TIA). The corrections did not include CHA_2DS_2 VASc or the $CHADS_2$ scores since both gender and age are included into these scores. The models were fit by an enter method, in which all variables were entered into the original model and then variables with P-values of >.10 were removed. All reported P-values were two-sided and a value <.05 was considered statistically significant. The analyses were performed using the SPSS 24.0 (SPSS, Chicago, IL).

3 | RESULTS

3.1 | Patients

There were 2493 patients who filled out the ASTA questionnaire prior to catheter ablation of AF. This represented 92 % of the total population eligible for evaluation. The mean age was 64.5 years for women, $n = 698$ patients, SD $\pm$ 8.6 and 59.6 years for men, $n = 1795$ patients, SD $\pm$9.7, $P < .001$, 72 % of the patients were men. For baseline characteristics, please see Table 1.

The most commonly used antiarrhythmic medication was beta blockers (70%) followed by amiodarone (22%) and Class IC antiarrhythmic drugs (15%). For further data regarding baseline characteristics, please see Table 1.

3.2 | Missing data

During the study period, a total of 2710 patients were ablated for AF and 2493 of those (92%) did fill out the ASTA questionnaire. Missing data for any one item in the nine-item symptom scale was 1.9-2.0% for women and 3.0% for men, and corresponding values for patients <65 years and ≥65 years were 2.8 and 2.5-2.6%, respectively. For the 13-item HRQoL scale, there were 1.9-2.6% and 3.0-3.3% missing items for women and men, respectively and for patients <65 years versus those ≥65 years the corresponding missing items were 2.9-3.2% and 2.5-3.0%. None of the above mentioned differences were significant.

3.3 | ASTA part I—When did you last experience tachycardia?

Arrhythmia "on and off every day" was reported by 27% of the women and 22% of the men ($P = .003$), "less than 1 week ago" 30% women, 25% men ($P = .009$) while the remaining intervals did not differ between the genders. Between the age groups only "on and off every day" showed a difference between the groups: age <65 years 26%, ≥65 years 20% ($P = .001$).

3.4 | ASTA part II—Symptoms

3.4.1 | Palpitations

The ASTA questionnaire contains seven questions regarding how the patients perceive the arrhythmia. Women experienced palpitations more often than men did, and patients <65 years reported experiencing palpitations more often than patients ≥65 years (Figure 1A and 1B).

3.4.2 | On specific occasions

Thirty one percent of the patients reported that the arrhythmia occurred on specific occasions. "Specific occasions" mentioned were, for example, during sleep, when exercising, in conjunction with mental stress, in connection with drinking alcohol, after meals, and when experiencing insomnia. This was more common for men compared to women (32 vs 27 %, $P < .05$). Patients <65 years more frequently experienced the arrhythmia on specific occasions then patients aged ≥65 years (34 vs 26%, $P < .001$). For further details, see Supporting Information.

3.4.3 | The ASTA 9-items symptom scale

The most frequently reported symptoms in connection with AF were breathlessness during activity, weakness/infirmity, and tiredness. There were significant differences between women and men in eight of the nine symptoms in the ASTA symptom scale, and there were differences between patients <65 years and those ≥65 years in five of the nine symptoms. Women and patients ≥65 years scored worse, that is, higher scores (Table 2).

3.4.4 | Close to fainting and fainting

Outside the ASTA symptom scale, the patients were questioned about the more disabling symptoms close to fainting and fainting. Women reported being both close to fainting (50%) and fainting (14%) significantly more often than men but no age differences were found (Table 2).

4 | ASTA PART III—HEALTH-RELATED QUALITY OF LIFE

4.1 | The ASTA 13-items HRQoL scale

There was a more pronounced negative impact due to the arrhythmia on physically related items compared to mental items. The most frequently experienced negative influence on daily life concerns due to AF were: "impaired physical ability," "deteriorated life situation," "feel unable to work, study, or carry out daily activities," and "avoid planning things you would like to do" (Table 3).

There were significant differences between women and men in 10 of the 13 HRQoL items. There was only one item where men were more negatively affected than women and this was regarding AF's negative effects on the patient's sexual life (Table 3).

Patients ≥65 years more often reported a negative influence in four of the items, compared to patients <65 years, for example, concerning feeling unable to work, study or carry out daily activities, spending less time with family/relatives and friends, as well as with acquaintances and avoiding planning things they would like to do such as travelling and leisure activities.

TABLE 1 Continuous variables are expressed as means ± standard deviation (±SD) and categorical data are presented as counts and percentages

Patients characteristics	Female	Male	P- value	<65 years	≥65 years	P-value
Number of patients%	698 (28)	1795 (72)		1434 (58)	1059 (42)	
Age mean (±SD)	64.5 (±8.6)	59.6 (±9.7)	<.001	54.6 (±7.5)	69.6 (±3.6)	<.001
Gender (% men)				80	61	<.001
	Female %	**Male %**	**P-value**	**< 65 years %**	**≥65 years %**	**P-value**
Type of atrial fibrillation						
Paroxysmal	49	48	.90	49	48	.63
Persistent	49	49	.75	48	50	.34
Long-standing persistent	2	3	Ns	3	2	ns
Ischemic heart disease	6	4	.40	30	28	.70
Hypertension	39	37	.13	41	40	.55
Diabetes	5	6	.86	7	7	.68
TIA/Stroke	5	5	.32	7	7	.53
CHADS$_2$	%	%		%	%	
Female N = 204, Male N = 530						
0	34	44	.01	44	39	.18
<65 years = 433, ≥65 years = 301						
1	42	36	.11	37	39	.62
2	18	13	.09	13	17	.10
3	6	6	.09	6	5	.10
4	0	0.6	Ns	1	0.3	ns
5	0	0.4	Ns	1	0	ns
CHA$_2$DS$_2$ VASc	%	%		%	%	
Female N = 488, Male N = 1,250						
0	-	27	-	27	29	.19
<65 years = 985, ≥65 years = 753						
1	55	29	-	30	27	.19
2	23	24	.41	24	24	.89
3	15	12	.15	13	13	.81
4	5	6	.22	6	5	.58
5	2	1	Ns	2	1	ns
6	1	1	Ns	1		ns
7	0	0	Ns	0	0	ns
8	1	0	Ns	0	1	ns
Body Mass Index (kg/m^2) mean (±SD)	27.8 (±4.5)	27.8 (±4.2)	.76	27.8 (±4.2)	27.8 (±4.4)	.99
Antiarrhythmic drugs	%	%		%	%	
Beta blockers	70	71	.51	70	71	.54
Calcium antagonists	4	2	.02	2	3	.19
Digitalis	4	3	.11	3	4	.25
Class 1A	1	1	Ns	1	1	ns
Class 1C	14	15	.42	14	16	.33
Class III Sotalol	4	4	.57	5	4	.11
Amiodarone	21	22	.98	23	20	.14
Dronerdarone	9	9	.42	10	8	.29
Anticoagulants						
Warfarin	61	59	.50	58	63	.01
NOAC	39	41	.50	42	37	.01

CHADS$_2$, congestive heart failure; hypertension, age≥75, diabetes, stroke.
CHA$_2$DS$_2$ VASc: congestive heart failure, hypertension, age ≥75 years, diabetes, stroke, vascular disease, female sex.
N = number of patients; TIA = transient ischemic attack.
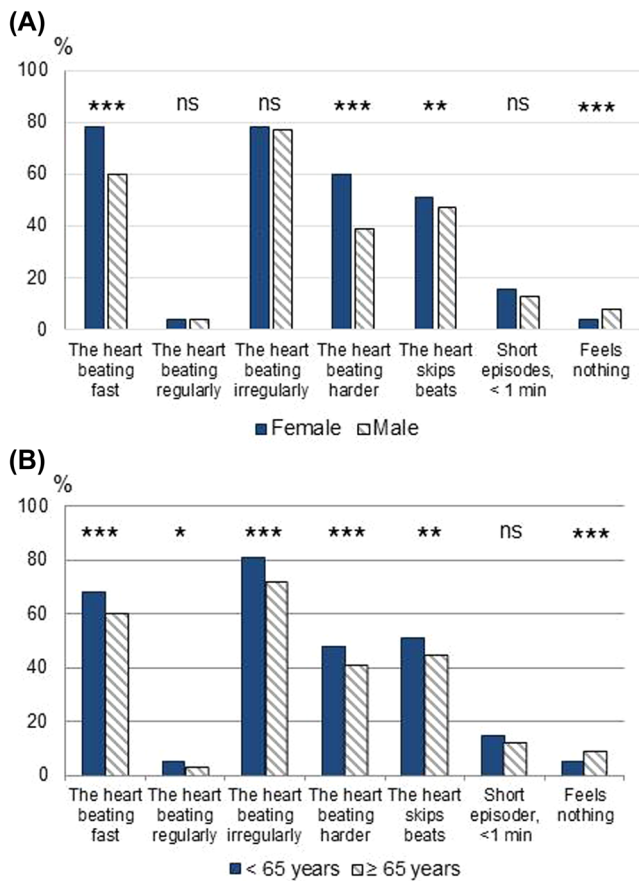
FIGURE 1 (A) Description of palpitations for women and men. Note that more than one answer was allowed. *** indicates a P-value < .001, ** indicates a P-value < .01, * indicates a P-value < .05, and ns = not significant. (B) Description of palpitations for patients <65 years and for those ≥65 years. Note that more than one answer was allowed. *** indicates a P-value < .001, ** indicates a P-value < .01, * indicates a P-value < .05, and ns = not significant
[Color figure can be viewed at wileyonlinelibrary.com]

Those <65 years were more negatively affected in one item: a more impaired ability to concentrate (Table 3).

4.2 | The ASTA symptom and HRQoL scale scores, gender, and age comparisons

Women scored significantly higher than men for the degree of severity in all the four scale scores (P < .001). This was true for both the mental and physical subscales (Table 4). This difference remained unchanged when corrected for covariates including age.

No differences were seen between the age groups (<65, ≥65 years) in the ASTA HRQoL total scale score. However, patients ≥65 years reported a significantly worse HRQoL in the ASTA HRQoL physical scale score (P = .002) while patients <65 years reported a significantly worse HRQoL in the mental scale score (P = .012). This age difference remained unchanged when corrected for covariates including gender. Patients <65 years scored significantly worse in the ASTA symptom scale score (P = .001).

Internal consistency was evaluated with the Cronbach's α and considered adequate for all four scales. The ASTA symptom scale: 0.795, the ASTA HRQoL total scale: 0.893, the ASTA HRQoL physical subscale: 0.874, and the ASTA HRQoL mental subscale: 0.773.

5 | DISCUSSION

The main results in this large Scandinavian, clinical cohort of patients with AF, referred for catheter ablation, were the pronounced differences between how women and men experienced symptoms, including palpitations, and how AF influenced daily life concerns. There were also differences, although less pronounced, between patients <65 years and those ≥65 years. To our knowledge, this is by far the largest study reporting disease-specific assessments used in clinical routine prior to catheter ablation in a patient cohort with AF.

TABLE 2 Experienced symptoms during arrhythmia

Percent of patients experiencing the respective symptoms in connection with arrhythmia (Yes/No)	Female %	Male %	P- value	<65 years %	≥65 years %	P-value
Breathlessness during activity	91	90	.175	91	89	.115
Breathlessness even at rest	59	54	.037	57	52	.016
Dizziness	71	58	<.001	62	61	.5398
Cold sweats	59	52	.001	57	50	<.001
Weakness/fatigue	94	87	<.001	88	90	.237
Tiredness	94	87	<.001	88	91	.007
Chest pain	40	36	.035	39	35	.043
Pressure/discomfort in chest	72	63	<.001	68	63	.026
Worry/anxiety	74	63	<.001	67	64	.122
Close to fainting	50	32	<.001	38	37	.467
Fainting	14	8	<.001	8	9	.534

ASTA = The Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia.
Nine symptoms included in the ASTA symptom scale while "close to fainting" and "fainting" are outside of the scale.

TABLE 3 The 13 items in the ASTA HRQoL evaluation and included in the ASTA HRQoL scale

Percent of patients experiencing negative influence on daily life concerns due to arrhythmia (Yes/No)	Female %	Male %	P-value	< 65 years %	≥ 65 years %	P-value	Domain
Feel unable to work, study, or carry out daily activities	84	74	<.001	73	82	<.001	P
Spend less time with your family/relatives and friends	67	48	<.001	50	58	<.001	P
Spend less time with acquaintances (people you do not know that well)	63	48	<.001	50	56	.008	P
Avoid planning things you would like to do, like travelling and leisure activities	84	74	<.001	73	81	<.001	P
Impaired physical ability	83	82	.399	92	93	.725	P
Impaired ability to concentrate	69	65	.060	68	63	.031	M
Feel dejected or sad	80	72	<.001	73	73	.983	M
Feel irritated or angry	52	55	.205	56	53	.162	M
Experience sleep problems	79	65	<.001	70	68	.295	M
Negatively affected sexual life	53	63	<.001*	61	60	.537	P
Afraid of dying	56	39	<.001	45	42	.118	M
Deteriorated life situation	90	90	.614	90	91	.564	P
Feel worried that your symptoms will reoccur during arrhythmia-free periods	76	71	.009	73	71	.440	M

ASTA = The Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia;HRQoL = Health-related quality of life.
The physical subscale (*P*) includes questions 1-5, 10, and 12. The mental subscale (*M*) includes questions 6-9, 11, and 13. The one item where men scored worse than women is marked with an asterix.[*]

TABLE 4 Scale scores are calculated for the symptom scale and for the HRQoL scales

Overall scoring in the ASTA symptom and HRQoL scales				
Gender	Female	Male	P-value, univariate linear regression	P-value, multivatiate linear regression
Symptom score 9 items	44 (30, 56)	37 (22, 48)	<.001	<.001
HRQoL total score 13 items	41 (26, 60)	36 (21, 54)	<.001	<.001
Physical score 7 items	48 (29, 71)	38 (24, 62)	<.001	<.001
Mental score 6 items	33 (22, 50)	28 (17, 44)	<.001	<.001
Age groups	<65 years	≥65 years	P-value, univariate linear regression	P-value, multivatiate linear regression
Symptom score 9 items	37 (26, 52)	37 (26, 52)	.182	.001
HRQoL total score 13 items	36 (21, 54)	38 (23, 56)	.036	.42
Physical score 7 items	38 (24, 62)	48 (29, 67)	<.001	.002
Mental score 6 items	33 (17, 50)	28 (17, 50)	.241	.012

ASTA = The Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia.
The scale scores are presented as medians and within brackets 25th-75th percentiles.
Scores can be calculated for the symptom scale if at least eight of the nine items are filled out and for the HRQoL scale if 11 of the 13 items are completed.
Values range from 0 to 100 where higher scores reflect a higher symptom burden and a worse effect on HRQoL, due to arrhythmia.The *P*-values in the third column are the results from linear regression analysis while the multiple regression analysis is presented in the fourth column: The analyses were corrected for: hypertension, diabetes, BMI (body mass index) ≥30, previous TIA or stroke, age and gender.

5.1 | Symptoms of arrhythmia from a gender and age perspective

It has been reported in several studies that there is a prominent difference in how women experience AF, in that they show both a higher symptom burden and a more negatively affected HRQoL compared to men. However, most of these studies have used generic question-naires and these are influenced not only by the arrhythmia but also by other causes, for example, concomitant diseases.[9] In two recent studies, disease-specific questionnaires were used[6,16] confirming previously reported gender differences.

It makes intuitive sense that younger, more active patients may find AF significantly more disruptive than older patients, particularly those

with additional health problems. The results of our study, in which older age was associated with lower AF symptom frequency and severity scores, support this notion and are consistent with analysis from the RACE trial, which reported that age <69 years was associated with a greater likelihood of improved QoL during study follow-up.[17] Our data confirm that women are older when they are referred for catheter ablation treatment.[18] In our study, 39% of the age group 65 years or above were women; the corresponding number for the younger age group was only 20%.

Bhave et al showed in patients with newly diagnosed AF, a sizeable gender- and race-based disparity in both treatment and care, with women being less likely to undergo treatment with catheter ablation than men.[19] It is known that female patients with supraventricular arrhythmia had more difficulties getting diagnosed and being referred for catheter ablation compared to men and they also struggled to be believed.[20]

Men and those ≥65 years significantly more often experienced persistent arrhythmia before the ablation and they perceived longer duration of AF, both typical as well as longest experienced duration. Women more often had AF "less than 1 week ago" and patients <65 years had, like women, daily episodes more often.

We found no difference in AF type, either between the genders or between the age groups. The impact of gender on arrhythmia duration varies in different studies, probably due to large differences in the cohorts.[3,21,22] The reasons for the differences we found are unclear; one explanation is that many patients report repeated episodes of arrhythmia even during continuous AF and, thus, patients with a lower threshold for AF symptoms will report a higher frequency of episodes even during ongoing AF.[21]

In the ASTA questionnaire, patients are asked how they experience palpitations. Twice as many men than women reported that they did not experience any palpitations at all while arrhythmia-related descriptions of fast, irregular, and hard heart beats were significantly more often reported by women. In the present study, women more often reported that they experienced their hearts to beat more rapidly during AF.

Almost one third of the patients in our study found a pattern of arrhythmia occurrence. It was more common that male patients found a connection to specific occasions, as well as those <65 years. Arrhythmia provoking factors have been described previously regarding patients with paroxysmal AF.[23] As in our study, common situations for AF occurrences were during sleep, in connection with physical effort or mental stress, while drinking alcohol, when having big meals or eating spicy food, or for some when tired and suffering from insomnia.

It is worth noting the very high frequency of three symptoms: "breathlessness during activity," "weakness/fatigue," and "tiredness," all three reported by approximately 90 % of the population, regardless of age and gender. Our data are in line with what is known to be the most common experienced symptoms, and that less common is chest pain in connection to the arrhythmia.[21]

There is no obvious explanation for why women experienced almost all symptoms more frequently than men did and with a higher degree

of severity. The only exception was the most commonly reported symptom "breathlessness during activity." The fact that women felt more dizziness, cold sweats, and weakness/fatigue during AF may be an explanation for the higher frequency of being close to fainting and fainting among women. There are several reports indicating that women with AF are more symptomatic than men,[24,25] a higher heart rate has been suggested as one possible mechanism.[22,25]

Walters et al investigated factors predicting AF-related symptoms and impact on HRQoL in a group of patients with symptomatic AF and found a high prevalence of severe psychological distress (35%).[26] In the SMURF-study,[27] we investigated factors predicting AF-related symptoms and HRQoL prior to catheter ablation of AF. We found that both anxiety and depression, as indicated by the HADS questionnaire (HADS: Hospital Anxiety Depression Scale),[28] and low-grade inflammation played a central role in arrhythmia-related symptoms and HRQoL. Obesity was the most significant predictor of general physical status.[12] Reynolds et al conclude that a better understanding of the factors that underlie these differences will be needed to optimize outcomes for women with AF.[4]

Regarding the ASTA symptom scale score and influence of age, we did not find any differences between patients <65 years and those ≥65 years even though the mean age differed in the groups by as much as 15 years.

5.2 | Health-related quality of life from a gender and age perspective

Women also experienced more negative impact on HRQoL, with one important exception: men were more negatively affected regarding their sexual life. In the answer to the question: "Is your sexual life affected negatively by your arrhythmia?" more than half of the women and two thirds of the men judged the arrhythmia to negatively affect their sexual life.

There is not much data exploring this important HRQoL concern in this patient population.

A study by Platek et al highlights that sexual dysfunction is highly prevalent in patients with AF and there is a need to routinely screen these patients for sexual dysfunctions. AF itself may cause a decreased HRQoL, including disturbed sexual life, but also concomitant diseases, such as hypertension and diabetes, and other cardiovascular risk factors, as well as pharmaceutical agents, particularly beta blockers, may contribute to the impairment.[29] We found no such differences in the present study. The question on whether AF has impact on the patients' sexual life is important and needs to be addressed in the care.

The more negative impact on most of the HRQoL items for women is in line with previous reports on women with AF.[3,30,31] In several investigations, in a variety of settings women scored a more negative impact on both Quality of Life and HRQoL than men did. The reasons suggested range from socioeconomic factors to fundamental gender differences regarding perception of illness.[3,4,7] Bazemore et al made use of disease-specific questionnaires but merely states that "this gender gap in enrolment for catheter ablation is unclear and likely due to multiple patient and provider factors."[6] Walters et al evaluated symptom

severity and HRQoL also with disease-specific instruments and found that psychological factors outweighed clinical predictors.[16]

The main finding that older patients report a more severe impact on HRQoL, particularly on the physical subscale, is not surprising. That increasing age correlates with reduced HRQoL is a common finding.[9]

Whatever the cause, it is evident that women with AF differ from men in their demographic and clinical characteristics, their subjective experience of the condition, and possibly in how they are managed and how they respond to therapy.[4,12,31] Better understanding of the factors that underlie these differences is needed to optimize outcomes for women with AF.

6 | METHODOLOGICAL CONSIDERATIONS/LIMITATIONS

This was a cross-sectional study from five Scandinavian ablation centers including patients with AF referred for catheter ablation. As such, this was a group of symptomatic patients comprising a large number of patients clinically accepted for ablation, and not a selected study group. We cannot completely rule out an influence from a selection bias regarding referral for catheter ablation. An argument against such a bias being the main reason for the large differences found is the fact that regardless of disease the same pattern for gender differences has been reported.

Using PROMs in clinical routine requires good logistics, where the patients fill out the assessments preferably before the planned intervention. A vast majority of patients in this study answered the ASTA questionnaire in its web version, which had the advantage that the volume of missing data was minimized and input errors were avoided. The patients filled out the ASTA questionnaire at home before the planned ablation treatment and it was, therefore, not combined with an ECG registration. However, when using the ASTA questionnaire, patients were questioned about their overall experiences in connection with episodes and not specifically at the time of filling out the questionnaire.

Not all patients did in fact fill out the questionnaire, 8% did not. The main reason was of logistical nature: failure to make certain that the questionnaire was filled out prior to the procedure due to among other reasons a tight schedule at the respective ablation laboratory.

There were no differences between those who did and those who did not fill out the questionnaire regarding age, gender, or comorbidities.

7 | CONCLUSIONS

We analyzed a large number of patients referred for catheter ablation of AF regarding symptoms, HRQoL, and perception of arrhythmia from a gender and age perspective, making use of a disease-specific questionnaire. There were large differences between women and men, where women scored worse in almost all measured symptoms and items regarding HRQoL, with one important exception where men reported a worse impact on their sexual life. The differences were less pronounced between the age groups. Regardless of the reasons for these differences, they should be considered when evaluating patients with AF and their treatment options. PROMs in a clinical setting add important information in the care of patients with AF.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace* 2016;18:1609-1678.
2. Lane DA, Aguinaga L, Blomstrom-Lundqvist C, et al. Cardiac tachyarrhythmias and patient values and preferences for their management: The European Heart Rhythm Association (EHRA) consensus document endorsed by the Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLEACE). *Europace* 2015;17:1747-1769.
3. Ong L, Irvine J, Nolan R, et al. Gender differences and quality of life in atrial fibrillation: The mediating role of depression. *J Psychosom Res.* 2006;61:769-774.
4. Reynolds MR, Lavelle T, Essebag V, Cohen DJ, Zimetbaum P. Influence of age, sex, and atrial fibrillation recurrence on quality of life outcomes in a population of patients with new-onset atrial fibrillation: The Fibrillation Registry Assessing Costs, Therapies. Adverse events and Lifestyle (FRACTAL) study. *Am Heart J.* 2006;152:1097-1103.
5. Piccini JP, Simon DN, Steinberg BA, et al. Differences in clinical and functional outcomes of atrial fibrillation in women and men: Two-year results from the ORBIT-AF registry. *JAMA Cardiol.* 2016;1:282-291.
6. Bazemore TC, Bolger LE, Sears SF, Sadaf MI, Gehi AK. Gender differences in symptoms and functional status in patients with atrial fibrillation undergoing catheter ablation. *Pacing Clin Electrophysiol.* 2019;42:224-229.
7. Thrall G, Lip GY, Carroll D, Lane D. Depression, anxiety, and quality of life in patients with atrial fibrillation. *Chest* 2007;132:1259-1264.

8. Ong L, Cribbie R, Harris L, et al. Psychological correlates of quality of life in atrial fibrillation. *Qual Life Res.* 2006;15:1323-1333.

9. Thrall G, Lane D, Carroll D, Lip GY. Quality of life in patients with atrial fibrillation: A systematic review. *Am J Med.* 2006;119:448 e1-448e1-19.

10. Walfridsson U, Arestedt K, Stromberg A. Development and validation of a new arrhythmia-specific questionnaire in tachycardia and arrhythmia (ASTA) with focus on symptom burden. *Health Qual Life Outcomes.* 2012;10:44.

11. Walfridsson U, Stromberg A, Arestedt K. Development and validation of an arrhythmia-specific scale in tachycardia and arrhythmia with focus on health-related quality of life. *J Cardiovasc Nurs.* 2015;30: 98-108.

12. Charitakis E, Barmano N, Walfridsson U, Walfridsson H. Factors predicting arrhythmia-related symptoms and health-related quality of life in patients referred for radiofrequency ablation of atrial fibrillation: An observational study (the SMURF study). *JACC Clin Electrophysiol.* 2017;3:494-502.

13. Rickham PP. Human experimentation. code of ethics of the world medical association. Declaration of Helsinki. *British Med J.* 1964;2:177.

14. Cronbach LJ. Coefficient alpha and the internal structure of tests. *Psychometrika* 1951;16:297-334.

15. Fayers P . Patient-reported outcomes. Quality of Life: The Assessment, Analysis, an Interpretation of Patient-Reported Outcomes. New York, NY: Wiley. 2008.

16. Walters TE, Wick K, Tan G, et al. Symptom severity and quality of life in patients with atrial fibrillation: Psychological function outweighs clinical predictors. *Int J Cardiol.* 2019;279:84-89.

17. Hagens VE, Ranchor AV, Van Sonderen E, et al. Effect of rate or rhythm control on quality of life in persistent atrial fibrillation. Results from the Rate Control Versus Electrical Cardioversion (RACE) study. *J Am Coll Cardiol.* 2004;43:241-247.

18. Dagres N, Nieuwlaat R, Vardas PE, et al. Gender-related differences in presentation, treatment, and outcome of patients with atrial fibrillation in Europe: A report from the Euro heart survey on atrial fibrillation. *J Am Coll Cardiol.* 2007;49:572-577.

19. Bhave PD, Lu X, Girotra S, Kamel H, Vaughan Sarrazin MS. Race- and sex-related differences in care for patients newly diagnosed with atrial fibrillation. *Heart Rhythm* 2015;12:1406-1412.

20. Wood KA, Wiener CL, Kayser-Jones J. Supraventricular tachycardia and the struggle to be believed. *Eur J Cardiovasc Nurs.* 2007;6:293-302.

21. 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;12:658-665.

22. Hnatkova K, Waktare JE, Murgatroyd FD, Guo X, Camm AJ, Malik M. Age and gender influences on rate and duration of paroxysmal atrial fibrillation. *Pacing Clin Electrophysiol.* 1998;21:2455-2458.

23. Hansson A, Madsen-Hardig B, Olsson SB. Arrhythmia-provoking factors and symptoms at the onset of paroxysmal atrial fibrillation: A study based on interviews with 100 patients seeking hospital assistance. *BMC Cardiovasc Disord.* 2004;4:13.

24. Paquette M, Roy D, Talajic M, et al. Role of gender and personality on quality-of-life impairment in intermittent atrial fibrillation. *Am J Cardiol.* 2000;86:764-768.

25. Humphries KH, Kerr CR, Connolly SJ, et al. New-onset atrial fibrillation: Sex differences in presentation, treatment, and outcome. *Circulation* 2001;103:2365-2370.

26. Walters TE, Wick K, Tan G, et al. Psychological distress and suicidal ideation in patients with atrial fibrillation: Prevalence and response to management strategy. *J Am Heart Assoc.* 2018;7:e005502.

27. Charitakis E, Walfridsson U, Nystrom F, et al. Symptom burden, metabolic profile, ultrasound findings, rhythm, neurohormonal activation, haemodynamics and health-related quality of life in patients with atrial fibrillation (SMURF): A protocol for an observational study with a randomised interventional component. *BMJ Open.* 2015;5: e008723.

28. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983;67:361-370.

29. Platek AE, Hrynkiewicz-Szymanska A, Kotkowski M, et al. Prevalence of erectile dysfunction in atrial fibrillation patients: A cross-sectional, epidemiological study. *Pacing Clin Electrophysiol.* 2016;39: 28-35.

30. Smith D, Lip GY, Lane DA. Impact of symptom control on health-related quality of life in atrial fibrillation patients: The psychologist's viewpoint. *Europace* 2010;12:608-610.

31. Lane DA, Langman CM, Lip GY, Nouwen A. Illness perceptions, affective response, and health-related quality of life in patients with atrial fibrillation. *J Psychosom Res.* 2009;66:203-210.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.