Women with atrial fibrillation undergoing pulmonary vein isolation are more symptomatic but improve more in health-related quality of life and symptom burden than men

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ABSTRACT

Gender differences in symptoms and perceived health-related quality of life (HRQOL) in patients with atrial fibrillation (AF) referred to pulmonary vein isolation (PVI) have been reported previously. Women experience a lower HRQOL, faster heart rate, and more symptoms such as palpitation and dyspnea than men. Furthermore, they experience worse physical functioning independently of other heart diseases or age. This study evaluates referral patterns and symptoms, morbidity, functional impairment, and HRQOL from a gender perspective in patients with AF before and 6 months after PVI. The study includes 242 patients (121 men), mean age 62 ± 9 years, referred for PVI. Symptoms were assessed with the Symptom Checklist: Frequency and Severity (SCL), HRQOL with Short Form 36 (SF-36), and the functional impairment with Sickness Impact Profile (SIP). The patients’ own experiences of the referral process and history of their disease were evaluated with a supplementary questionnaire. The results showed that women improved more than men in HRQOL, SIP, and SCL 6 months post PVI. There were no sex differences in proportion of paroxysmal and persistent AF or ablation outcome. At baseline, women scored higher than men in both scales of the SCL (\(p < 0.001\)), scored lower in all components in SF-36, and scored higher in five categories of the SIP. Women were not more reluctant to accept referral for ablation when offered. The conclusion is that women with AF undergoing PVI are more symptomatic but also improve more in HRQOL and in symptom burden than men.

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Introduction

Pulmonary vein isolation (PVI) of atrial fibrillation (AF) is an alternative to drug treatment in symptomatic patients [1]. Gender differences in symptoms and perceived health-related quality of life (HRQOL) in patients with AF have been reported previously. Women experience a lower HRQOL, faster heart rate, and more symptoms such as palpitation and dyspnea than men [2,3]. Furthermore, they experience worse physical functioning independently of other heart diseases or age.

Despite more symptoms, women are less often referred for cardioversion and PVI [4–6]. The reasons are unclear although it seems likely that these differences are not limited to the fact that typically women are older at AF onset. We and others have recently reported that in patients with paroxysmal supraventricular tachycardia (PSVT), women more often than men are incorrectly diagnosed as suffering from stress, anxiety, or panic attacks, delaying referral for curative ablation for several years [7,8]. It is unknown whether female AF patients in Sweden experience similar conditions. To address this gap in knowledge, this study evaluates symptoms, morbidity, referral patterns, experience of information given, functional impairment, HRQOL, and perceived improvement from a gender perspective in patients with AF before and 6 months after ablation.

Material and methods

Design

The study is a single center, cohort study with a prospective design using a baseline investigation before PVI and a follow-up 6-month post ablation.

Patients

Between February 2013 and February 2016, a total of 197 consecutive men and 167 consecutive women referred for a de novo PVI were contacted by mail 7–30 days before the procedure requesting their participation.

The mail contained an informed consent, a postage paid envelope, and a folder with the Symptom Checklist-Frequency and Severity Scale (SCL), Medical Outcomes Short Form-36 (SF-36), Sickness Impact Profile (SIP), and a supplementary questionnaire regarding the referral history,
experience of information given in regard to the arrhythmia, number of years with symptomatic AF, and previous evaluations and diagnoses of their arrhythmia symptoms.

Symptom duration was defined as the time interval from the first symptoms reported by patients that suggested an episode of AF and confirmed in patients’ medical records when possible until the time, they answered the questionnaires.

Clinical, demographic, and electrophysiological (EP) data were collected at the time of the procedure. According to pre-study power calculations, 120 men and 120 women were needed to demonstrate a 20% difference in HRQOL parameter. Exclusion criteria were inability to read or understand Swedish or cognitive impairment.

Ablation procedure and follow-up
The ablation procedure was performed as described previously at our institution [9]. All patients underwent transesophageal echocardiography prior to the ablation procedure to exclude intra-atrial thrombosis. The ablation procedures were performed under conscious sedation and analgesia. In all procedures, PVI was performed either by radiofrequency or cryoablation technique. Additional ablation (empirical lines, complex fractionated electrograms, substrate ablation) was performed in persistent AF according to operator’s discretion.

The clinical follow-up included outpatient visits, review of medical records from other hospitals and outpatient clinics, and in some cases telephone contact with both patients and referring physicians. An ambulatory ECG and/or 24-h Holter ECG was routinely obtained during follow-up visits as well as during unscheduled ambulatory visits related to suspected AF recurrences. Recurrence was defined as at least one documented episode of AF after the index procedure. Furthermore, Patient Reported Outcome Measures (PROM) were collected at 6 months.

Questionnaires

Referral process
The questionnaire regarding the referral history was based on six interviews of patients who had undergone catheter ablation of AV nodal re-entrant tachycardia, atrial tachycardia, and atrial fibrillation. The interviews were written down verbatim and analyzed using the qualitative content analysis method [10]. Themes found were anxiety and worries they would not be believed or would not be treated politely when seeking medical help for their arrhythmias. The final version of the questionnaire consisted of questions that covered the described themes, symptom duration, referral history, and socioeconomic status.

Symptoms checklist: Frequency and severity scale
Developed by Bubien and Jenkins, the Symptom Checklist: Frequency and Severity Scale measures frequency and severity of arrhythmia symptoms [11]. The frequency scale has five answer options: never = 0, rarely = 1, sometimes = 2, often = 3, and always = 4. The severity scale has three answer options: mild = 1, moderate = 2, and extreme = 3. Range for the frequency scale is 0–64 and for the severity scale 0–48. The two scales sum independently of each other, but the severity scale depends on the frequency scale. When a patient mark “never” on the frequency scale, the severity scale is left empty. Lower values indicate less symptom burden. In this study we used the Swedish translated validated version of SCL. The data show good reliability and validity for our specific study group with a Cronbach’s alpha of 0.87 (an index of 0.70 is used as a minimal acceptable value) [12].

The short form 36 health survey questionnaire
The HRQOL was assessed with the Swedish short form 36 (SF-36) survey elaborated within the framework of International Quality of Life Assessment (IQOLA) to match the original US SF-36 Health Survey manual and Interpretation guide. On a 0 to 100 scale, the survey evaluates eight health domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. Higher scores reflect better HRQOL status and well-being. Missing items and scoring were considered according to the SF-36 manual [13].

Sickness impact profile
The self-rated functional capacity to perform daily activities was assessed with the Sickness Impact Profile (SIP). The instrument was developed by Bergner et al. [14] in the United States and was translated and validated for Swedish conditions by Sullivan et al. [15]. The instrument includes 136 items forming 12 scales. Points can be shown as total index (i.e. all 12 categories merged) for the physical and psychosocial index along with the remaining five categories or for the 12 categories separately without losing validity. Lower values indicate less functional impairment and better HRQOL. We excluded the categories body care, movement, and food intake because we judged these questions to be unfit for our study population. That is, we believed that excluding these items would not affect the validity of the scale. SIP has previously been used in studies of arrhythmia patients [16,17].

Statistical analyses
The statistical analyses were performed using IBM corp. SPSS statistics for Windows, Version 22.0, released 2013, Armonk, NY, USA. Descriptive analyses were used to describe the sample and study variables presented as mean and standard deviation or number and percent. Student’s t-test was used to compare changes in HRQOL, SIP subscales, and SCL symptom score and to evaluate differences between the sexes. Parametric methods were chosen over non-parametric ones because the variables were visually normally distributed. The summation of results from different questions to subscales and overall main scales allowed parametric
methods [4]. Categorical variables were expressed as total number and compared between the groups using the \(\chi^2\) test. To measure correlation between self-reported time with arrhythmia, education, marital status, ethnicity and occupational status, a Spearman’s correlation test was used. A \(p\) value <0.05 was considered significant.

**Ethics**

The investigation conforms to the principles outlined in the Declaration of Helsinki and were approved by the Regional Institutional Ethics Committee (2011/1903-31/2). The studies were performed in accordance with the international conference on Harmonization in Good Clinical Practice (ICH-GCP) guidelines to protect the rights, integrity, confidentiality, and well-being of the trial subjects. All participants received written information and informed consent was obtained from all patients.

**Results**

Of 364 patients contacted, 66% (\(n = 242\)) gave informed consent, completed the questionnaires, and ultimately were included in the study. The 122 patients who declined participating (76 men and 46 women) were younger than the study group, mean age 58±11 vs. 62±9 years (\(p = 0.0002\)). In the final study group, 121 women and 121 men participated. Since fewer women are referred for PVI, the inclusion time were longer for women compared to men, 35 vs. 18 months. The men were younger than the women, 60±9.6 vs. 63±8.7 years (\(p = 0.01\)). Clinical characteristics and socioeconomic data of the 242 patients are presented in Table 1.

**Missing data**

At 6 months after PVI, 92% (\(n = 222\)) of the patients completed and returned the folder with the questionnaires. The patients who did not complete the study (14 men and 6 women) did not differ in age or comorbidities when compared with those that completed the study. There were few missing data from the questionnaires. Only one patient did not fully complete the SF-36 at baseline. This was handled according to the recommendations in the SF-36 manual. The SCL and SIP had no missing data.

| Table 1. Baseline characteristics of the study subjects. |
|--------------------------------------------------------|
| **Total** \(n = 242\) | **Men** \(n = 121\) | **Women** \(n = 121\) | **p** |
| Age  | 62±9 | 60±10 | 63±9 | 0.01 |
| Systolic blood pressure  | 132±19 | 132±17 | 132±20 | 0.8 |
| Diastolic blood pressure  | 76±10 | 79±10.1 | 76±10 | 0.07 |
| BMI  | 27±4 | 27±3 | 26±4 | 0.3 |
| Diagnosis  |  |  |  |  |
| Paroxysmal atrial fibrillation  | 178 (74) | 85 (70) | 93 (77) | 0.3 |
| Persistent atrial fibrillation  | 64 (26) | 36 (30) | 28 (23) | 0.2 |
| Comorbidities  |  |  |  |  |
| Hypertension  | 91 (38) | 47 (39) | 44 (36) | 0.8 |
| Heart disease\[^a\]  | 15 (6) | 11 (9) | 4 (3) | 0.1 |
| Heart failure  | 10 (4) | 5 (4) | 5 (4) | 1.0 |
| Diabetes  | 16 (7) | 12 (10) | 4 (3) | 0.07 |
| Stroke/transient ischemic attack  | 23 (10) | 11 (9) | 12 (10) | 0.8 |
| Chronic obstructive pulmonary disease  | 3 (1) | 1 (1<1) | 2 (2) | 0.6 |
| Tested antiarrhythmic drugs  |  |  |  |  |
| Amiodarone  | 30 (12) | 11 (9) | 19 (16) | 0.2 |
| Disopyramide  | 15 (6) | 5 (4) | 10 (8) | 0.3 |
| Dronedarone  | 111 (46) | 55 (45) | 57 (47) | 0.9 |
| Flecaïnide  | 95 (39) | 57 (47) | 41 (34) | 0.05 |
| Propafenone  | 3 (1) | 2 (2) | 1 (<1) | 0.6 |
| Quinidine  | 2 (<1) | 1 (<1) | 1 (<1) | 1.0 |
| Sotalol  | 72 (30) | 35 (29) | 38 (31) | 0.8 |
| Others  |  |  |  |  |
| Beta-blockers  | 181 (75) | 84 (69) | 99 (81) | 0.04 |
| Calcium channel blockers  | 16 (7) | 3 (2) | 13 (11) | 0.02 |
| Digoxin  | 24 (10) | 4 (3) | 20 (17) | 0.001 |
| Marital status and socioeconomic data  |  |  |  |  |
| Married  | 192 (79) | 107 (88) | 85 (70) | <0.001 |
| Single  | 39 (16) | 11 (9) | 28 (23) | 0.005 |
| Widowed  | 8 (3) | 1 (<1) | 8 (7) | 0.04 |
| Unknown  | 3 (1) | 2 (2) | 1 (<1) | 0.6 |
| Education level  |  |  |  |  |
| Primary  | 33 (14) | 16 (13) | 18 (15) | 0.9 |
| High school  | 74 (31) | 36 (30) | 38 (31) | 0.9 |
| University/College  | 120 (50) | 59 (49) | 61 (50) | 0.9 |
| Unknown  | 14 (6) | 10 (8) | 4 (3) | 0.2 |
| Occupational status  |  |  |  |  |
| Employed or self-employed  | 106 (44) | 37 (31) | 69 (57) | <0.001 |
| Temporary worker, hourly employee, unemploy  | 11 (5) | 4 (3) | 7 (6) | 0.5 |
| Retired  | 97 (40) | 39 (32) | 58 (48) | 0.02 |
| Long-term sick leave\[^b\]  | 7 (3) | 2 (2) | 5 (4) | 0.4 |

\[^a\]Coronary artery disease, valvular heart disease, coronary bypass surgery.

\[^b\]More than 3 months, disability leave.
Type of AF, procedure success, and complications

The proportion of paroxysmal (episodes lasting for ≤7 days) and persistent (episodes lasting for ≥7 days) lasting AF did not differ between men and women (70% paroxysmal AF in men and 77% in women, \( p = 0.3 \)) [18]. In addition, there were no differences in acute success rate or recurrence rate at 6 months. During the procedure, <1% of all the patients experienced serious adverse events (pseudo aneurysm, pericardial tamponade, or stroke). During the 6-month follow-up, 14 patients (5 men and 9 women) had an additional ablation procedure. In total, 18% (n = 22) of men and 13% (n = 16) of women (\( p = 0.4 \)) had a redo procedure within the first year. More ablation data are presented in Table 2.

Symptom duration and referral history

Results from the questionnaire regarding the patient’s experience with AF, symptom duration, and referral history are presented in Table 3. Before the PVI, the patients had visited an emergency clinic on average 4.6 times (in total 1087 times) and an outpatient clinic on average 3.1 times (in total 727 times) due to symptomatic AF for a mean period of 7.5 years. There were no differences between the sexes and number of visits. When a diagnosis of AF was made, 49% (n = 59) of the men and 66% (n = 80) of the women were offered drug therapy (\( p = 0.009 \)). Men were more often referred for cardioversion than women (mean 3.8 ± 5.2 times vs. 1.9 ± 3.4 times, \( p = 0.001 \)) before the PVI. For all patients, 32% (n = 78) reported that they would have preferred to have been referred for ablation, 24% (n = 57) had demanded a PVI procedure, and 10% (n = 24) were offered a referral for PVI but chose to wait. In most cases, reasons for waiting were a moderate AF burden, drugs were preferred, or hesitation due to presumptve procedure complications.

Results from the questionnaires at baseline and 6 months

Symptoms checklist: Frequency and severity (SCL)

At baseline, women generally scored higher than men both on the frequency scale (24 ± 9 vs. 16 ± 9, \( p < 0.001 \)) and the severity scale (20 ± 8 vs. 13 ± 8, \( p < 0.001 \)) (Table 4). Compared to men, women reported more types of symptoms such as fatigue, heart fluttering/skipping, heart racing, headache, difficulties concentrating, dyspnea, feeling warm/flushed, sweating, weakness, poor appetite, and nausea.

At 6 months, women had improved more than men measured as a decrease in the symptom frequency scale (37% vs. 31%, \( p < 0.001 \)) and a decrease in the severity scale (38% vs. 30%, \( p < 0.001 \)) Despite greater improvement, women still experienced more heart racing (\( p = 0.02 \)), dizziness (\( p = 0.01 \)), and dyspnea (\( p = 0.04 \)) compared to men. Women also had more unspecific symptoms such as weakness, headache, sweating, loss of appetite, feeling of warmth, and difficulties sleeping.

Medical outcomes short form-36 (SF-36)

At baseline, women reported lower HRQOL scores in all scales than men, except for general health. At the 6-month follow-up, women had improved more than men in two scales, social functioning \( p < 0.001 \) and role-emotional, \( p = 0.04 \), but there were still differences compared with men in physical functioning and role physical scales (\( p = 0.05 \) and \( p = 0.04 \), respectively), where women scored lower. Men improved in all scales except for physical functioning, which remained unchanged (Table 4).

Sickness impact profile

Women assessed five categories of the SIP higher than men at baseline: ambulation, mobility, home management (all \( p < 0.001 \)), social interaction (\( p = 0.002 \)), and recreation and past time (\( p = 0.007 \)). The most commonly endorsed items in psychosocial dimension and social interaction for both sexes were “I am going out less to visit people and participate in less social activities with groups of people”, 22% (n = 53) and “My sexual activity is decreased”, 35% (n = 85). In the physical dimension, the items “I walk shorter distances or often stop to rest”, 26% (n = 63) and “I walk more slowly”, 43% (n = 104) were most common. In the independent dimension, the largest impact of the AF was found within the categories sleep and rest and recreation and pastimes, which contained the following statements: “I sleep less at night, for example wake up too early, don’t fall asleep for a long time, awaken frequently”, 50% (n = 121), “I am cutting down on some of my usual physical recreation or activities” 54% (n = 131), and “I am going out for entertainment less often”, 32% (n = 77). In the category home management, the most common statement was “I am doing less of the regular daily work around the house than I would usually do” 26% (n = 63). At the 6-month follow-up, men and

| Table 2: Ablation data. |
|------------------------|
|                       |
|                       |
|                       |
|                       |

Data are presented as mean SD, or number and percentage.
women only differed in ambulation and home management, where women scored higher. After 6 months, women had improved in eight out of nine dimensions whereas men had improved in six out of nine dimensions (Table 4). Proportionally, women improved more than men in all dimensions except communication.

Table 3. Results from the questionnaire regarding the patients’ own experience of the AF, symptom duration and referral history.

| Questions and claims                                                                 | Men (n = 121) | Women (n = 121) | p     |
|-------------------------------------------------------------------------------------|---------------|-----------------|-------|
| How many years have you had symptomatic AF?                                         | 6 ± 6         | 6 ± 5           | 0.9   |
| Correct diagnosis at the first consultation                                        | 8(67)         | 72(60)          | 0.3   |
| Have never felt any palpitation                                                    | 20(17)        | 8 (7)           | 0.03  |
| Experience at the outpatient’s clinic                                              |               |                 |       |
| How many times did you visit the GP, occupational health service, or cardiologist due to the AF? | 3 ± 6         | 3 ± 4           | 0.3   |
| How many times did you visit the Emergency care due to the AF?                     | 5 ± 7         | 4 ± 5           | 0.2   |
| I didn’t feel that the health care staff believed in me when I consulted for my arrhythmia symptom. | 9 (7)         | 12 (10)         | 0.6   |
| I feel that I have been incorrectly diagnosed.                                     | 3 (2)         | 4 (3)           | 0.7   |
| Number of times you have been converted, mean SD                                  | 4 ± 5         | 2 ± 3           | 0.001 |
| Experiences of the referral                                                        |               |                 |       |
| Referral for ablation at first consultation                                        | 5 (4)         | 1 (<1)          | 0.2   |
| I accepted instantly when I was offered PVI ablation for my AF                    | 90(74)        | 89 (74)         | 0.9   |
| I had wished to be referred for ablation earlier                                  | 41 (34)       | 37 (31)         | 0.7   |
| I had to ask for referral of ablation myself                                       | 24 (20)       | 33 (27)         | 0.2   |
| I was offered a referral for ablation but chose to wait                            | 13 (11)       | 11 (9)          | 0.8   |
| When you had received the correct diagnosis, what treatment were you offered?      |               |                 |       |
| Drug therapy                                                                       | 59 (49)       | 80 (66)         | 0.009 |
| Drug therapy and conversion                                                        | 67 (55)       | 52 (43)         | 0.07  |
| Drug therapy while waiting for ablation                                           | 41 (34)       | 30 (25)         | 0.2   |
| Ablations treatment directly                                                       | 5 (4)         | 1 (<1)          | 0.2   |
| Information about AF                                                              |               |                 |       |
| I would have liked more or better information about AF                             | 74 (61)       | 102 (84)        | <0.001|
| Yes, I got enough information about AF                                             | 39 (32)       | 18 (15)         | 0.002 |
| Unknown                                                                           | 8 (7)         | 1 (<1)          | 0.04  |
| Information of how to act if a new episode occurs                                 |               |                 |       |
| Felt well informed about how to react if a new AF episode should occur            | 40 (33)       | 38 (31)         | 0.9   |
| I needed no information                                                           | 36 (30)       | 30 (25)         | 0.5   |
| No, would have liked more information                                             | 32 (26)       | 50 (39)         | 0.02  |
| Unknown/ no answer                                                                 | 13 (8)        | 3 (2)           | 0.02  |
| AF, atrial fibrillation.                                                          |               |                 |       |

Data are presented as mean SD or n (%), p value < 0.05 was considered significant.

Table 4. Symptoms and Functional impairment pre- and post PVI, comparison between the sexes.

| Symptom checklist | Baseline | 6 months |
|-------------------|----------|----------|
|                   | Men      | Women    | p      |
|                   | n = 121  | n = 121  |        |
| Frequency         | 15.5 ± 8.6 | 24.4 ± 9.1 | <0.001 |
| Severity          | 13.1 ± 7.5 | 20.2 ± 7.6 | <0.001 |
| SF-36 dimensions  |          |          |        |
| Physical functioning | 80.1 ± 17.9 | 64.1 ± 22.8 | <0.001 |
| Bodily pain       | 76.0 ± 24.1 | 64.7 ± 27.5 | 0.001 |
| General health    | 61.4 ± 19.1 | 56.4 ± 21.2 | 0.05  |
| Vitality          | 53.3 ± 21.7 | 46.0 ± 22.7 | 0.01  |
| Social functioning | 76.7 ± 23.3 | 61.3 ± 28.3 | <0.001 |
| Role emotional    | 73.9 ± 38.2 | 60.6 ± 44.2 | 0.01  |
| Mental health     | 74.1 ± 18.0 | 69.9 ± 20.6 | 0.004 |
| A higher score indicates more symptoms                                             |          |          |        |
| Sickness Impact Profile Dimensions*                                              |          |          |        |
| Physical          |          |          |        |
| Ambulation        | 2.2 ± 1.3 | 3.5 ± 1.8 | <0.001 |
| Mobility          | 1.6 ± 0.5 | 3.1 ± 2.1 | <0.001 |
| Psychosocial      |          |          |        |
| Social interaction | 2.0 ± 1.8 | 3.1 ± 2.4 | 0.002 |
| Alertness behavior | 3.4 ± 2.8 | 3.7 ± 2.7 | 0.6   |
| Emotional behavior | 2.7 ± 2.1 | 3.2 ± 1.9 | 0.3   |
| Communication     | 1.9 ± 0.9 | 2.2 ± 1.2 | 0.05  |
| Independent categories |      |          |        |
| Sleep and rest    | 41.2 ± 2.5 | 40.0 ± 2.1 | 0.09  |
| Home management   | 2.7 ± 1.7 | 4.4 ± 2.5 | <0.001 |
| Recreation and Pastimes | 2.7 ± 1.7 | 3.5 ± 1.9 | 0.007 |

*Excluded items: work and food intake. Higher score indicates poorer functional impairment.

Data are presented as mean ± SD, p value < 0.05 was considered significant.
Information

More women than men (81% (n = 99) vs. 60% (n = 72); \( p < 0.01 \)) experienced they had not received adequate information or no information at all regarding AF. About 33% (n = 80) of the patients reported that they would have liked better information about their arrhythmia and how to act when experiencing an AF episode (Table 3).

Comorbidity and anti-arrhythmic drug therapy

There were no differences in comorbidity. Women were more often treated with betablockers, calcium antagonists, and digoxin than men. In all, women had tested more anti-arrhythmic drugs than men (2.5 ± 1.0 vs. 2.1 ± 0.9, \( p = 0.008 \)) (Table 1).

Patients considered procedural failures

Patients considered ablation failures assessed their HRQOL lower at 6 months, had more symptoms, and had a higher functional impairment compared with the successfully treated patients (see Table 5). However, notably patients with persistent AF and recurrences improved in physical function, role physical, vitality, social functioning, and role emotional. The same results were seen in patients with paroxysmal AF and recurrences, except for physical function and role emotional that remained unchanged (Table 6). The symptom frequency scale showed an improvement in following items; tiredness/lack of energy, heart racing, hard to catch and shortness of breath, sweating, weakness, difficulty sleeping, and chest pain when the heart is racing. On the severity scale, they were less bothered by heart fluttering/skipping, heart racing, to concentrate. The SIP showed less impairment in sleep and rest and alert behavior.

Women considered ablation failures improved less than the men considered ablation failures in both SCL frequency and severity score. Women had more headache, less appetite, and nausea. No differences were found in the HRQOL or the functional impairment except for in home management were the women scored a higher functional impairment than men (Table 5).

Discussion

Main findings

Women with AF were more symptomatic but notably improved more than men in HRQOL and in symptoms after PVI. In contrast to previous reports, there were no gender differences in this cohort regarding duration of AF before referral to PVI. In addition, there were no gender differences regarding paroxysmal and persistent AF. However, when referred, women were older, had tried more drugs, had more drug failures, and had less often been offered cardioversion despite more severe symptoms. Women reported lower HRQOL and worse functional impairment before the PVI than men. Patients considered procedural failures at follow-up also showed significant
improvement in HRQOL, functional status, and experienced less direct arrhythmia-related symptoms, but improved less than patients considered procedural successes. This improvement was less pronounced in women.

**HRQOL and symptom burden**

The women were more symptomatic and experienced lower HRQOL than the men before PVI. Similar results have been described in other reports [2,19]. This is probably due to higher ventricular response rate and longer episodes with AF in the women than the men [6,19]. Mohanty et al. [20] reported a faster rate with recurrent atrial tachycardia and atrial flutter post ablation in women. Moreover, they had more unspecific symptoms such as headaches, feeling of warmth, and sweating than men before as well as after PVI. Similar symptoms are seen in women who has undergone successful ablation of PSVT [7]. It is unclear whether this indicate episodes of AF or are caused by other mechanisms such as premature atrial contractions or menopausal symptoms.

Improvement regarding symptoms and HRQOL after PVI are seldom reported from a sex aspect in ablation studies. In the present study, women improved proportionally more than men in several categories describing health related issues and experienced proportionally less palpitation symptoms. The larger improvement could relate to that woman scored lower than men at baseline. Women might therefore benefit more from the procedure than men. In most ablation studies as well as in data from ablation registries, women are underrepresented and constitute 25–30% of PVI patients while the prevalence of women with AF patients is 40% [21,22]. In the present study, women were not more reluctant than men to undergo an ablation procedure, which has been suggested as one reason for this discrepancy. In contrast to patients with PSVT, they did not report being misdiagnosed or that they were not being taken seriously [7].

Significantly more women than men would have liked more and better information regarding AF and treatment options. Earlier studies have shown a lack of AF-related knowledge in AF patients even when they had been given both verbal and written information [23–25]. Aliot et al. [26] found that more than one-third of the patients were worried or fearful about their AF. In the same study, 23% of the patients reported that they did not know how, where, or whom to contact to receive information about AF.

There is no reason to suspect that information given to patients with AF regarding ablation differ between female and male patients. This indicates that women with AF inquire other aspects of an ablation procedure than information on how the procedure is done, success rate, and the risk for adverse events. Hypothetically, these might be questions regarding how a successful procedure affects aspects of daily life such as social functioning and interaction, physical functioning, and recreation and pastimes. These are all parameters where women scored lower than men. To

**Table 6. Differences in HRQOL between ablation success in persistent and PAF patients.**

| Dimensions                     | Persistent atrial fibrillation (n=9) | Persistent atrial fibrillation (n=3) | PAF atrial fibrillation (n=65) | PAF atrial fibrillation (n=28) |
|--------------------------------|-------------------------------------|-------------------------------------|-------------------------------|-------------------------------|
| **Physical functioning**       | 70.9 ± 20                           | 85.6 ± 18                           | 63.2 ± 19                     | 73.6 ± 20                     |
| **Role physical**              | 44.4 ± 44                           | 79.8 ± 34                           | 29.5 ± 37                     | 51.8 ± 44                     |
| **Bodily pain**                | 81.5 ± 24                           | 81.5 ± 25                           | 71.0 ± 26                     | 77.8 ± 22                     |
| **General health**             | 64.4 ± 19                           | 74.7 ± 18                           | 52.2 ± 24                     | 55.4 ± 24                     |
| **Vitality**                   | 54.2 ± 19                           | 72.0 ± 20                           | 43.9 ± 16                     | 59.1 ± 22                     |
| **Social functioning**         | 72.6 ± 26                           | 89.9 ± 18                           | 62.9 ± 19                     | 79.9 ± 22                     |
| **Role emotional**             | 83.3 ± 32                           | 88.9 ± 25                           | 51.5 ± 44                     | 73.8 ± 41                     |
| **Mental health**              | 68.3 ± 21                           | 79.9 ± 19                           | 70.0 ± 18                     | 75.3 ± 20                     |

Data are presented as mean ± SD. A higher value indicate better HRQOL.
adequately answer these questions, further studies are necessary.

**Gender differences in referral for PVI**

Previous studies have reported longer duration of AF as well as more comorbidities in women compared to men in patients undergoing PVI [4,5]. We did not find any differences between the sexes regarding years with AF or comorbidities before referral for PVI. Zylly et al. [27] suggested that the reason for previously reported delay in referral of women for PVI might be that women are more reluctant to undergo an invasive procedure as an early treatment option. This is contrary to our results. Almost 75% of the women accepted when they were offered PVI and 27% asked actively to be referred for ablations. The same proportions were reported among men, 75% and 20%, respectively.

**Sickness impact profile (SIP)**

The impact of AF on the self-rated functional capacity to perform daily activities was considerable. Similar results have been described in previous reports by both Dorian et al. [28] and Wagner et al. [29]. AF patient’s disease-related impairment was as poor or worse as seen in patients post percutaneous coronary intervention [28,29].

The impact on the recreation and pastime was significant before the PVI. Sleeping disturbances were common in both sexes before PVI. In a study including over 2000 patients, AF was associated not only with sleep disordered breathing but also with sleep quality, including slow wave sleep [30]. The sexual activity was decreased in 35% of the patients, but it is unclear whether this is due to AF itself, its psychological consequences, or linked to antiarrhythmic drugs.

**Cardioversion**

Paradoxically, even though women were more symptomatic, they were less often referred for cardioversion than men. This finding is not new and have been reported in several previous studies [4–6]. The reason is unclear. One might suspect or speculate that the cause is gender related. In patients with supraventricular tachycardias, it has been shown that women’s symptoms are often neglected or falsely interpreted compared to men’s symptoms [7]. It is not unreasonable to consider the same mechanism as partly responsible for the finding that less women than men are being referred for cardioversion.

**Limitations**

Our results may suffer from selection bias. It is reasonable to expect that the patients who gave their informed consent to participate were more motivated than those who did not, which may correlate to a different symptom burden or experiences with referral. Furthermore, we do not know if the improvement of the HRQOL and reduction of symptoms are exclusively due to the PVI or partly due to the reduction of antiarrhythmic drugs. As recurrences in AF tend to increase with extended follow-up, the results in improved HRQOL might decrease during longer follow-up. Both radiofrequency energy and cryo energy were used in this study, which might be a confounding factor since cryo energy usually is less painful. However, there were no differences in success rate, recurrence rate or improvement comparing the two energy sources.

**Conclusion**

Women with AF improve proportionally more than men in HRQOL, functional impairment, and symptoms after PVI. However, women are more symptomatic than men at baseline and still after PVI. Women are not more reluctant to accept referral for ablation when offered.

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