



Published in final edited form as:

J Cardiovasc Nurs. 2018 ; 33(2): 137–143. doi:10.1097/JCN.0000000000000421.

Atrial Fibrillation Symptoms and Sex, Race, and Psychological Distress: A Literature Review

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Abstract

Background—Atrial Fibrillation (AF) symptoms are a major component of treatment decisions for AF patients and impact quality of life and functional ability, yet are poorly understood.

Objective—This review aimed to determine what is known about the prevalence of symptoms, and the association of symptoms to AF characteristics, psychological distress, sex, and race.

Methods—We performed a structured review of AF symptoms as of March 2016 using PubMed, EMBASE, and CINAHL, and reference searches of retrieved articles. Full-text, published, peer-reviewed, English language articles were examined. Articles were included if they reported original research data on symptom prevalence and type among patients with AF.

Results—The three most common symptoms were dyspnea, palpitations, and fatigue. The results suggested that while AF characteristics are not a significant predictor of symptoms, tachycardia, female sex, race and psychological distress have a positive association to symptoms.

Conclusions—There is a scarcity of research examining symptoms in AF. Furthermore, the inconsistency in measurement methods and the failure to include diverse populations in AF research makes it difficult to draw definitive conclusions from current literature. Given the prevalence of AF in the United States and the impact of symptoms on quality of life and healthcare utilization, further research examining predictors of symptoms and interventions to alleviate symptoms is crucial.

Keywords

Atrial Fibrillation; Symptoms; Psychology; Sex; Race

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Disclosures

Dr. Nazarian is a scientific advisor to Biosense Webster Inc. and CardioSolv Inc. and principal investigator for research funding to Johns Hopkins from Biosense Webster, Inc. (Diamond Bar, California). All other authors have no conflicts of interest

INTRODUCTION

Atrial Fibrillation (AF) is the most common adult cardiac rhythm disorder. It is estimated that there are 5.2 million cases of AF in the United States (US), and this number is projected to increase to 12.1 million cases by 2030.(1) Conservative estimates suggest that healthcare expenditures due to AF-specific care in the US cost \$6 billion a year.(2) The main driver for seeking medical attention by persons with AF is the symptoms they experience.(3, 4) AF symptoms are associated with increased healthcare utilization, decreased quality of life (QOL), and poor health outcomes.(5–11) Clinical decisions for procedural symptom management strategies, including cardioversions, ablations, and rhythm and rate control medications are largely guided by patients' symptom reports.(12, 13) The symptoms are highly variable. Between 25 to 30% of patients with AF are asymptomatic, while other patients report severe symptoms that affect their QOL.(4, 14) Among patients with symptomatic AF, a significant percentage has episodes that are asymptomatic and the specific symptoms reported vary by type of AF.(15)

The causal mechanism of AF symptoms and why symptoms are present in some patients and absent in others is unknown.(4, 16) There is limited understanding of the variability of symptoms with respect to psychosocial, race, and sex related differences. Females and non-whites are significantly underrepresented in cardiovascular clinical trials.(17–20) Since there are tremendous costs and potential complications related to AF treatment strategies, a thorough comprehension of symptoms caused by AF is essential. The purpose of this review is to improve understanding of what is known about the prevalence and type of symptoms in AF patients, and the association of AF symptoms to AF characteristics, psychological distress, sex, and race.

METHODS

A structured literature search of the PubMed, CINAHL, and EMBASE databases was conducted with the assistance of a university librarian in March 2016 (Figure 1). Search terms included the MeSH term “atrial fibrillation.” For symptom burden, the terms “symptom burden,” “functional impairment,” “functional capacity,” “symptom,” “asymptomatic” and “burden of symptoms” were used. Functional impairment and functional capacity were included because they are often measured in studies of symptoms' effect on an individual. Reference lists were reviewed to identify relevant articles. No time limitations were imposed to ensure the inclusion of key, seminal articles examining AF symptoms. This search of online databases yielded a total of 4085 articles. 26 articles were removed after screening for duplicates. Abstracts and titles were reviewed for inclusion criteria. Articles that were potentially relevant were reviewed in full text. Where it was unclear if a study should be included, the co-author team was consulted. 11 articles were identified by hand review. After screening, 38 articles remained and were reviewed using the following inclusion and exclusion criteria. The inclusion criteria were: Full text, published, peer-reviewed, English language, 100% of participants diagnosed with AF, and data on symptom prevalence and type were collected and analyzed.

Data were extracted from each article included: prevalence and type of symptoms, the association between symptoms, sex, psychological distress, race, and AF characteristics, and instruments used. The extracted data are depicted in tables 1, 2, 3, and 4. Quality assessments of each quantitative study were conducted using the Strengthening of the Reporting of Observational Studies in Epidemiology (STROBE) checklist.(21) The STROBE checklist does not include a scoring system.

Our review is not intended to be all-inclusive or systematic. It represents the main studies examining psychological distress, sex, race, AF characteristics, and AF symptoms. This review is organized by discussing the prevalence and type of symptoms in AF, and associations among AF characteristics, psychological distress, sex, race, and AF symptoms.

RESULTS

Prevalence and Type of Symptoms

Fourteen studies that reported data on the prevalence and type of symptoms experienced by individuals with AF were examined (Table 1). AF symptom measurement instruments typically include palpitations, dyspnea, fatigue, chest pain, and dizziness. However, there is variance in the type and number of symptoms, time frame, and wording included in commonly used instruments (Table 2). In three prospective, cross-sectional studies that used the European Heart Rhythm Association (EHRA) symptom classification for AF, between 56 to 62% of patients had one or more AF symptoms in the past seven days.(7, 10, 22) While one study used a sample (n=510) consisting only of symptomatic AF patients,(22) the other two had larger samples (n=9665 and 9542) that included asymptomatic and symptomatic patients and had comparable findings.(7, 10) Three studies similarly reported that 63% to 70% of study participants reported AF symptoms in the baseline data collection prior to tests of rhythm control interventions.(23–25) Two of these studies did not describe the use of any instrument to measure AF symptoms, which may explain their findings of a slightly higher prevalence of current AF symptoms.(4, 23, 24)

Dyspnea, fatigue, and palpitations were the three most commonly reported symptoms.(6, 7, 10, 11, 22, 26–29) Results from one qualitative study supported the reports of symptoms experienced in the quantitative studies.(30) Participants (n=15) reported distress from abrupt occurrences of palpitations often accompanied by fatigue and shortness of breath, which they perceived as an AF episode. Most of the participants reported fatigue during AF episodes that lasted for a few days following the episode.

Association of AF Characteristics and Symptoms

Eleven studies examining the association of AF characteristics to symptoms were reviewed (Table 3). AF characteristics, including AF burden, heart rate when in AF, sinus rhythm rate, and frequency and severity of pauses, were measured through a pacemaker, continuous looping monitor, or an electrocardiogram (EKG) recorder. Seven studies found essentially no association between the number and frequency of symptoms of AF reported by patients and AF characteristics measured by a continuous monitor.(27, 28, 31, 43–46) In contrast, two studies found a significantly greater AF burden in patients who reported symptoms in

comparison to asymptomatic patients.(41, 42) In the study by Manganiello and colleagues, continuous subcutaneous EKG monitoring was utilized to measure AF burden, and the sample (n=113) consisted of participants at a single center who had undergone ablation for AF, which may explain the differing results.(42)

Eight studies examining the association between heart rate and AF symptoms were reviewed.(11, 31, 34, 41, 42, 45, 48, 49) The findings of seven studies support that there is a significant association of tachycardia to prevalence of symptomatic AF episodes ($P<0.001$). (11, 34, 41, 42, 45, 48, 49) A heart rate greater than 100 beats per minute (bpm) was associated with increased symptoms.(11, 42) One study did not find a significant association between heart rate and AF symptoms by measuring symptoms prior to applying a continuous monitor for seven days to measure AF characteristics.(31) This data collection timing contrasts with the other studies described, where data were collected on the patients' reported symptoms in parallel with the monitoring period. Seven studies analyzed the sensitivity and positive predictive value of self-reported symptoms to detect the pacemaker's report of an AF episode. The reported findings of four studies suggested a similar sensitivity of 19% or lower,(43–46) with the exception of two studies that reported a sensitivity of 53% (47) and 91%.(41) However, the studies reported divergent positive predictive values of symptoms, ranging from values of a positive predictive 21% or lower,(44, 46) to 63% and higher.(41, 43, 45, 47, 48) A weight reduction and cardiometabolic risk factor management intervention study found that AF symptoms, the number of episodes, and the cumulative duration of episodes were significantly reduced following the intervention, though whether the reduction in symptoms was correlated to the reduction in number of episodes and duration was not examined.(50)

Association of Psychological Distress and AF Symptoms

Seven studies examining the association of psychological distress to AF symptom burden were reviewed.(14, 27, 32, 51–54) The findings from five studies supported a significant ($p<0.05$) association between depression and anxiety and AF symptoms.(27, 32, 51, 53, 54) The studies measured AF characteristics through EKGs, continuous looping monitors and implanted cardioverter defibrillators (ICD), and included these measurements in the analyses. The majority of the studies used different measurements of psychological distress: the State Trait Anxiety Inventory (STAI), Profile of Mood States (POMS), participant report of psychological stress, Beck's Depression Inventory (BDI), Type D personality (DS14), and the Perceived Stress Scale (PSS-10), the hospital anxiety and depression scale (HADS-A), and the Patient Health Questionnaire (PHQ-9). Three of the studies adjusted for sex and age in the analysis; one study also adjusted for ethnicity, working status, education, smoking and congestive heart failure(53) and another study additionally adjusted for physical activity and body mass index (BMI).(32) A study that examined emotional response to symptoms found that 67% of participants (n=150) reported that their symptoms worried them to some degree, and 50% reported being frustrated by their symptoms.(55)

A randomized-controlled trial (n=49) examined the effects of yoga on AF measured both pre- and post- anxiety and depression scores using the Zung self-assessment anxiety score (56) and Zung self-assessment depression score (SDS) in addition to AF symptoms using a

symptom diary and cardiac nonlooping event monitors and found that changes in anxiety and depression did not significantly correlate with changes in AF symptom experience, though the findings indicated a significant improvement in AF symptom burden, anxiety and depression following the intervention.(52) Findings from the one qualitative study supported the quantitative results in that most of the participants (n=15) reported that emotional distress could precipitate an AF episode.(30)

Association of Sex and AF Symptoms

The majority of studies reported a significant, positive association between symptomatic AF and female sex ($p<0.05$)(7, 11, 26, 31, 35, 57, 58) with the exception of five studies that found no association between symptomatic AF and sex (Table 4).(27, 32, 42, 59, 60) The studies that found a significant association had larger sample sizes than the studies without findings indicative of a significant association. With the exception of one,(26) all of the studies that examined sex differences in symptoms were prospective cohort studies.

Association of Race and AF Symptoms

Notably, only three of the studies reviewed examined racial differences in symptom experience.(7, 22, 31) In each of these studies' samples, over 85% of the participants were Caucasian. The studies found that nonwhites were significantly more likely to experience symptoms than Caucasians ($p<0.05$).(7, 31)

DISCUSSION

The findings indicate that there is limited research examining the associations between AF symptoms and AF characteristics, psychological distress, race, and sex. The lack of standardized assessment of AF symptoms, homogenous samples, and observational designs limits most prior research.(7) The research reviewed was mainly observational studies, and the findings were largely inconclusive. Few of the studies in this review were designed for the exclusive purpose of examining symptoms in AF.(49, 50, 52, 61) Many of the articles reported on symptoms through subsample analysis where part of the data and sample was taken from a larger study.(5, 8, 57, 62)

One of the key methodological weaknesses of the prior research is the inconsistent measurement of AF symptoms. This variation in measurement complicates drawing conclusions from the literature because the studies used instruments with differing symptoms and time periods.(10, 46, 53, 62) For example, the EHRA includes a time frame of one week and one year to survey patients on symptoms, whereas ATSSS surveys about symptoms experienced in that past month.(63) Some instruments include as many as sixteen symptoms whereas others include four.(37, 38) Differences in instruments display a lack of agreement among AF researchers over which symptoms can be attributed to AF and the appropriate time period to understand patients' experiences with AF symptom burden. Additionally, all commonly used instruments for the measurement of AF symptoms have limited reported evidence of reliability and validity for use among different race and ethnicity groups.(29, 38, 39, 64) The majority of the tools to measure symptoms were tested

on predominantly Caucasian male samples,(29, 38, 39) making the applicability of the tools to females and non-Caucasian populations questionable.

AF symptoms are the primary reason patients seek medical treatment.(4) They are known to negatively affect quality of life.(65, 66) Patients' report of symptoms is a major component of the treatment path for AF.(12) Yet, there is a universal inadequate understanding of AF symptoms.(4) The differences that exist among the AF symptom measurement tools are both reflective of the lack of a thorough comprehension of AF symptom burden and an impediment to developing a deeper understanding of AF symptoms. There is a notable lack of qualitative studies,(30) which are necessary to understanding the subjective and highly variable experience of AF symptom burden. Qualitative studies could also be used to better inform AF symptom measurement instruments, which currently vary in their measurements of the number, type, and time-frame of symptoms,(38, 40, 64) and to enrich understanding of the different predictors of AF symptom burden.(30)

In an examination of the existing literature on sex differences in AF symptoms, it is important to note that the majority of the sample was male in each study described in this review. While estimates suggest that a male's lifetime risk for AF at age 40 is 26% while a female's lifetime risk of 23% at age 40, the difference is not large enough to account for the lack of female representation in the study samples.(67) Since the limited research investigating sex differences in symptom burden suggests that females may be more symptomatic than males, the prevalence of symptoms may not be generalizable to women since females were not equally represented in the samples. Findings from Rienstra and colleagues suggest that asymptomatic patients have better outcomes;(24) differences in symptoms may be contributing to disparate outcomes in marginalized populations.(68)

While the limited research examining race and AF symptoms suggests non-whites experience more symptoms, the majority of research in AF is done on largely Caucasian samples. Efforts must be made to determine the potential causes that contribute to non-whites being more symptomatic. The current findings reflect a need for improved symptom management for minorities.

It is difficult to draw conclusions based on the studies included in this review on the association of psychological distress and symptoms. Individuals with high levels of psychological distress prior to diagnosis of AF may be more likely to experience symptoms, psychological distress may precipitate a symptomatic AF episode, and the symptoms of AF may result in high levels of psychological distress.(14, 30, 53, 54) The randomized-controlled trial examining the effects of yoga on AF symptoms and found that changes in anxiety and depression did not significantly correlate with changes in AF symptom experience. While a causal relationship cannot be determined from the studies in this review, the relationship may be bidirectional. However, future studies specifically designed to examine psychological distress and AF symptoms are needed to draw definitive conclusions.

There are limitations to the findings of this review. It is possible that informative articles were not found in the review due to the lack of consistency and broadly defined term "symptoms." The review was not systematic and it is possible articles with valuable

symptoms data were not found. There were limited studies that were designed for the specific purpose of examining symptoms and the associated variables found in the literature. The results from this review remain valuable in highlighting knowledge gaps and methodological shortcomings that restrict the ability to draw evidence-based conclusions.

Research gaps exist in understanding the association between race and ethnicity, sex, psychological distress and symptoms. The few studies that did include data on race and ethnicity reported a largely homogenous patient population. Findings suggest that psychological distress may be associated with symptoms. Improved understanding of AF patients' symptom experience and reliable, valid, and clinically-feasible methods to measure symptom experience may lead to effective, tailored strategies to improve the quality and outcomes of AF care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding Sources

Kelly T. Gleason received support from predoctoral fellowship in Interdisciplinary

Training in Cardiovascular Health Research, T32 NR012704, and Predoctoral Clinical Research Training Program, TL1 TR001078.

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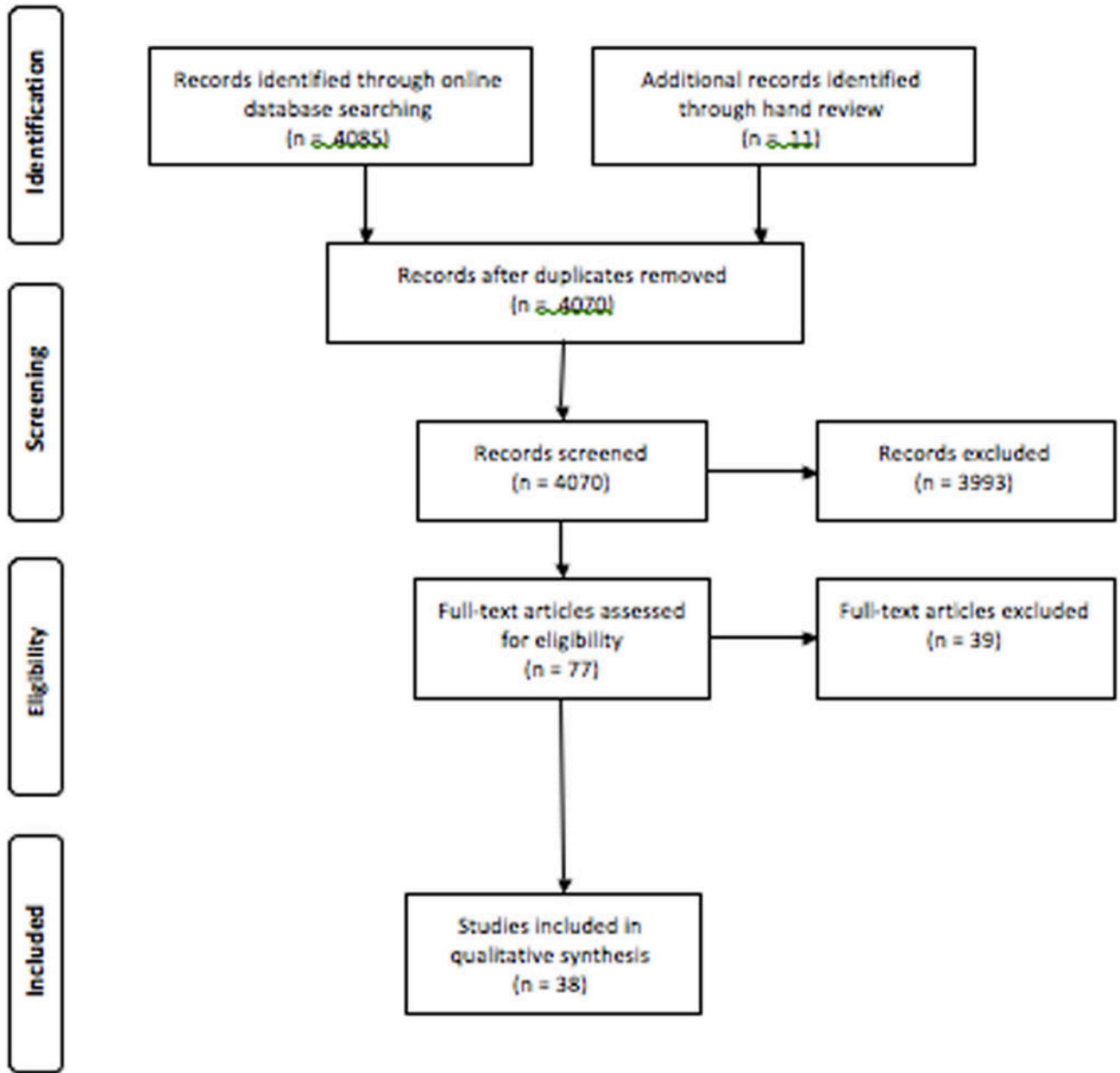


Figure 1.
Flow Diagram

Identification

Screening

Eligibility

Included

Table 1

Prevalence of Symptoms

Study	Sample	Prevalence of Symptoms	Symptom Type	Instrument	Important to Note
Diker, 2015, Turkey(22)	N=510, 56% permanent, 21% persistent, 13% paroxysmal	56% had symptoms in past 7 days, 78.8% had symptoms in past year	34.5% dyspnea, 34.4% palpitations, and 32.5% fatigue	EHRA	EKG findings indicated that 88.4% of patients were in AF at time data was collected
Dorian, 2000, US, Canada, Germany and England(29)	N=152, 60% paroxysmal, 40% persistent	90% reported symptoms during AF	68% palpitations, 62% fatigue, 60% shortness of breath	AFSS	Permanent AF patients were excluded
Golwala, 2016, US(7)	N=9542, 51% paroxysmal, 45% persistent/permanent, 4% Undetermined	62% reported symptoms	32% palpitations, 28% dyspnea, 26% fatigue	EHRA, AFEQT	The EHRA classification, done by physicians, and AFEQT, done by patients, were highly correlated, though findings suggest physicians may underestimate mild AF symptoms
Ha, 2014, 21 countries(8)	N=2439, 52% paroxysmal, 43% persistent, 5% Undetermined	Baseline score of 8.7 SD 7	Not described	AFSS	Cohort consists of recent-onset AF patients
Patel, 2014, US(31)	N=286, 40% persistent, 60% paroxysmal	25% reported severe AF symptoms	Not described	AFSS	Stable outpatient sample
Kupper, 2013, Netherlands(32)	N=52, persistent	9 symptoms on average with an average frequency of 2.5 during AF	92% tiredness, 76% dyspnea, 70% heart racing	ATSSS	Persistent AF sample that was a substudy, pre-ablation data examined
Murin, 2014, 26 countries(33)	N=4869, permanent N=6622, Nonpermanent	Permanent: 25% reported severe symptoms Nonpermanent: 19.7% EHRA Class III reported severe symptoms	Not reported	EHRA	50% of permanent AF patients did not have controlled AF in this sample
Nieuwlaet, 2005, 35 countries(23)	N=5333, 28% paroxysmal, 21% persistent, 29% permanent	69% currently symptomatic	75% palpitations and/or syncope	Not described	Majority of the patients were recruited from university and specialized centers
Patten, 2006, Germany(34)	N=1033, Symptomatic paroxysmal		Palpitations, tachycardia, and dyspnea most prevalent in EKG-confirmed AF episodes, palpitations, angina, and vertigo most common in perceived AF episodes in SR	Self-monitoring event recorder system	Study reviewed of patient-reported symptomatic AF events against the EKG-report
Rienstra, 2005(26)	N=522, Recurrent persistent	70% reported symptoms	39% fatigue, 35% dyspnea, 27% palpitations	Not described	No data of how symptom information was collected, and how patients were questioned about symptoms

Study	Sample	Prevalence of Symptoms	Symptom Type	Instrument	Important to Note
Sears, 2005, US(27)	N=96	Average of 8.89 AF symptoms across participants	Tiredness and difficulty sleeping two most frequently experienced	ATSSS	Sample consisted of symptomatic, drug refractory AF patients
Singh, 2006, US(25)	N=496, Persistent	63% perceived symptomatic AF	AF symptom burden score 13.4, SCL frequency 18.15, SCL severity of 14.6	SCL, AFSS	Symptom prevalence reported as baseline data from a longitudinal study on AF control
Siontis, 2016, US(35)	N=476	66% reported symptoms	40% palpitations, 26% symptoms other than palpitations		No standardized measurement of symptoms, data was based on information from chart review
Steg, 2012, 26 countries located in Europe, the Middle East, Africa, Asia & America (10)	N=9665,	61% reported symptoms in past 7 days, 22% reported severe symptoms	39.4% dyspnea, 35.5% fatigue, 33.8% palpitations	EHRA	Study has unprecedented geographical relevance, includes developing low- and middle-income countries
Vermond, 2014, Netherlands(11)	N=558, Permanent	35% reported a high symptom severity, 34% moderate symptom severity	76% dyspnea, 75% fatigue, 53% palpitations	AFSS	Self-reported AFSS scores were more sensitive than the history taking by treating physician, 70% of patients who reported mild symptoms were classified as asymptomatic by physician

Abbreviations: AF, atrial fibrillation; EKG, electrocardiogram; EHRA, European Heart Rhythm Association score of AF-related symptoms; AFSS, Atrial Fibrillation Symptom Severity Scale; SCL, Symptom Checklist; SR, sinus rhythm; ATSSS, Atrial Tachyarrhythmia Symptom Severity Scale, AFEQT Atrial Fibrillation Effect on Quality of Life

Table 2

Description of Commonly Used AF Symptom Assessment Instruments

Measure, Year Created	Description	Symptoms Included	Time Period
European Heart Rhythm Association symptom classification (EHRA), EHRA, 2007(36)	Provider rating of patients' symptom severity and symptoms' impact on daily activities	Does not assess specific symptoms, provider rates severity and impact on daily activities of symptoms attributable to AF	At time of visit, past 7 days, and past 12 months excluding previous 7 days
Symptom Checklist-Frequency and Severity Scale (SCL), Bubien et al., 1996(37)	Score based on severity and frequency of symptoms	Tiredness/lack of energy, heart fluttering/skipping, heart racing, lightheadedness/dizziness, hard-to-catch breath, shortness of breath, chest pain, pressure, or fullness when the heart is racing or fluttering, and chest pain, pressure, or fullness, when heart is not racing or fluttering, headache, trouble concentrating, feeling warm/flushed, sweating, weakness, poor appetite, nausea, difficulty sleeping	Present
AF Effect on Quality of Life (AFEQT), Spertus et al., 2011(38)	A measure of quality of life based on self-report of extent symptoms have bothered patient and interfered with activities of daily living	Palpitations (described as heart fluttering, skipping, or racing), irregular heart beat, pause in heart activity, lightheadedness or dizziness	Over the past 4 weeks
University of Toronto AF Severity Scale (AFSS), Dorian et al., 2000(29)	Subjective and objective ratings of AF disease burden, including frequency, duration, and patient-perceived severity of episodes, and healthcare use	Palpitations, shortness of breath at rest, shortness of breath with activity, exercise intolerance, fatigue at rest, lightheadedness/dizziness, and chest pain/pressure	Present
Canadian Cardiovascular Society Severity of AF Scale (CCS-SAF), Dorian et al., 2006(39)	Scored by providers in collaboration with patients, score determined by identification of major AF-related symptoms, determination of symptom-rhythm correlation, and assessment of symptom impact of daily activities and quality of life	Palpitations, dyspnea, dizziness/syncope, chest pain, weakness/fatigue	Present
Quality of Life in AF patients (QL-AF), Braganca et al., 2010(40)	Score determined by symptoms and treatments	Palpitations, breathlessness, chest pain, dizziness	Present, asks patient to specify how frequent palpitations are

Table 3

AF Characteristics' Association to Symptoms

Study	Samples	Design	Symptom Measurement	Assessment of cardiac rhythm	Findings	Limitations
Bhandari (1992), US(41)	N=113, 100% Paroxysmal, Age 50 (±15), 69% Female	Substudy of a randomized-controlled trial	Patient report	Trans telephonic EKG monitoring	Symptomatic calls significantly associated with documented AF, 91% AF, 91% sensitivity	Symptomatic AF was an inclusion criteria
Mangianello (2014), Italy(42)	N=113, 9% paroxysmal, 91% persistent, Age 64 (±20), 78% Male	Prospective cohort	Symptom diary	Insertable cardiac monitor	47% of patients had asymptomatic AF episodes, Significant association of symptoms to AF rhythm (P<0.01)	Symptomatic AF was inclusion criteria for the sample, all participants had undergone ablation, univariate analysis
Mehall, (2007), US(43)	N=50, Age 69, 74% Male	Prospective cohort	Manual activator when symptomatic episode perceived	Continuous home EKG monitoring	15% sensitivity, No significant association between symptoms and AF episode, 52% PPV	Long periods of AF were sometimes interrupted by EKG artifact, caused the monitor to record a new episode of AF
Quirino (2009), Italy(44)	N=102, 100% Paroxysmal AF, Age 73 (±7), 58% Male	Prospective Cohort	Symptom diary	Pacemaker	81% of device-stored episodes were asymptomatic, sensitivity was 19% and 21% PPV, duration of episodes was significantly related to symptomatic episode	Participants each had a pacemaker, symptoms were measured through self-report rather than a standardized tool
Sears (2005), US(27)	N=96, Age 62 (±12) 72% Male	Prospective cohort	ATSSS	Implantable cardioverter defibrillator	Insignificant association	All patients had an

Study	Samples	Design	Symptom Measurement	Assessment of cardiac rhythm	Findings	Limitations
Silbauer (2009), UK(45)	N=79, 100% paroxysmal, Age 70 (±9), 57% Male	Prospective cohort substudy	Symptom diary	Pacemaker	Sensitivity of 13% and PPV of 63%, no significant difference in AF episode frequency between symptomatic and asymptomatic follow-up periods, Heart rate and length of episodes significantly related to symptomatic episodes (p<0.001)	Implantable cardioverter defibrillator Symptomatic AF sample, patients to complete symptom diaries, the participants each had a pacemaker
Strickberger (2005), US(46)	N=48, Age 76 (±10), 58% Male	Prospective randomized single-blind parallel study	Manual activator when symptomatic episode perceived, & symptom diary	Pacemaker	6% of AF episodes were symptomatic, 17% PPV, did not find a significant difference in ventricular rate and symptoms	Relied on patients to use the activator to identify symptomatic episodes over a 12-month period, sample consisted of patients with symptomatic bradycardia
Tondo (2014), Italy(47)	N=143, Age 59 (±9), 85% Male, 55% paroxysmal, 45% persistent	Prospective cohort	Manual activator when symptomatic episode perceived, & symptom diary	Implanted cardiac monitor	53% sensitivity, 89% PPV	Study was performed following catheter ablation
Patel (2014), US(31)	N=286, Age 62 (±13), 65% Male, 60% paroxysmal, 40% persistent	Prospective single-center cohort study	AFSS	Continuous looping monitor	No AF monitor characteristic was predictive of severe AF symptom burden, including HR	Since symptoms were measured using the AFSS prior to the 7-day cardiac

Study	Samples	Design	Symptom Measurement	Assessment of cardiac rhythm	Findings	Limitations
Patten (2006), Germany(34)	N=1033, Symptomatic paroxysmal	Longitudinal cohort	Self-monitoring event recorder system	Tele-EKG recorder	46% documented AF associated with specific symptoms. Symptoms were significantly correlated with heart rate (p<0.001), 37% perceived symptomatic AF episodes were genuine EKG-episodes, 69% of patients reported symptoms when in SR	Inclusion criteria was a history of symptomatic paroxysmal AF, the Tele-EKG monitoring did not collect data about the onset and duration of episodes because it a maximal EKG recording time of 1 minute
Verma (2013), Canada(48)	N=50, 80% paroxysmal, 10% persistent	Prospective cohort	Standardized symptoms diary	Continuous implanted cardiac monitoring	Symptoms had a 87% PPV, 69% of all AF episodes were asymptomatic	Inclusion criteria was first-time ablation procedure

Abbreviations: EKG, electrocardiogram; PPV, positive predictive value; SR, sinus rhythm; ATSSS, Atrial Tachyarrhythmia Symptom Severity Scale; AFSS, University of Toronto Atrial Fibrillation Severity Scale

Table 4

The Association of Gender and Symptoms

Study	Study Design	Significant Association with Sex and AF Symptoms (p<0.05)	Measurement Tool	Other Variables in Analysis	Women Were More Symptomatic
Boriani (2015)(57)	Prospective cohort, n=3119, 60% Male	Yes	EHRA	Age, previous myocardial infarction	Yes
Clair (1993)(59)	Prospective cohort, N=150, 53% Male	No	Patient report	Age	
Golwalia (2016)(7)	Prospective cohort, N=9542	Yes	EHRA, AFEQT	Not specified	Yes
Henry (2013)(58)	Prospective cohort, N=540, 66% Male	Yes	SCL	Age, left atrial size, duration of AF (months), coronary artery bypass graft surgery, valve surgery, CHF; EuroSCORE	Yes
Mangiello (2014)(42)	Prospective cohort, N=113, 78% Male	No	Symptom diary	Univariate comparisons	
Kang (2006)(60)	Prospective cohort, n=81, 51% Male	No	SCL	Not specified	
Kupper (2013)(32)	Prospective cohort, N=52, 61% Male	No	ATSSS	Age, emotional distress, cardiac disease, BMI, physical activity	
Patel (2014)(31)	Prospective cohort, N=286, 65% Male	Yes	AFSS	Age, comorbidities, heart rate, AF characteristics, PVC and PAC burden	Yes
Rienstra (2005)(26)	Randomized control trial, N=522, 63% Male	Yes	Report of: Palpitations, dyspnea, or fatigue	Age, underlying heart disease, DM, left ventricular function	Yes
Sears (2005)(27)	Prospective cohort, N=96, 72% Male	No	ATSSS	Age, AF characteristics, negative emotion	
Vermond (2014)(11)	Post hoc analysis, N=558, 67% Male	Yes	AFSS	Not specified	Yes
Siontis, 2016(35)	Retrospective evaluation, N=476, 53% Male	Yes	Not specified	Age, CHADS score, comorbidities	Yes

Abbreviations: EHRA, European Heart Rhythm Association score of AF-related symptoms; AFEQT, Atrial Fibrillation Effect on Quality of Life; SCL, Symptom Checklist; ATSSS, The Atrial Tachyarrhythmia Symptom Severity Scale; BMI, Body Mass Index; PVC, Premature ventricular contractions; PAC, Premature atrial contractions; DM, Diabetes Mellitus