Journal of the American Heart Association

ORIGINAL RESEARCH

Clinically Meaningful Change in Quality of Life and Associated Factors Among Older Patients With Atrial Fibrillation

Hawa O. Abu, MD, PhD, MPH; Jane S. Saczynski, PhD; Jordy Mehawej, MD; Mayra Tisminetzky, MD, PhD, MPH; Catarina I. Kiefe, MD, PhD; Robert J. Goldberg, PhD; David D. McManus, MD, ScM

BACKGROUND: Among older patients with atrial fibrillation, there are limited data examining clinically meaningful changes in quality of life (QoL). We examined the extent of, and factors associated with, clinically meaningful change in QoL over 1-year among older adults with atrial fibrillation.

METHODS AND RESULTS: Patients from cardiology, electrophysiology, and primary care clinics in Massachusetts and Georgia were enrolled in a cohort study (2015–2018). The Atrial Fibrillation Effect on Quality-of-Life questionnaire was used to assess overall QoL and across 3 subscales: symptoms, daily activities, and treatment concern. Clinically meaningful change in QoL (ie, difference between 1-year and baseline QoL score) was categorized as either a decline (≤–5.0 points), no clinically meaningful change (–5.0 to +5.0 points), or an increase (≥+5.0 points). Ordinal logistic models were used to examine factors associated with QoL changes. Participants (n=1097) were on average 75 years old, 48% were women, and 87% White. Approximately 40% experienced a clinically meaningful increase in QoL and 1 in every 5 patients experienced a decline in QoL. After multivariable adjustment, women, non-Whites, those who reported depressive and anxiety symptoms, fair/poor self-rated health, low social support, heart failure, or diabetes mellitus experienced clinically meaningful declines in QoL.

CONCLUSIONS: These findings provide insights to the magnitude of, and factors associated with, clinically meaningful change in QoL among older patients with atrial fibrillation. Assessment of comorbidities and psychosocial factors may help identify patients at high risk for declining QoL and those who require additional surveillance to maximize important clinical and patient-centered outcomes.

Key Words: atrial fibrillation ■ elderly ■ quality of life

Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia worldwide and has often been associated with impaired quality of life (QoL).[1,2] The onset of AF symptoms including palpitations, fatigue, chest pain, and dyspnea, and the consequences of AF treatment, such as medication side effects as well as frequent hospitalizations, could negatively impact patients' QoL.[3,4] Consequently, one of the primary objectives in AF management is to alleviate patients' suffering or discomfort through rate or rhythm control with the goal of improving their functional status and QoL.[5] Understanding the factors that may influence clinically meaningful changes in QoL is important in the delivery of patient-centered care and to improve the long-term health outcomes in older patients with AF and other chronic diseases.

Although previous cross-sectional studies have examined generic and disease-specific QoL in patients with AF,[6–8] only limited research has prospectively examined changes in QoL over time reporting findings based on statistical, rather than clinically significant changes in QoL, thus lacking clinical relevance

Correspondence to: Hawa O. Abu, MD, PhD, MPH, Division of Cardiovascular Medicine, Department of Medicine, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655. E-mail: hawa.abu@umassmed.edu

Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.016651

For Sources of Funding and Disclosures, see page 11.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- We observed that 1 in 5 older adults with atrial fibrillation had clinically meaningful decline in quality of life over 1-year.
- Clinically meaningful decline in quality of life was associated with sex, symptoms of depression, anxiety, fair/poor self-rated health, lower social support, previously diagnosed comorbidities, and polypharmacy.

What Are the Clinical Implications?

- Prompt recognition and addressing the poor psychosocial factors and comorbidities in older adults with atrial fibrillation may potentially improve patient-centered outcomes, including quality of life.

Nonstandard Abbreviations and Acronyms

AF	atrial fibrillation
AFEQT	Atrial Fibrillation Effect on Quality-of-Life
ORBIT-AF	Outcomes Registry for Better Informed Treatment of Atrial Fibrillation
QoL	quality of life
SAGE-AF	Systematic Assessment of Geriatric Elements in Atrial Fibrillation

or implication on patient's long-term clinical course and health outcomes.[9,10] Because of the intrinsically subjective nature of patient reported outcomes such as QoL, there is no gold standard for defining clinically meaningful change in QoL.[11] Still, a few studies among patients with AF have suggested approaches that could be used for defining clinically meaningful change in QoL based on patient reported magnitude of change in their QoL.[12,13] Yet, no prior studies have examined the extent of clinically meaningful change in QoL, and patient and clinical factors that are associated with clinically meaningful change in QoL among older patients with AF.

Using data from the prospective multi-center study, SAGE-AF (Systematic Assessment of Geriatric Elements in Atrial Fibrillation), we examined clinically meaningful changes in QoL over a 1 year follow-up period in patients aged ≥65 years with AF and examined a variety of patient sociodemographic, psychosocial, and clinical factors associated with clinically meaningful change in QoL among these patients.

METHODS

The data, analytic methods, and study materials will be made available to other researchers upon reasonable request made to the SAGE-AF study principal investigators (J.S., D.M.).

Study Population

The present study used data from an ongoing prospective study: SAGE-AF.[14,15] Between 2015 and 2018, patients were recruited from 1 of 4 clinical sites in Central Massachusetts (University of Massachusetts Memorial Health Care internal medicine, cardiology, electrophysiology, or Heart Rhythm Associates of Central MA), 1 clinical site in Eastern Massachusetts (Boston University cardiology), or 1 of 2 practices in Central Georgia (Family Health Center and Georgia Arrhythmia Consultants). Eligible participants were (1) aged ≥65 years; (2) diagnosed with AF if this arrhythmia was detected on Holter monitor, electrocardiography tracings, or was documented in any clinic or hospital record; and (3) had a CHA_2DS_2-VASC risk score ≥2. Patients were ineligible for study enrollment if they had documentation of an absolute contraindication to the use of oral anticoagulants, or an indication for oral anticoagulation other than AF (ie, mechanical heart valve, deep venous thrombosis, or pulmonary embolism); if they were unable to provide signed informed consent; did not speak English; were scheduled for an invasive procedure with high risk for uncontrolled bleeding; if they were pregnant; were incarcerated; or if they were unwilling or unable to attend scheduled 1- and 2-year study follow-up visits. Of the 6507 individuals screened, a total of 1244 participants were enrolled in this prospective study and completed their baseline examination (Figure).

Trained research personnel abstracted data from hospital medical records and conducted face-to-face or telephone interviews with each participant at baseline, and 1 and 2 years of follow-up. The Institutional Review Boards at the University of Massachusetts Medical School, Boston University, and Mercer University approved this investigation. Each eligible participant provided written informed consent before formal study enrollment.

Assessment of QoL

At the time of study enrollment and at 1 year of follow-up, we assessed participants' QoL using the Atrial Fibrillation Effect Quality-of-Life (AFEQT) Questionnaire.[16] This 20-item questionnaire is a validated and reliable disease specific measure that asks participants to self-report the extent to which their experience of AF may have affected their QoL in the prior 4 weeks with 7 response options in a Likert scale

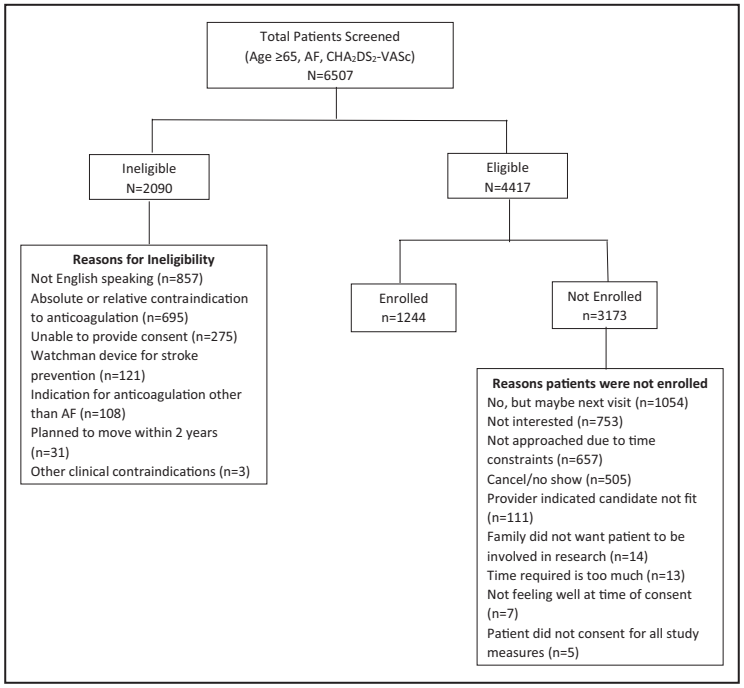

Figure. Baseline SAGE-AF study enrollment flowchart, 2016 to 2018. AF indicates atrial fibrillation; and SAGE-AF, Systematic Assessment of Geriatric Elements in Atrial Fibrillation.

that include: "Not at all bothered Or I did not have this symptom", "Hardly bothered", "A little bothered", "Moderately bothered", "Quite a bit bothered", "Very bothered", and "Extremely bothered". Based on the developers' guidelines, the overall AFEQT summary score was derived from summing up responses to the 18 items belonging to 3 subscales: symptoms (4 items), daily activities (8 items), and treatment concerns (6 items) subscale, with a total score ranging from 0 to 100 with higher scores indicating better QoL. In addition, each subscale, namely symptoms, daily activities, and the treatment concern subscale was scored separately with scores ranging from 0 (worst QoL score) to 100 (best QoL score). The symptoms subscale assessed the extent to which patients' physical symptoms (palpitations, light headedness, or dizziness) may have been bothersome to them in the prior 4 weeks. The daily activities subscale measured the extent of difficulty patients experienced in carrying out their regular physical activities, exercising, walking briskly, or doing vigorous activities. The treatment concern subscale assessed whether patients were worried or anxious that there AF could begin at any time or worsen their coexisting medical conditions. The Treatment satisfaction subscale (2-items) scores were not included in the overall AFEQT summary score.[16]

A difference of at least 5 points between the baseline and 1-year AFEQT overall score and for each subscale was considered a clinically meaningful difference based on recent reports by the AFEQT developers using data from the ORBIT-AF (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation) registry.[13] We categorized patients into the following 3 groups: (1) clinically meaningful decline in QoL (1-year QoL score—Baseline QoL score ≤–5.0 points); (2) no clinically meaningful change in QoL (1-year QoL score—Baseline QoL score between –5.0 to +5.0 points); and (3) clinically meaningful increase in QoL (1-year QoL score—Baseline QoL score ≥+5.0 points.

Baseline Participant Characteristics

Participant sociodemographic data including measures of age and sex were derived from the review of electronic medical records. Other sociodemographic characteristics such as race/ethnicity, marital status, and highest level of education were obtained during the baseline face-to-face or telephone interviews. Clinical measures assessed from medical records included type of AF (paroxysmal, persistent, and permanent), time since AF diagnosis, receipt of rate or rhythm control therapy, previously diagnosed comorbidities including hypertension, dyslipidemia, diabetes mellitus, heart failure, arthritis, anemia, and cancer, polypharmacy (receipt of ≥5 medications). Calculated risk scores including CHA_2DS_2-VASc, HASBLED, and Charlson Comorbidity index were derived from patient's relevant medical history.[17,18] Psychosocial and geriatric elements were obtained from comprehensive

structured interviews including measures of social support, cognitive impairment, frailty, symptoms of depression and anxiety, independent functioning, hearing and visual impairment, self-rated health, and history of falls. Social support was assessed with the 5-items Medical Outcomes Social Support Survey Instrument.[19] Cognitive impairment was assessed using the 30-item Montreal Cognitive Assessment Battery with scores ranging 0 to 30 (higher scores indicative of better cognitive functioning) and a cut-off of ≤23 suggestive of cognitive impairment.[20,21] Frailty was assessed by the Cardiovascular Health Survey frailty scale (0: not frail, 1–2: pre-frail, and ≥3: frail).[22] Symptoms of depression were measured with the 9-item Patient Health Questionnaire (≤4: no depressive symptom, 5–9: mild, ≥10: moderate to severe depressive symptoms).[23] Anxiety symptoms were assessed with the 7-item Generalized Anxiety Disorder questionnaire (no anxiety symptom [≤4], mild [5–9], moderate to severe [≥10] anxiety symptoms).[24] Level of independence was examined with the instrumental activities of daily living including basic communication skills, transportation, meal preparation, shopping, housework, managing medications and personal finances.[25] Self-rated health status was evaluated with a reliable and validated single-item measure with responses on a 5-point Likert scale which asked: "In general, would you say your health is excellent, very good, good, fair, or poor?".[26] Participants provided self-reports of hearing and visual impairment, history of falls, whether they had experienced AF symptoms in the preceding 4 weeks and health behaviors including alcohol use and smoking history (Variables and measures assessed in the present study and method of data collection are summarized in Table S1).

Statistical Analysis

All the study data were accessible to the lead author (H.A.) who takes full responsibility for the integrity of the data and accuracy of results obtained from data analysis.

In deriving the analytic sample, we excluded participants with missing information on the AFEQT QoL measure at the 1 year of follow-up contact (n=147). At baseline, all participants provided responses to the AFEQT measure with no missing data. The analytic sample consisted of 1097 of the original 1244-member study cohort. Descriptive statistics were used to examine participant's baseline characteristics according to whether they experienced a clinically meaningful decline, increase, or no clinically meaningful change in their QoL between baseline/study enrollment and 1-year of follow-up. We used independent sample t tests to compare differences in mean AFEQT QoL scores overall and according to the 3 subscales from baseline to 1 year of follow-up.

In examining the factors associated with clinically meaningful change in QoL, ordinal logistic regression models were constructed to calculate the crude and multivariable adjusted odds ratios (ORs) and accompanying 95% CI. The 3-level outcomes were either a clinically meaningful decline, no clinically meaningful change, or clinically meaningful increase in QoL. The proportional odds assumption for the ordinal logistic regression models was not sufficiently met when evaluated with the Brant test.[27] Thus, we used the partial proportional odds model with less restraints on the proportionality assumption.[28] Separate regression models were constructed to examine factors independently associated with clinically meaningful change in the overall AFEQT score and the respective subscales: symptoms, daily activities, and treatment concerns. We sequentially examined patient characteristics and clinical factors significantly associated with changes in QoL. Our a priori selection of variables was based on clinical judgement by identifying those factors assessed in our study that may impact patients' QoL and those described in previous studies as being significantly associated with QoL among patients with AF. First, in univariable models we separately examined the association between each variable and clinically meaningful change in QoL according to the following groups: sociodemographic characteristics (age, sex, race/ethnicity, and education), clinical and health behavior variables (previously diagnosed comorbidities, type of AF, AF symptoms in prior 4 weeks, anticoagulation therapy, rhythm versus rate control therapy, risk scores, smoking, and alcohol use), and psychosocial/geriatric measures (symptoms of depression and anxiety, social support, frailty, self-rated health, independent functioning, previous history of falls, hearing, visual, and cognitive impairment). Subsequently, in each multivariable adjusted model, we included only variables that were independently associated with a clinically meaningful change in QoL from the univariable analysis. Additionally, since the baseline QoL score may impact change in QoL over time with regression to the mean,[29] we adjusted for baseline overall QoL score and baseline subscale score in the respective univariable and multivariable regression models. A 2-sided $P<0.05$ was considered statistically significant.

RESULTS

Participant Baseline Characteristics

In comparison with included participants (n=1097), the 147 participants with missing data on the AFEQT QoL

score at 1-year of follow-up were more likely to be of a racial/ethnic minority group (12.6% versus 23.1%) and a higher proportion reported mild/moderate symptoms of depression (24.2% versus 35.4%), had higher risk scores (CHA_2DS_2-VASc, HASBLED, and Charlson Comorbidity index), and were more likely to be cognitively impaired (33.2% versus 59.2%) and frail (12.5% versus 23.8%) ($P<0.05$ for all comparisons). The mean (SD) score for the overall AFEQT QoL measure at baseline was significantly higher for those who were included in the analytic sample compared with excluded participants (80.4 [SD=17.8] versus 77.1 [SD=18.8]; $P=0.04$).

The mean age of study participants (n=1097) was 75 years, 48% were women, and 87% were White. Approximately two thirds had paroxysmal AF, 14% had persistent AF, and 18% had permanent AF. There were no differences in terms of changes in the QoL scores according to type of AF. One third had symptoms of AF during the 4 weeks before study enrollment, and 59% of patients were on rhythm control (cardioversion or ablation therapy). No significant differences were observed in terms of change in QoL scores according to whether patients received rhythm versus rate control therapy. In addition, symptoms of depression or anxiety did not differ according to the type of treatment patients received. A majority of patients (95%) were prescribed ≥5 medications. There were no differences in changes in QoL based on the individual groups of commonly prescribed medications. About one quarter of study participants had mild/moderate symptoms of depression or mild/moderate symptoms of anxiety (Table 1).

Participant QoL at Baseline and 1-Year Follow-Up

Among the 1097 study participants, 21.8% had a clinically meaningful decline in their overall AFEQT QoL score (≥−5.0 points), 38.0% had no clinically meaningful change in QoL (between −5.0 to +5.0 points), and 40.2% experienced a clinically meaningful increase in their QoL score (≥+5.0 points). The average baseline overall AFEQT score was notably low (mean [SD]=69.1 [18.0]) among those who experienced a clinically meaningful increase in their QoL during follow-up compared with those who had a decline (mean [SD]=86.1 [13.1]) or no clinically meaningful change (mean [SD]=89.1 [12.6]) in their overall QoL (Table 2).

Overall, study participants experienced a 4.3-point increase in their mean AFEQT from a baseline score of 80.4 to 84.8 at the 1-year follow-up ($P<0.001$). With regards to the 3 QoL subscales, participants reported the highest QoL score at baseline on the symptom subscale, with a mean of 88.3, and the lowest QoL score on the daily activity subscale, with an average score of 74.4. Patients had the greatest improvement in QoL over 1 year in the daily activity subscale (mean change: +5.6) and the least improvement in the symptom subscale (mean change: +1.8) (Table 2). On the treatment concern subscale, the average change was +4.4 points between baseline and 1 year from an initial mean score of 83.1 (19.3) at baseline.

The proportion of participants with a clinically meaningful decline in their QoL over 1 year on the daily activity, symptom, and treatment concern subscales were 25.7%, 20.7%, and 22.0%, respectively (Table 2). The proportion of those with a clinically meaningful increase in the daily activity subscale was 40.9% which was higher than the values observed on the symptom (25.9%) and treatment concern (40.8%) subscales (Table 2).

Patient and Clinical Factors Associated With Clinically Meaningful Change in QoL

In the multivariable adjusted model examining factors associated with clinically meaningful change in overall QoL, patients with symptoms of mild/moderate depression and fair/poor self-rated health were more likely to experience a clinically meaningful decline versus no clinically meaningful change or clinically meaningful increase in their overall QoL scores than patients without symptoms of depression or those who rated their health as good/excellent, respectively (Table 3). With regards to the symptom's subscale, those who self-reported their health as being fair/poor versus good/excellent, and women compared with men, were more likely to experience a clinically meaningful decline versus no clinically meaningful change or clinically meaningful increase in their QoL (Table 4). On the daily activities' subscale, participants with a prior diagnosis of diabetes mellitus or heart failure, and those taking ≥5 medications (polypharmacy), were more likely to experience clinically meaningful decline in their QoL (Table 5). With regards to the treatment concerns subscale, patients who were non-Whites compared with White, those who reported symptoms of mild/moderate depression versus none, or moderate anxiety versus none, or those with low social support were more likely to experience a clinically meaningful decline in their QoL (Table 6). In the overall QoL regression models, and the respective subscale models, higher baseline QoL scores were associated with clinically meaningful decline over the 1-year period of follow-up.

DISCUSSION

In this large prospective study, we described the extent of clinically meaningful change in QoL, and factors associated with clinically meaningful change in QoL,

Table 1. Baseline Characteristics of Study Participants According to Clinically Meaningful Changes in QOL From Baseline—1 Year of Follow-Up in the SAGE-AF Study

Characteristics	Overall Analytic Sample (n=1097)	Clinically Meaningful Decline in QoL* (n=239)	No Clinically Meaningful Change in QoL† (n=417)	Clinically Meaningful Increase in QoL‡ (n=441)
Socio-demographic				
Age (y, mean [SD])	75.2 (7.0)	75.6 (7.1)	75.1 (7.0)	75.0 (7.2)
Age categories, %				
65–74 y	52.0	51.5	53.7	50.6
75–84 y	36.1	33.0	35.5	38.3
≥85 y	11.9	15.5	10.8	11.1
Women, %	48.3	50.6	42.2	52.8
Race/Ethnicity, %				
White	87.4	82.8	88.7	88.6
Non-White	12.6	17.2	11.3	11.4
Married, %	57.4	55.5	60.4	55.5
Education				
≤ High school	36.4	41.8	33.3	36.4
Some college	19.4	19.0	16.8	22.1
College graduate	44.2	39.2	49.9	41.5
Clinical				
AF type, %				
Paroxysmal	67.7	71.1	66.2	67.3
Persistent	14.4	15.6	13.4	14.6
Permanent	17.9	13.3	20.4	18.1
Time since AF diagnosis, (y, mean [SD])	5.3 (4.3)	5.3 (4.2)	5.5 (4.0)	5.2 (4.5)
Symptoms of AF in past 4 wk, %	29.4	27.4	22.3	37.4
Anticoagulation therapy, %				
DOAC	37.1	39.3	31.7	41.0
Warfarin	48.6	47.3	50.8	47.2
None	14.3	13.4	17.5	11.8
AF treatment approach, %				
Rhythm control therapy	58.5	61.5	56.3	59.0
Rate control therapy	41.5	38.5	43.7	41.0
Polypharmacy (≥5 medications), %	95.3	97.1	95.2	94.6
Commonly prescribed medications, %				
ACE-inhibitors	33.8	32.6	36.4	32.0
ARBs	23.0	23.8	22.1	23.4
Beta-blockers	79.1	80.1	80.4	77.3
Calcium channel blockers	31.4	35.6	28.1	32.4
Digoxin	3.0	2.6	2.5	3.7
Diuretics	50.0	51.9	45.1	52.8
Statins	68.2	70.7	68.1	66.9
CHA_2DS_2-VASc >2, %	88.3	90.0	85.1	90.5
HASBLED ≥3, %	73.2	73.2	70.0	76.2
Charlson comorbidity index, (mean, SD)	5.9 (2.5)	6.2 (2.5)	5.8 (2.5)	5.9 (2.5)
Medical history, %				
Hypertension	89.8	94.6	88.0	88.9
Dyslipidemia	80.2	77.8	80.8	81.0
Diabetes mellitus	29.9	36.0	25.2	31.1
Heart failure	34.9	39.7	30.9	36.0

(Continues)

Table 1. (Continued)

Characteristics	Overall Analytic Sample (n=1097)	Clinically Meaningful Decline in QoL* (n=239)	No Clinically Meaningful Change in QoL† (n=417)	Clinically Meaningful Increase in QoL‡ (n=441)
Arthritis	50.4	51.5	47.2	52.8
Anemia	30.6	29.3	28.3	33.6
Cancer	31.0	32.2	33.6	27.9
Psychosocial and geriatric				
Depressive symptoms§, %				
None	73.2	73.2	80.8	66.0
Mild/moderate	24.3	25.5	18.2	29.2
Moderately severe/severe	2.5	1.3	1.0	4.8
Anxiety symptoms‖, %				
None	76.9	75.7	84.7	70.1
Mild/moderate	21.4	23.4	14.6	20.8
Severe	1.7	0.9	0.7	3.2
Low social support, %	26.3	27.6	24.5	27.4
Cognitive impairment, %	33.2	38.8	30.9	32.4
Hearing impairment, %	35.5	33.9	32.4	39.5
Visual impairment, %	33.2	34.3	27.8	37.6
Previous history of fall, %	21.4	20.9	18.0	24.8
Frailty, %				
Not frail	34.6	32.6	44.4	26.5
Pre-frail	52.9	55.7	48.4	17.9
Frail	12.5	11.7	7.2	55.6
Self-rated health, %				
Fair/poor	15.4	16.4	10.1	19.9
Good/excellent	84.6	83.6	89.9	80.1
Independent functioning (IADLs) (mean, SD)	6.8 (0.8)	6.8 (0.8)	6.8 (0.8)	6.7 (1.0)
Baseline overall AFEQT score (mean, SD)	80.4 (17.8)	86.1 (13.1)	89.1 (12.6)	69.1 (18.0)
Health behaviors				
Alcohol use, %	57.0	53.2	62.9	53.5
Smoking status, %				
Never smoker	46.8	44.9	44.9	49.7
Former smoker	50.1	51.7	52.7	46.9
Current smoker	3.1	3.4	2.4	3.4
Study sites				
Georgia, %	22.3	26.4	18.9	23.5
Massachusetts, %	77.7	73.6	81.1	76.5

ACE indicates angiotensin-converting enzymes; AFEQT, Atrial Fibrillation Effect Quality-of-Life; ARBs, Angiotensin Receptor Blockers; CHA_2DS_2-VASc, Congestive heart failure, Hypertension, Age (≥65=1 point, ≥75=2 points), Diabetes Mellitus, and Prior Stroke/Transient Ischemic Attack (2 points), Vascular Disease (peripheral artery disease, previous myocardial infarction, aortic atheroma) and female sex; DOAC, direct oral anticoagulant; HAS-BLED, determines 1-year risk of major bleeding (Hypertension, Abnormal Renal and Liver Function, Prior Stroke, Prior Bleeding, Labile INR, Elderly, Drugs or Alcohol; IADLs, Instrumental Activities of Daily Living (score ranging from 0 to 7; INR, International Normalized Ratio; QoL, quality of life; and SAGE-AF, Systematic Assessment of Geriatric Elements in Atrial Fibrillation.

*Clinically meaningful decline in quality of life based on Atrial Fibrillation Effect on Quality of Life score at year 1—baseline score ≤−5.0.

†No clinically meaningful change in QoL based on Atrial Fibrillation Effect on Quality of Life score at year 1—baseline score −5.0 to +5.0.

‡Clinically meaningful increase in QoL based on Atrial Fibrillation Effect on Quality of Life score at year 1—baseline score ≥+5.0.

§Patient Health Questionnaire 9-item score (5–9 mild; 10–14 moderate; 15–19 moderately severe; and ≥20 severe depression).

‖General Anxiety Disorder 7-item score (5–9 mild; 10–14 moderate; ≥15 severe anxiety).

over 1-year of follow-up among patients ≥65 years with AF. Approximately 40% of patients experienced a clinically meaningful increase in their overall QoL whereas 20% experienced a clinically meaningful decline in their overall QoL. Factors independently associated with clinically meaningful change in participants' overall

Table 2. Overall AFEQT QoL Score and Subscale Scores at Baseline and 1 Year of Follow-Up: SAGE-AF

AFEQT Overall and Subscales	Baseline Score (Mean, SD)	1-Y Score (Mean, SD)	Mean Change	*P* Value	Proportion With Clinically Meaningful Decline in QoL (%)*	Proportion With No Clinically Meaningful Change in QoL (%)†	Proportion With Clinically Meaningful Increase in QoL (%)‡
Overall	80.4 (17.8)	84.8 (15.3)	+4.3	<0.001	21.8	38.0	40.2
Symptoms	88.3 (17.5)	90.2 (14.7)	+1.8	0.001	20.7	53.4	25.9
Daily activities	74.4 (24.5)	80.0 (21.6)	+5.6	<0.001	25.7	33.4	40.9
Treatment concern	83.1 (19.3)	87.6 (16.5)	+4.4	<0.001	22.0	37.2	40.8

AFEQT indicates Atrial Fibrillation Effect on Quality of Life questionnaire; QoL, quality of life; and SAGE-AF, Systematic Assessment of Geriatric Elements in Atrial Fibrillation.

*Clinically meaningful decline in quality of life based on Atrial Fibrillation Effect on Quality of Life score at year 1—baseline score ≤−5.0.

†No clinically meaningful change in quality of life based on Atrial Fibrillation Effect on Quality of Life score at year 1—baseline score <+5.0 to −5.0.

‡Clinically meaningful increase in quality of life based on Atrial Fibrillation Effect on Quality of Life score at year 1—baseline score ≥+5.0.

QoL or at least 1 of its subscales included several patient sociodemographic and psychosocial characteristics, the presence of previously diagnosed comorbid conditions, polypharmacy, and higher baseline QoL scores.

Consistent with findings from the few existing studies of older patients with AF in the outpatient setting,[12,13] most of our study participants did not experience a major deterioration in their overall QoL during the 1-year follow-up period. We postulate that since our study participants were recruited from cardiology, electrophysiology, and primary care outpatient clinics as opposed to the hospital in-patient setting, they may have been relatively stable with greater functional status and overall well-being as reflected by their high baseline overall QoL score (mean=80.4), and may have adapted to their chronic illness, thus being less likely to report a deterioration in their QoL.

In the present study, sociodemographic characteristics including sex and race were independently associated with change in QoL. Women were more likely to experience a clinically meaningful decline in their QoL as assessed by the symptom subscale than men. Similarly, prior studies that have examined the association between sex and baseline QoL in patients with AF[30–32] and coronary heart disease[33,34] have shown that women have greater impairment in their QoL than men. Perception of one's symptoms, threshold for reporting AF symptoms, and the presence of psychosocial or comorbid factors have been identified as plausible reasons for observed sex differences in QoL.[35] Our prospective findings suggest that not only

Table 3. Factors Independently Associated With Clinically Meaningful Change ("Decline" vs "No Clinically Meaningful Change" or "Increase") in Overall AFEQT QoL Scores Between Baseline and 1 Year of Study Follow-Up: SAGE-AF

Characteristics	Unadjusted OR (95% CI)	*Adjusted OR (95% CI)
Race (non-White vs White)	1.80 (1.25–2.59)	1.46 (0.98–2.16)
Diabetes mellitus	1.43 (1.10–1.86)	1.16 (0.87–1.54)
Hypertension	1.60 (1.08–2.36)	1.33 (0.89–1.98)
Heart Failure	1.42 (1.10–1.83)	1.27 (0.97–1.66)
Visual impairment	1.37 (1.05–1.78)	1.12 (0.84–1.48)
Cognitive impairment	0.75 (0.58–0.97)	0.93 (0.71–1.22)
Polypharmacy	1.85 (1.05–3.27)	1.68 (0.94–2.99)
Fair/poor vs good/excellent self-rated health	2.08 (1.43–3.01)	1.57 (1.05–2.35)†
Mild Anxiety vs none	1.71 (1.23–2.39)	1.44 (0.99–2.08)
Mild/moderate depression vs none	1.92 (1.40–2.62)	1.62 (1.14–2.31)†

AFEQT indicates Atrial Fibrillation Effect on Quality of Life; OR, odds ratio; QoL, quality of life; and SAGE-AF, Systematic Assessment of Geriatric Elements in Atrial Fibrillation study.

*Adjusted model includes only variables associated with change in QoL in the univariable models and the overall baseline Atrial Fibrillation Effect on Quality of Life score.

†Statistically significant results.

Table 4. Factors Independently Associated With Clinically Meaningful Change ("Decline" vs "No Clinically Meaningful Change" or "Increase") in AFEQT Symptom Subscale Scores Between Baseline and 1 Year of Study Follow-Up: SAGE-AF

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Sex (women vs men)	1.60 (1.24–2.06)	1.45 (1.10–1.91)†
Marital status (married vs not married)	0.73 (0.57–0.95)	0.87 (0.66–1.15)
Cognitive impairment	0.72 (0.55–0.94)	0.80 (0.60–1.06)
Vision impairment	1.40 (1.06–1.83)	1.11 (0.83–1.49)
Mild/moderate depression vs none	2.25 (1.56–3.23)	1.00 (0.64–1.56)
Mild anxiety vs none	1.59 (1.13–2.24)	1.28 (0.47–1.87)
Moderate anxiety vs none	3.06 (1.38–6.77)	1.91 (0.82–4.41)
Independent activities of daily living	0.85 (0.74–0.97)	0.97 (0.79–1.20)
Fair/poor vs good/excellent self-rated health	2.00 (1.40–2.86)	1.64 (1.12–2.42)†

AFEQT indicates Atrial Fibrillation Effect on Quality of Life; OR, odds ratio; and SAGE-AF, Systematic Assessment of Geriatric Elements in Atrial Fibrillation study.

*Adjusted model includes only variables associated with change in quality of life in the univariable models and baseline symptom subscale score.

†Statistically significant results.

Table 5. Factors Independently Associated With Clinically Meaningful Change ("Decline" vs "No Clinically Meaningful Change" or "Increase") in AFEQT Daily Activity Subscale Scores Between Baseline and 1 Year of Study Follow-Up: SAGE-AF

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Race (non-White vs White)	1.44 (1.01–2.07)	1.14 (0.76–1.73)
Type of AF (persistent vs paroxysmal)	1.45 (1.01–2.07)	1.44 (0.99–2.09)
Diabetes mellitus	1.74 (1.34–2.26)	1.45 (1.07–1.96)†
Hypertension	1.68 (1.13–2.50)	1.27 (0.82–1.97)
Heart failure	1.67 (1.29–2.16)	1.33 (1.00–1.78)†
Cognitive impairment	0.73 (0.57–0.94)	0.84 (0.63–1.12)
Vision impairment	1.43 (1.10–1.85)	1.14 (0.86–1.52)
Mild/moderate depression vs none	1.77 (1.24–2.51)	1.30 (0.93–1.81)
Pre-frail vs not frail	1.30 (1.00–1.67)	1.30 (0.94–1.79)
Frail vs not frail	2.05 (1.31–3.19)	1.27 (0.76–2.11)
Polypharmacy	2.21 (1.26–3.88)	1.80 (1.00–3.21)†
BMI (≥30 kg/m^2 vs <25 kg/m^2)	1.46 (1.05–2.02)	1.25 (0.87–1.79)
Fair/poor self-rated health vs good/excellent	2.22 (1.48–3.33)	1.32 (0.87–2.02)

AF indicates atrial fibrillation; AFEQT, Atrial Fibrillation Effect on Quality of Life; BMI, body mass index; OR, odds ratio; and SAGE-AF, Systematic Assessment of Geriatric Elements in Atrial Fibrillation study.

*Adjusted model includes only variables associated with change in quality of life in the univariable models and baseline daily activity subscale score.

†Statistically significant results.

Table 6. Factors Independently Associated With Clinically Meaningful Change ("Decline" vs "No Clinically Meaningful Change" or "Increase") in AFEQT Treatment Concern Subscale Scores Between Baseline and 1 Year of Study Follow-Up: SAGE-AF

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Race/Ethnicity (non-White vs White)	2.26 (1.57–3.27)	1.63 (1.09–2.45)†
Some College vs ≤ High School	0.67 (0.47–0.94)	0.78 (0.55–1.12)
College Graduate vs ≤ High School	0.70 (0.54–0.92)	0.88 (0.66–1.18)
Diabetes mellitus	1.51 (1.16–1.97)	1.30 (0.98–1.73)
Mild/moderate depression vs none	2.08 (1.52–2.84)	1.63 (1.13–2.33)†
Mild anxiety vs none	2.15 (1.50–3.06)	1.77 (1.20–2.61)†
Moderate anxiety vs none	2.18 (1.07–4.46)	1.50 (0.68–3.27)
Fair/poor self-rated health vs good/excellent	1.97 (1.37–2.85)	1.46 (0.97–2.21)
Pre-frail vs not frail	1.34 (1.03–1.73)	1.07 (0.81–1.40)
Frail vs not frail	1.77 (1.11–2.81)	0.99 (0.59–1.67)
Visual impairment	1.56 (1.20–2.03)	1.22 (0.92–1.62)
Cognitive impairment	0.68 (0.53–0.88)	0.86 (0.65–1.15)
Low social support	1.54 (1.17–2.03)	1.47 (1.11–1.94)†

AFEQT indicates Atrial Fibrillation Effect on Quality of Life; OR, odds ratio; and SAGE-AF, Systematic Assessment of Geriatric Elements in Atrial Fibrillation study.

*Adjusted model includes only variables associated with change in quality of life in the univariable models and baseline treatment concern subscale score.

†Statistically significant results.

do women have poorer QoL than men at a given point in time, but that they may be more likely to experience deterioration in their QoL over the course of their illness as compared with men. These data suggest that during routine follow-up visits, healthcare providers should regularly assess how women's experience of their AF symptoms may negatively impact their overall well-being and functional status.

Study participants from racial/ethnic minority groups were more likely to experience clinically meaningful decline in their QoL on the treatment concern subscale compared with Whites. There has been limited study of racial disparities in QoL among patients with AF. Recent findings from the ORBIT-AF registry of 9542 American adults with incident and prevalent AF, showed that Black individuals, who comprised only 5% of their study population, had a higher symptom burden of AF and lower QoL at baseline and 2 years of follow-up in comparison with Whites.[36] Reports from various clinical and epidemiological studies have consistently shown a lower incidence and prevalence of AF in racial/ethnic minority groups.[37,38] To enhance our understanding of patient-centered outcomes in racial/ethnic minority groups with AF, implementing targeted strategies for recruiting and retaining more minorities in population-based studies and clinical trials may enhance our understanding of racial variations in treatment strategies, QoL changes, and long-term health outcomes.[39]

We observed that several psychosocial factors, such as symptoms of depression, anxiety, and fair/poor self-rated health were independently associated with clinically meaningful change in QoL. Patients with symptoms of mild/moderate depression and those who rated their health as fair/poor were more likely to experience decline in their overall QoL over the 1-year follow-up period. Similarly, those who rated their health as fair/poor as opposed to good/excellent experienced a clinically meaningful decline versus an increase or no clinically meaningful change on the symptom QoL subscale. Participants with symptoms of mild/moderate depression and those with mild anxiety experienced declining QoL on the treatment concern subscale. Prior studies conducted in patients with AF have reported an association between symptoms of depression, anxiety, poorly perceived health status, stress, and impaired QoL.[40–42] In a cross-sectional study among 207 patients recruited from an outpatient arrhythmia clinic and those hospitalized in a cardiac progressive care unit, poor illness perception of AF such as attributing serious consequences to AF and a lack

of understanding of their AF condition was associated with greater psychological distress, anxiety, and depression.[43] Our findings further highlight an important temporal relationship between symptoms of depression or fair/poor self-rated health at baseline and an increased risk of experiencing declines in QoL over time. Living and coping on a daily basis with symptoms of AF, depression, and/or anxiety, as well as perceiving one's health to be fair/poor may be particularly burdensome for patients from the perspective of disordered mind-body interactions,[44] which may lead to deterioration in one's perception of their overall well-being. These findings reinforce the need for early assessment of patient's psychological well-being including symptoms of depression, anxiety, and self-reports of their health status, which provides an opportunity to institute treatment strategies that may be pivotal in improving patient's psychological symptoms, QoL, and could ultimately impact their response to AF treatment. In addition, we recommend improved approaches for clinical practice with standardized screening of self-rated health, depression, and anxiety in high-risk older patients with AF.

Furthermore, reports of low social support among our study participants were associated with a decline in QoL as assessed by the treatment concerns subscale. Our finding is in keeping with those from previous studies that emphasize the important role of caregivers in periods of illness or having a strong support system which fosters well-being and QoL.[45,46] For a more holistic approach to patient care, addressing the social determinants of health, including access to care, transportation, safe environment, and availability of caregiver support may help identify patients with low social support and those in need of referral for social workers intervention and assistance.

The presence of a number of comorbid conditions, most notably heart failure and diabetes mellitus, and the use of ≥5 medications (polypharmacy) at baseline were associated with clinically meaningful decline in QoL assessed on the daily activity subscale. Our study participants were older men and women with a high burden of several comorbid conditions which have been identified as risk factors for the development of AF.[47,48] Previous studies have shown an association between comorbidities and poor QoL in patients with AF.[6,9] Our observation that the presence of several comorbid diseases was associated with greater decline in QoL over 1-year of follow-up further emphasizes that older patients with AF who have coexisting cardiometabolic diseases may have reduced physical reserve and experience increasingly worsening AF symptoms over the period of their illness.[6] Furthermore, the high proportion of study participants who were prescribed ≥5 medications is reflective of the considerable burden of comorbidities among this cohort of patients. The burden of ingesting multiple pills for co-existing medical conditions and dealing with potential side effects of these medications may be overwhelming and could negatively impact patients' QoL. These results and those from prior studies buttress the need for a more holistic approach in patient management to address the presence of comorbid conditions while simultaneously providing rate/rhythm control in patients with AF for sustained improvement in QoL and overall well-being.

An important goal of AF management is symptom improvement through rate or rhythm control.[5] Interestingly, we observed that during the 1-year period of follow-up, study participants experienced the greatest improvement in their QoL on the daily activity subscale reporting that they were able to function more optimally while carrying out their daily activities and spending time with their loved ones as opposed to alleviation of their cardiac related symptoms. This finding suggests the need for a better understanding of those aspects of one's illness experience that matter most to patients as they undergo treatment for AF. However, we recognize that there may have been a potential ceiling effect, since the symptom subscale had the highest mean score at the time of baseline study enrollment with less likelihood for improvement compared with the daily activity subscale which had the lowest mean value at baseline.

Although previous research has shown that treatment approaches to restoring sinus rhythm are associated with improvement in QoL,[49,50] we did not observe any significant association between rate or rhythm control strategies and clinically meaningful changes in overall QoL over our 1-year period of follow-up. Future longitudinal studies should examine the impact of rate or rhythm control on clinically meaningful changes in QoL over longer periods of follow-up to better evaluate if there are sustained effects of various treatment approaches on patient-reported outcomes including their QoL.

Study Strengths and Limitations

To the best of our knowledge, this is the first contemporary inquiry into the factors associated with clinically meaningful change in QoL among a well characterized cohort of older men and women diagnosed with AF with a detailed assessment of their clinical, psychosocial, and geriatric characteristics. In addition, the AFEQT questionnaire used to assess the impact of AF on QoL among our study participants is a well-established and widely accepted measure, enhancing the validity and reproducibility of our study findings. However, our results should be interpreted in the light of several limitations. We recognize that a majority of our study participants were recruited from study sites only in the North Eastern and South Eastern regions of the United

States which could lead to potential selection bias and limited generalizability of our results to more ethnically diverse populations. We acknowledge that the assessment of QoL among our study participants is entirely subjective and may be influenced by one's personal illness experience and their cultural beliefs and values, which may limit the generalizability of our study findings to sicker populations diagnosed with AF and those of varying socio-cultural groups. In addition, the cut point used for defining clinically meaningful decline in QoL may not be applicable in different patient populations with AF. Given our observational study design, there may be unmeasured factors that could impact clinically meaningful changes in patients QoL which were not accounted for in our study and potentially bias our effect estimates. Future longitudinal studies should use a multi-stake holder approach to directly assess the factors that may influence change in QoL from both the perspective of patients, their caregivers, and healthcare providers. These studies should also conduct multiple assessments of QoL during longer follow-up periods to identify particularly high-risk periods where interventions may be most beneficial and enhance the depth of our understanding of long-term changes in QoL while managing men and women from different age groups diagnosed with AF.

CONCLUSIONS

In this large multicenter prospective study among older adults with AF, we observed that ≈2 in every 5 patients experienced clinically meaningful increases in their QoL over 1 year of follow-up and 1 in 5 patients had a clinically meaningful decline in their overall QoL. Female participants reported mild/moderate symptoms of depression and anxiety, fair/poor self-rated health, had lower social support, and those with previously diagnosed comorbidities and polypharmacy were more likely to experience clinically meaningful decline in their overall QoL and on the symptom, daily activities, and treatment subscales. Our study provides timely and clinically relevant information for healthcare providers to assess potential factors that may lead to a progressive decline in QoL among patients with AF, and further reinforces the need for a more holistic approach in patient management to improve the functional status and overall well-being of older men and women with AF.

ARTICLE INFORMATION

Received May 4, 2020; accepted July 22, 2020.

Affiliations

From the Division of Cardiovascular Medicine, Department of Medicine, University of Massachusetts Medical School, Worcester, MA (H.O.A., J.M., D.D.M.); Department of Pharmacy and Health Systems Sciences, School of Pharmacy, North Eastern University, Boston, MA (J.S.S.); Division of Geriatrics and Meyers Primary Care Institute, Department of Medicine (M.T.) and Department of Population and Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA (M.T., C.I.K., R.J.G.).

Sources of Funding

This work was supported by grant R01HL126911 from the National Heart, Lung, and Blood Institute. McManus is supported by other National Heart, Lung, and Blood Institute grants: R01HL137734, R01HL137794, R01HL13660, and R01HL141434. Tisminetzky is supported by grants from the National Institute on Aging (R33AG057806 and RO1AG062630). The funding source had no role in the study concept and design, participant recruitment, data acquisition, analysis, interpretation of study results, article preparation; and decision to submit the article for publication.

Disclosures

McManus has received research grant support from Apple Computer, Bristol-Myers Squibb, Boeringher-Ingelheim, Pfizer, Samsung, Philips Healthcare, and Biotronik; consulting fees from Bristol-Myers Squibb, Pfizer, Flexcon, and Boston Biomedical Associates, and has inventor equity in Mobile Sense Technologies, Inc (Farmington, CT). The remaining authors have no disclosures to report.

Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. Variables assessed in the present SAGE-AF Study.

Variables and Measures	Patient Interviews	Medical Records Abstraction
Outcome Measure		
Quality of Life (Atrial Fibrillation Effect Quality-of-Life (AFEQT) Questionnaire [16]	✓	
Sociodemographic characteristics		
Age		✓
Sex		✓
Race/ethnicity	✓	
Level of Education	✓	
Marital status	✓	
Clinical variables		
Type of AF		✓
Time since AF diagnosis		✓
Symptoms of AF in past 4 weeks	✓	
Anticoagulation therapy		✓
AF treatment approach		✓
Medication use		✓
Medical history		✓
Psychosocial and Geriatric characteristics		
Social Support (Medical Outcomes Social Support Survey) [19]	✓	
Cognitive Assessment (Montreal Cognitive Assessment Battery (MoCA)) [20, 21]	✓	
Frailty (Cardiovascular Health Survey (CHS) frailty scale) [22]	✓	
Symptoms of Depression (PHQ-9) [23]	✓	
Symptoms of Anxiety (GAD-7) [24]	✓	
Independent functioning (Instrumental activities of daily living) [25]	✓	
Self-Rated Health [26]	✓	
Self-reported hearing impairment	✓	
Self-reported visual impairment	✓	
History of Fall	✓	
Health Behaviors		
Alcohol use	✓	
Smoking history	✓	