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Psychosocial and cognitive multimorbidity and health-related quality of life and symptom burden in older adults with atrial fibrillation: The systematic assessment of geriatric elements in atrial fibrillation (SAGE-AF) cohort study

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ABSTRACT

Background: Depression, anxiety, and cognitive impairments occur in up to 40 % of adults with AF and are associated with poorer health-related quality of life (HRQoL) and higher symptom burden. However, it is unknown how often these impairments co-occur, or multimorbidity, and how multimorbidity effects HRQoL and symptom burden.

Methods: Patients with AF age ≥ 65 years with a CHA_2DS_2VASC risk score ≥ 2 and eligible for oral anticoagulation therapy were recruited from five clinics in a prospective cohort study. Participants completed validated measures of depression (PHQ9) and anxiety (GAD7), cognitive impairment (MoCA), and HRQOL and AF symptom burden (AFEQT). Multinomial logistic regression was used.

Results: Participants (N = 1244, 49 % female) were on average 76 ± 7 years; 86 % were non-Hispanic white. Approximately 35 % of participants had 1 impairment, 17 % had 2 impairments and 8% had 3 impairments; 39 % had none of the 3 impairments examined. Compared to participants with no impairments, patients with 1, 2 and 3 impairments had higher odds of poor HRQoL (adjusted OR [AOR] = 1.77, 95 % CI 1.21, 2.60; AOR = 6.64, 95 % CI 4.43, 9.96; and AOR = 7.50, 95 % CI 4.40, 12.77, respectively) and those with 2 and 3 impairments had higher odds of high symptom burden (AOR = 3.69 95 % CI 2.22, 6.13; and AOR = 5.41 95 % CI 2.85, 10.26).

Conclusions: Psychosocial/cognitive multimorbidity is common among older adults with AF and is associated with poor HRQoL and high symptom burden. Clinicians might consider incorporating psychosocial and cognitive screens into routine care as this may identify a high-risk population.

1. Introduction

With an estimated prevalence of 3–5 million adults, atrial fibrillation (AF) represents the most common cardiac rhythm abnormality. (Wändell et al., 2016) Considering an aging population in the US and that AF primarily affects older adults, prevalence of AF is expected to more than double to 12 million by 2050. (Go, Hylek, & Phillips, 2001; Wändell et al., 2016) Further, AF represents a significant economic burden with health-related costs about $8700 higher per year than those living without AF. (Roger, Go, & Lloyd-Jones, 2011) Treatment of AF by attempting restoration of sinus rhythm with cardioversions, anti-arrhythmic medications and catheter ablation has been shown to reduce symptoms and improve quality of life, but has no incremental benefits on stroke, bleeding or mortality. (Packer, Mark, & Robb, 2019) Further, guidelines suggest the use of health-related quality of life (HRQoL) as a marker for treatment success in clinical practice and HRQoL is increasingly included in clinical trials as an important patient reported outcome of treatment. (Packer et al., 2019; McNamara, Brass, & Drozda, 2004; Baron, Arnold, & Wang, 2017; Feldman, Mauri, & Kahwash, 2018; Tan, Koh KWL, Lim, & Wang, 2018 Additionally, symptom burden, an important driver of HRQoL, (Tan et al., 2018; Randolph, Simon, & Thomas, 2016; Ha, Breithardt, & Camm, 2014 has

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been associated with poor outcomes including heart failure hospitalization, stroke and mortality (Vermond, Crijns, & Tijssen, 2014); and also influences anticoagulation prescription. (Steinberg, Kim, & Thomas, 2014) Therefore, the assessment of HRQoL and symptom burden and their association with other patient specific factors is an important consideration.

Among patients with AF, it is estimated that 2 million patients also live with a psychosocial (i.e., depression or anxiety) or cognitive impairment. (Akintade, Chapa, Friedmann, & Thomas, 2015; Thrall, Lip, Carroll, & Lane, 2007; Frasure-Smith, Lespérance, & Habra, 2009 Patients with psychosocial or cognitive impairments have poorer outcomes including a greater risk for cardiovascular events, increased healthcare utilization, increased symptom severity, poorer medication adherence, increased all-cause mortality (Frasure-Smith et al., 2009; Wändell et al., 2016; Flaker, Pogue, & Yusuf, 2010; Thrall, Lip, Carroll, & Lane, 2007; Gehi, Sears, & Goli, 2012 and poorer HRQoL. (Charitakis, Barmano, Walfridsson, & Walfridsson, 2017; Tan et al., 2018; Ong, Cribbie, & Harris, 2006; Akintade, Chapa, Friedmann, & Thomas, 2015 Although there is evidence that individual psychosocial and cognitive impairments may affect HRQoL and symptom burden in AF, little research has examined whether increased impairment (i.e., multimorbidity) is associated with poorer clinical outcomes. Multimorbidity, defined by WHO as "the existence of two or more chronic conditions in the same individual," has most often focused on the co-occurrence of physical medical conditions (i.e., chronic conditions, frailty) rather than psychosocial and cognitive conditions. (Vetrano, Palmer, & Marengoni, 2018; Mercer, Zhou, & Humphris, 2018; Violan, Foguet-Boreu, & Flores-Mateo, 2014; Forman, Maurer, & Boyd, 2018 Research suggests that physical multimorbidity is associated with poorer HRQoL in various chronic diseases including pulmonary disease, heart disease and diabetes. (Fortin et al., 2004) Given the prevalence of psychosocial and cognitive impairment in AF patients and the impact of physical multimorbidity on health outcomes, it is possible that psychosocial and cognitive multimorbidity may also impact health outcomes in AF patients.

Limited research in diabetes has found that psychosocial and cognitive multimorbidity is associated with lower adherence to self-care practices like physical activity and blood glucose monitoring. (Smith, Pedneault, & Schmitz, 2015) With regards to AF and psychosocial and cognitive multimorbidity, the literature is very limited. One study found significantly lower HRQoL with higher psychosocial and cognitive multimorbidity in patients with AF. (Bostrom, Saczynski, & Hajduk, 2017) However, the sample consisted of only symptomatic AF patients from one geographic location and did not evaluate the relationships between symptom burden and impairment. Utilizing a broader sample of AF patients and evaluating the association between multimorbidity and symptom burden, an important marker of AF severity, would provide a more complete view of the impact of psychosocial and cognitive multimorbidity in patients with AF. Further, little is known regarding patterns of psychosocial and cognitive multimorbidity in AF (for example, which conditions co-occur most frequently), nor regarding factors and patient characteristics associated with psychosocial and cognitive multimorbidity in AF. (Bostrom et al., 2017)

Given the importance of HRQoL as an endpoint of AF treatment and the potential impact impairment and multimorbidity may have on HRQoL and symptom burden, it is important to understand the burden of psychosocial and cognitive multimorbidity and the relationship between multimorbidity and important patient reported outcomes in AF. The objective of this study was to examine patterns of psychosocial and cognitive multimorbidity in older adults with AF, patient characteristics related to psychosocial and cognitive multimorbidity, and the association between multimorbidity and HRQoL and symptom burden.

2. Methods

2.1. Study sample

The Systematic Assessment of Geriatric Elements in Atrial Fibrillation (SAGE-AF) study is an ongoing prospective study of geriatric conditions (e.g., frailty, cognitive impairment) and their relationship to oral anticoagulation treatment in AF. The SAGE-AF study has been previously described. (Saczynski, Sanghai, & Kiefe, 2020) In brief, from June 2015 to June 2018, 1244 participants enrolled in SAGE-AF. Enrollment for SAGE-AF is complete and 2 year follow ups are ongoing. All 1244 participants were included in the analyses of the present study. Study participants were recruited from 5 ambulatory care sites in Massachusetts and Georgia. All sites were heterogeneous in provider type (e.g., geriatric and family medicine, cardiology, cardiac electrophysiology) and patient demographics, serve rural, suburban, and urban populations, include a range of socioeconomic status from middle class to extremely poor, and include private, academic and hospital-owned practices. Sites were selected for their heterogeneity to enhance the generalizability of our findings. Inclusion criteria included: 1) a history of AF; 2) Aged 65 years or older; and 3) A CHA_2DS_2VASC risk score ≥ 2; 4) taking or eligible for oral anticoagulation therapy with no contraindication to oral anticoagulation therapy. Participants were excluded if they had documentation of an absolute contraindication to anticoagulant therapy or an indication for anticoagulant therapy other than AF. Additionally, participants were not eligible for enrollment if they could not speak English, were pregnant, were in prison, could not provide informed consent, were diagnosed with dementia, had a planned invasive procedure with possible uncontrollable bleeding, or were unwilling or unable to participate in one and two year follow-up assessments. Study participants with mild-moderate cognitive impairment were included in this study. Although cognitive impairment may impact a participant's ability to self-report some factors such as medication adherence, or food diaries, previous research shows that even with moderate cognitive impairment patients are able to accurately report medical conditions and respond to questionnaires about how they feel, including depression and anxiety. (Snow, Kunik, & Molinari, 2005; McGivney, Mulvihill, & Taylor, 1994; Bradford, Brenes, & Robinson, 2013 Participants provided written informed consent. The University of Massachusetts Medical School and Mercer University Institutional Review Boards approved all study protocols.

2.2. Data abstraction

Data were collected through comprehensive baseline geriatric assessments, structured interviews and a review of medical records. Assessments and interviews were conducted by trained study staff following participants' routine clinical visits. Structured interviews were administered by study staff trained by SAGE-AF principal investigators. Medical record review protocol used "gold standard" medical records and required that each abstractor satisfactorily complete 10 practice cases before certification. Quality control checks were conducted via audited interviews and medical records abstracted in duplicate for 5% random samples. If error rates were high, staff were retrained, and additional quality controls were put into place until error rates declined. Geriatric assessments and structured interviews consisted of validated instruments to assess depression, anxiety, cognitive impairment, HRQoL and symptom burden. Information abstracted from the medical record by trained staff included participants' age, race/ethnicity, sex, comorbidities, type of AF, medication use and laboratory values used to calculate CHA_2DS_2VASC and HAS-BLED risk scores. Other demographic variables collected through structured interviews include marital status, education and living situation.

2.3. Health-related quality of life and symptom burden

HRQoL and symptom burden were measured using the validated Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) questionnaire. (Spertus, Dorian, & Bubien, 2010) The AFEQT consists of several sub-scales including symptom severity, AF burden, global well-being and impact on health care utilization. (Spertus et al., 2010) The AFEQT is a reliable measure (Cronbach's alpha > 0.8 for overall scale and sub-scales) and is scored on a 0–100 scale, with higher scores indicating better HRQoL. (Spertus et al., 2010) As there is no standard score to indicate low HRQoL, we defined low HRQoL as AFEQT scores in the lowest quartile (scores ≤69.8). Symptom burden was measured using 4 items assessing how bothered participants have been by palpitations, irregular heartbeats, pauses in heart activity and lightheadedness/dizziness over the past four weeks. Any participant who reported being quite, very, or extremely bothered by any of the symptoms were categorized as having high symptom burden.

2.4. Psychosocial and cognitive multimorbidity

Depressive symptoms were assessed using the 9-item Patient Health Questionnaire (PHQ-9). (Kroencke, Spitzer, & Williams, 2001; Spitzer, Kroenke, Williams, & Group PHQPCS, 1999) Scores range from 0 to 27 with higher scores indicating increased severity and 5 was used as a cutoff point indicating mild or more severe depressive symptomology. (Kroencke et al., 2001) The PHQ-9 has high sensitivity (0.88) and specificity (0.88) for major depression in CVD patients. (Gilbody, Richards, Brealey, & CJJogim, 2007; Stafford, Berk, & HJJGhp, 2007) Anxiety was assessed using the 7-item Generalized Anxiety Disorder-7 scale (GAD-7). (Spitzer, Kroenke, Williams, & Löwe, 2006) GAD-7 scores range from 0 to 27 with higher scores indicating increased severity (Spitzer et al., 2006) and a cutoff point of 5 was used to indicate mild or more severe symptoms of anxiety. The GAD-7 has demonstrated high sensitivity (0.89) and specificity (0.82) in a general population of adults. (Spitzer et al., 2006) Cognitive function was assessed using the validated 30-item Montreal Cognitive Assessment Battery (MoCA). Scores range from 0 to 30 with lower scores indicating increased cognitive impairment. A cutoff of 23 was used to indicate cognitive impairment. (Saczynski, Inouye, & Guess, 2015) Among cardiovascular patients, the MoCA demonstrates high internal consistency (0.83) and high sensitivity (0.90). (Nasreddine, Phillips, & Bédirian, 2005) To examine multimorbidity, patients were classified as having no impairments, 1 impairment, 2 impairments, or all 3 impairments, where 2 or 3 impairments represented any combination of depression, anxiety and cognitive impairment. Participants were categorized based on reported individual impairments and impairment combinations.

2.5. Statistical analyses

Patient characteristics according to burden of impairment (0, 1, 2, or 3 impairments) were compared using analysis of variance and Kruskal-Wallis tests for continuous variables and Mantel-Haenszel χ (Go et al., 2001) tests for categorical variables. Regarding 1 or 2, all impairments and all combinations of impairments were included in the analyses. Further, 3 impairments represent the presence of depression, anxiety and cognitive impairment. Characteristics included participants' age, race/ethnicity, sex, marital status, education, living situation, comorbidities, type of AF, medication use, CHA_2DS_2VASC and HAS-BLED risk scores. Characteristics that differed significantly by burden of impairment were included in a multinomial logistic regression to assess which participant characteristics were independently associated with multimorbidity, using no impairment as the common reference group. Similarly, using characteristics that differed significantly by burden of impairment, we used logistic regression to assess the association between multimorbidity and impaired HRQoL and high symptom burden. A priori statistical significance was set at

p < 0.05 for all statistical analyses. For any participant with missing data for depression, anxiety or cognitive impairment, multiple imputation analysis was performed to predict the missing values. All analyses were performed using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

3. Results

The results presented here include all 1244 SAGE-AF participants who have complete baseline psychosocial, cognitive, HRQoL and symptom burden data. Participants were on average 75.5 ± 7.1 years, 86 % were non-Hispanic White, and 49 % were female. Most participants were married (57 %) while less than half (43 %) had a college degree. In addition to having AF, the majority of participants had a diagnosis of hypertension (90 %) and hyperlipidemia (80 %). The majority of patients (86 %) were prescribed an oral anticoagulant; 36 % and 6% were prescribed aspirin and anti-platelets, respectively.

3.1. Psychosocial and cognitive impairment

The majority of participants (N = 755, 61 %) had at least one psychosocial or cognitive impairment (Fig. 1). Cognitive impairment occurred the most frequently among participants (42 %), followed by elevated depressive symptoms (28 %) and elevated symptoms of anxiety (24 %). Thirty-five percent of participants had 1 impairment, 17 % had 2 impairments, and 8% had 3 impairments; 39 % had none of the 3 impairments. Regarding specific co-occurrence of impairments, depression and anxiety more often co-occurred with another impairment rather than alone (Fig. 1). Conversely, cognitive impairment more often occurred alone.

Age, race/ethnicity, gender, education, marital status, CHADS2VASC score, HAS-BLED score and the prevalence of heart failure, coronary artery disease, hypertension, diabetes, renal failure, stroke and implantable cardiac devices differed by number of psychosocial and cognitive impairment (Table 1).

3.2. Factors associated with psychosocial and cognitive multimorbidity

After multivariate adjustment, several participant characteristics were significantly associated with psychosocial and cognitive multimorbidity (Table 2). The characteristic with the strongest association with multimorbidity was race/ethnicity where patients with races/ethnicities other than non-Hispanic White had 4x, 3x and 8x the odds of having 1 impairment (OR = 4.48, 95 % CI 2.69, 7.46), 2 impairments (OR = 2.95, 95 % CI 1.64, 5.34) and 3 impairments (OR = 8.18, 95 % CI 4.24, 15.79). Older participants and those with less formal education had significantly higher odds of having 1 impairment (Age OR = 1.05, 95 % CI 1.03, 1.07; Some college or less OR = 1.51, 95 % CI 1.13, 2.00) and 3 impairments (Age OR = 1.07, 95 % CI 1.03, 1.10; Some college or less OR = 2.01, 95 % CI 1.19, 3.39). Patients with implantable cardiac devices were more likely to have psychosocial and cognitive impairments (1 impairment OR = 1.80, 95 % CI 1.31, 2.48; 2 impairments OR = 1.84, 95 % CI 1.25, 2.70; 3 impairments OR = 2.78, 95 % CI 1.69, 4.57) than patients without implantable cardiac devices.

3.3. Psychosocial or cognitive multimorbidity and poor health-related quality of life

We examined the association between psychosocial and cognitive multimorbidity and poor HRQoL using logistic regression. The number of psychosocial and cognitive impairments showed a dose-response relationship with poor HRQoL after adjusting for age, race, sex, education and medical comorbidities. About 1 in 8 (12 %) of patients with no impairments had poor QOL compared to 20 % of patients with 1 impairment, 50 % of patients with 2 impairments, and 54 % of patients with 3 impairments (Table 3). Compared to participants without
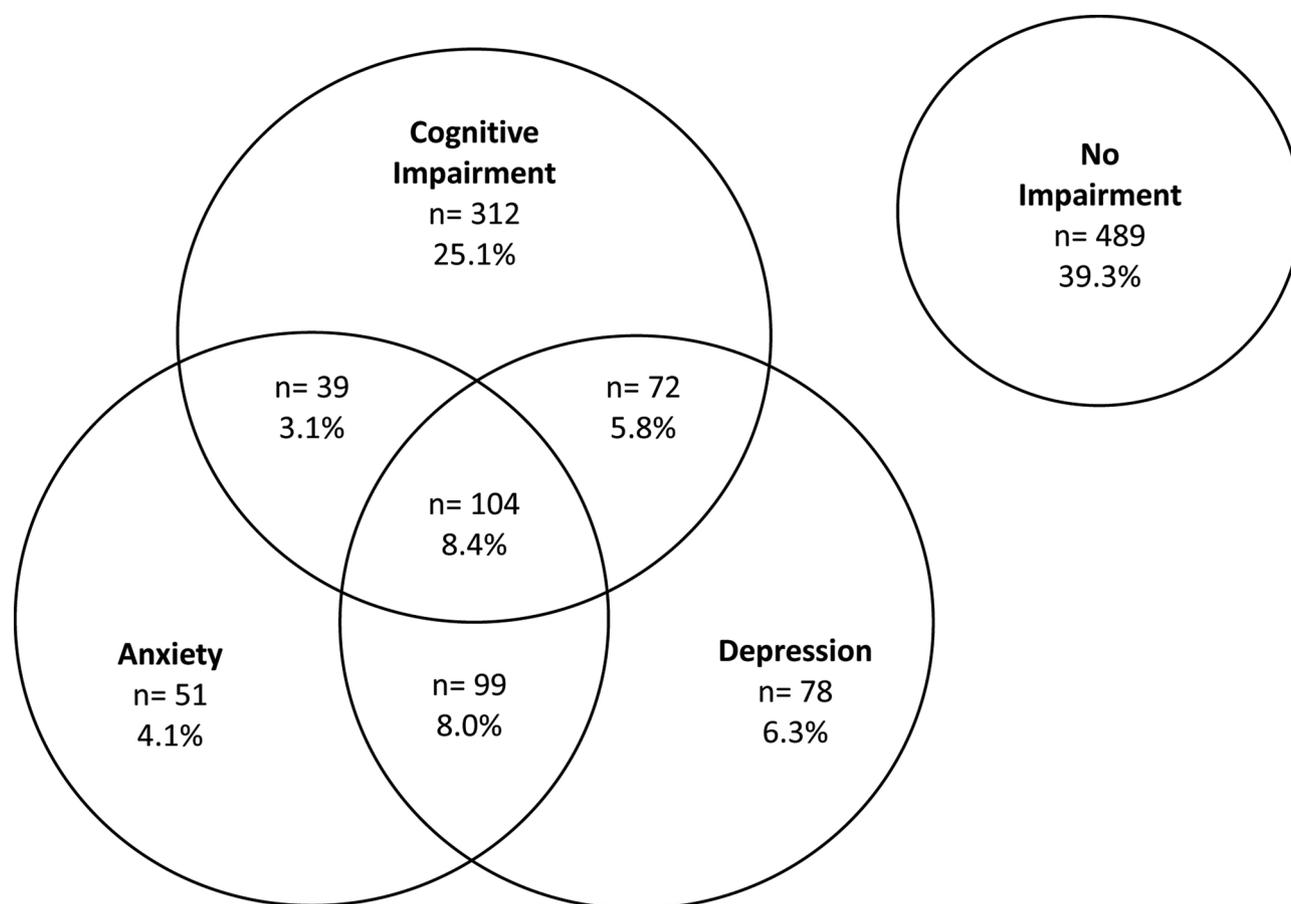
Fig. 1. Multimorbid Psychosocial and Cognitive Impairments among Older Adults with Atrial Fibrillation, The SAGE-AF Study (N = 1244).

psychosocial or cognitive impairments, those with 1 impairment had 1.8 times the odds of reporting poor HRQoL (Adjusted OR = 1.75, 95 % CI 1.19, 2.56), those with 2 impairments were 6.6 times as likely to report poor HRQoL (Adjusted OR = 6.60, 95 % CI 4.40, 9.89) and those with 3 impairments were more than 7.5 times as likely to report poor HRQoL (Adjusted OR = 7.59, 95 % CI 4.46, 12.91; Table 3). Associations between each individual impairment and low HRQoL are presented in supplemental Table 1. There was a significant relationship between participants with impairments and low HRQoL. Specifically, a greater proportion of participants with depression only; anxiety only; depression and anxiety; depression and cognitive impairment; anxiety and cognitive impairment; and depression, anxiety and cognitive impairment had low HRQoL compared to those with no impairment.

3.4. Psychosocial or cognitive multimorbidity and high symptom burden

We also examined the association between psychosocial and cognitive multimorbidity and high symptom burden using logistic regression (Table 4). There was a dose-response relationship between the number of psychosocial and cognitive impairments and high symptom burden after adjusting for age, race, sex, education and medical comorbidities. Less than a tenth (7%) of patients with no impairments had high symptom burden compared to 8% of patients with 1 impairment, 21 % of patients with 2 impairments, and 24 % of patients with 3 impairments (Table 4). Compared to participants without psychosocial or cognitive impairments, those with 2 impairments were 3.7 times as likely to report high symptom burden (Adjusted OR = 3.69 95 % CI 2.22, 6.13) and those with 3 impairments were more than 5.4 times as likely to report high symptom burden (Adjusted OR = 5.41 95 % CI 2.85, 10.26; Table 4). Associations between each individual impairment and high symptom burden are presented in supplemental Table 1. There

was a significant relationship between participants with impairments and high symptom burden. Specifically, a greater proportion of participants with depression only; depression and anxiety; depression and cognitive impairment; and depression, anxiety and cognitive impairment had high symptom burden compared to those with no impairment.

4. Discussion

In our sample of 1244 older adults with AF, we found 60 % of patients had at least 1 psychosocial and cognitive impairment, and 25 % were living with psychosocial and cognitive multimorbidity. Though multimorbidity has received increased attention in the treatment of chronic illness, few studies have explored psychosocial and cognitive multimorbidity. In the present study, we found that multimorbidity was more likely among participants who were racial/ethnic minorities, older, less educated and those with medical comorbidities. Additionally, few studies have evaluated psychosocial and cognitive multimorbidity and its effect on HRQoL and symptom burden in AF. In the present study we found that patients with greater psychosocial and cognitive multimorbidity were substantially more likely to experience poorer HRQoL and high symptom burden, two important patient-reported outcomes in AF.

Overall rates of psychosocial and cognitive impairments reported in this study are similar to those reported in previous studies evaluating the prevalence of psychosocial and cognitive impairment in AF samples. (Akintade et al., 2015a; Thrall et al., 2007a; Frasure-Smith et al., 2009, (Bostrom et al., 2017) The current study extends the literature by showing that among those with any impairment, 41 % had at least one additional psychosocial or cognitive impairment. Once a provider identifies or suspects a patient has an impairment, it may be prudent to

Table 1

Cohort Characteristics by Burden of Psychosocial or Cognitive Impairment (Elevated Depressive Symptoms, Elevated Anxiety Symptoms, and/or Cognitive Impairment) among Older Adults with AF: The SAGE-AF Study (N = 1244).

Characteristic	No Impairments (N = 489)	1 Impairment (N = 441)	2 Impairments (N = 210)	3 Impairments (N = 104)
Age (mean, std)	**74.2 (6)**	**76.9 (7)**	**74.9 (8)**	**77.6 (8)**
Race/ethnicity other than non-Hispanic White	24 (5)	82 (19)	34 (16)	35 (34)
Female	221 (45)	211 (48)	114 (54)	61 (59)
Married or Living as married	296 (61)	242 (56)	106 (52)	50 (50)
Education[a]	**229 (47)**	**269 (62)**	**121 (60)**	**74 (75)**
Some college or less	**257 (53)**	**163 (38)**	**82 (40)**	**25 (25)**
College graduate or more				
Living Situation[b]	138 (28)	120 (28)	59 (29)	33 (33)
Alone	348 (72)	315 (72)	144 (71)	68 (67)
With spouse or others				
Medical History	**134 (27)**	**187 (42)**	**84 (40)**	**58 (56)**
Heart failure	**39 (8)**61 (13)	**57 (13)**67 (15)	**20 (10)**33 (16)	**17 (16)**18 (17)
Coronary artery disease	425 (87)	402 (91)	195 (93)	100 (96)
Peripheral vascular disease	116 (24)384 (79)	122 (28)355 (81)	73 (35)175 (83)	35 (34)82 (79)
Hypertension	**38 (8)**	46 (10)	21 (10)	17 (16)
Diabetes	115 (24)	130 (29)	68 (32)	43 (41)
Hyperlipidemia	**105 (21)**	**177 (40)**	**80 (38)**	**59 (57)**
Stroke				
Renal failure				
Implantable cardiac device				
Clinical Characteristics	282 (58)	256 (58)**4.0 (3.0)**	143 (68)**5.0 (3.0)**	60 (58)**5.0 (2.0)**
AF Type- Paroxysmal	**4.0 (2.0)**	**3.0 (1.0)**	**3.0 (1.0)**	**3.0 (1.0)**
CHADS2VASC score (median, IQR)	**3.0 (2.0)**			
HASBLED score (median, IQR)				
Treatment Characteristics	423 (87)	372 (84)	174 (83)	95 (91)
Anticoagulant use	162 (33)	166 (38)	78 (37)	36 (35)
Aspirin use	24 (5)	28 (6)	17 (8)	10 (10)
Other anti-platelet use	1.3 (1.3)	2.6 (3.0)	7.3 (4.0)	10.0 (4.2)
Depression: PHQ-9 (mean, std)	0.9 (1.2)	1.7 (2.3)	5.8 (5.7)	9.2 (3.7)
Anxiety: GAD-7 (mean, std)	26.3 (1.7)	21.8 (4.1)	22.8 (4.5)	19.7 (3.4)
Cognitive Impairment: MoCA (mean, std)	85.6 (13.9)	82.3 (16.1)	69.3 (19.9)	65.6 (20.8)
Health-related Quality of Life: AFEQT (mean, std)				

Continuous variables are presented as mean ± standard deviation or median and IQR and categorical variables are presented as n (%).
Impairments = depression, anxiety or cognitive impairment; AF = Atrial Fibrillation, PHQ-9 = Patient Health Questionnaire, GAD-7 = Generalized Anxiety Disorder 7 Scale, MoCA = Montreal Cognitive Assessment Battery, AFEQT = Atrial Fibrillation Effect on QualiTy-of-life.
Bold indicates statistical significance p < 0.05.
[a] Some college or less = high school or less; some college. College graduate or more = college graduate; graduate degree.
[b] With spouse or others = with spouse; with family other than spouse; with people other than family; nursing home.

screen for other potential psychosocial or cognitive impairments, especially in the case of depression or anxiety, which most often co-occurred in our cohort.

Previous research in symptomatic AF adults with psychosocial and cognitive impairment found associations between impairment and older age and less formal education. (Bostrom et al., 2017) We found race/ethnicity was the characteristic most strongly associated with cognitive and psychosocial multimorbidity among older adults with AF. Reports are mixed regarding whether individual psychosocial and cognitive impairments occur more frequently in non-Hispanic White patients or patients of other races/ethnicities. (Sheffield & Peek, 2011; Lee et al., 2012; Steffens, Fisher, Langa, Potter, & Plassman, 2009; Williams, Gonzalez, & Neighbors, 2007; Weinberger et al., 2018; Asnaani, Richey, Dimaite, Hinton, & Hofmann, 2010; Williams, Gonzalez, & Neighbors, 2007; Kessler, Chiu, Demler, & Walters, 2005; Himle, Baser, Taylor, Campbell, & Jackson, 2009 There is evidence that rates of cognitive impairment are higher in racial/ethnic minorities (Lee et al., 2012; Sheffield & Peek, 2011) while depression (Steffens et al., 2009; Weinberger et al., 2018; Williams et al., 2007b) and anxiety (Asnaani et al., 2010; Himle et al., 2009; Kessler et al., 2005) are more common among non-Hispanic White adult and older adult patients. However, our results suggest that regardless of actual prevalence of individual impairments, the burden of psychosocial and cognitive multimorbidity disproportionately effects racial/ethnic minority older patients with AF. Though unexplored in previous research, this

increased burden may contribute to disparities that exist across race and ethnicity in AF. (Ugowe, Jackson, & Thomas, 2018; Goli, Thompson, & Sears, 2012; Golwala, Jackson, & Simon, 2016 For instance, there is strong evidence that in AF, racial/ethnic minorities have a 24–60 % higher risk of stroke, 2–4 times higher risk of intracranial hemorrhage and 46 % higher risk of death. (Ugowe et al., 2018) Additionally, racial/ethnic minorities report significantly more impaired functional status and poorer quality of life. (Goli et al., 2012; Golwala et al., 2016) It is possible that psychosocial and cognitive impairment in racial/ethnic minority patients may contribute to these disparities in racial/ethnic minority older patients with AF and that screening for cognitive impairment, depression and anxiety could identify a high-risk subgroup.

Findings from this study build on evidence regarding the importance of anxiety, depression and cognitive impairment in AF and extend the literature by highlighting the influence of psychosocial and cognitive multimorbidity, which has otherwise been neglected. With 1 impairment, patients were twice as likely to report poor HRQoL than those with no impairments, and this increased substantially to 7–8 times more likely in patients with 2 or 3 impairments. This suggests that the effects of multimorbidity on HRQoL may be multiplicative rather than additive, further highlighting the need to screen for these impairments. Additionally, we found that psychosocial and cognitive multimorbidity was associated with high symptom burden. This finding aligns with literature showing associations between individual

Table 2

Adjusted Odds Ratios (95 % Confidence Intervals) for Burden of Psychosocial or Cognitive Impairment in Relation to Cohort Characteristics: The SAGE-AF Study (N = 1244).

	1 Impairment (N = 441)	2 Impairments (N = 210)	3 Impairments (N = 104)
Age	**1.05** **(1.03, 1.07)**	1.01 (0.98, 1.03)	**1.07** **(1.03, 1.10)**
Non-White Race	**4.48** **(2.69 7.46)**	**2.95** **(1.64, 5.34)**	**8.18** **(4.24, 15.79)**
Female	1.04 (0.78, 1.37)	**1.44** **(1.02, 2.03)**	1.62 (1.00, 2.61)
Education[a]	**1.51**	1.30	**2.01**
Some college or less	**(1.13, 2.00)**	(0.92, 1.85)	**(1.19, 3.39)**
Medical History			
Heart failure	1.33 (0.97, 1.82)	1.14 (0.78, 1.68)	1.64 (0.99, 2.71)
Coronary artery disease	1.61 (1.02, 2.54)	1.06 (0.58, 1.93)	1.97 (0.99, 3.94)
Hypertension	1.12 (0.72, 1.77)	1.49 (0.81, 2.74)	1.95 (0.67, 5.70)
Diabetes	0.99 (0.71, 1.38)	1.33 (0.90, 1.97)	0.98 (0.57, 1.68)
Renal failure	0.88 (0.63, 1.23)	1.08 (0.72, 1.61)	1.02 (0.61, 1.72)
Implantable cardiac device	**1.80** **(1.31, 2.48)**	**1.84** **(1.26, 2.70)**	**2.78** **(1.69, 4.57)**
Stroke	1.15 (0.71,1.87)	1.04 (0.57,1.92)	1.46 (0.73,2.940)

No impairment is referent group. Impairments = depression, anxiety or cognitive impairment; AF = Atrial Fibrillation.

Bold indicates statistical significance p < 0.05.

[a] Some college or less = high school or less; some college. College graduate or more = college graduate; graduate degree.

impairments (e.g., depression only, anxiety only) and higher symptom burden (Walters, Wick, & Tan, 2019; Kang, 2006; Katon, Lin, & Kroenke, 2007; Thompson et al., 2014 and extends existing literature by showing associations between cognitive impairment only and higher symptom burden. Regarding associations of each impairment with HRQoL (supplemental Table 1), except for cognitive impairment only, a greater proportion of participants with all individual impairments and impairment combinations had low HRQoL compared to those with no impairment. These findings align with previous research evaluating individual impairments and also aligns with our interest in exploring the impact of psychosocial and cognitive multimorbidity on HRQoL. (Bostrom et al., 2017; Charitakis et al., 2017; Thrall et al., 2007a) Regarding associations of each impairment with symptom burden (supplemental Table 1), a greater proportion of participants with depression only or depression with any other impairment had high symptom burden compared to those with no impairment. To our knowledge, there are no studies evaluating the impact of cognitive impairment on symptom burden. There is limited evidence showing an association between symptom burden and anxiety (Charitakis et al., 2017; Thompson et al., 2014; Walters et al., 2019). Our findings suggest that depression may play a larger and unexplored role in the relationship between other impairments and symptom burden. More research is needed to further explore contributions of each impairment to symptom burden when there are 2 or more psychosocial a cognitive impairment.

Poor HRQoL and high symptom burden are linked to increased emergency department visits and hospitalizations in AF, (Freeman, Simon, & Go, 2015; Streur, Ratcliffe, Callans, Shoemaker, & Riegel, 2018) and it is possible that psychosocial and cognitive multimorbidity identifies a population at higher risk for increased health care utilization who may benefit from tailored interventions or who may have an optimal risk-benefit profile for treatment options aimed at restoration of sinus rhythm. Further, using psychosocial and cognitive multimorbidity as an indicator for poor HRQoL may be useful in clinical

Table 3

Unadjusted and Adjusted Odds Ratios (95 % Confidence Intervals) for Low Atrial Fibrillation Effect on Quality of Life (AFEQT) in Relation to Cohort Characteristics and Burden of Psychosocial or Cognitive Impairment: The SAGE-AF Study (N = 1244)[a].

	Low HRQOL N (%)	Unadjusted OR (95 % CI)	Adjusted OR (95 % CI)
Number of Impairments			
0 impairments	60 (12)	(Reference)	(Reference)
1 Impairment	86 (20)	**1.73** **(1.21, 2.48)**	**1.75** **(1.19, 2.56)**
2 Impairments	105 (50)	**7.15** **(4.88, 10.48)**	**6.60** **(4.40, 9.89)**
3 Impairments	56 (54)	**8.34** **(5.21, 13.36)**	**7.59** **(4.46, 12.91)**
Demographic Covariates			
Age			**0.95** **(0.93, 0.97)**
Female			**2.16** **(1.61, 2.92)**
Race/ethnicity other than non-Hispanic White			1.00 (0.65, 1.52)
Education[b]			0.84
Some college or less			(0.61, 1.14)
College graduate or more			
Clinical Covariates			
Heart failure			**1.54** **(1.11, 2.13)**
Coronary artery disease			1.20 (0.75, 1.91)
Hypertension			1.12 (0.66, 1.89)
Diabetes			1.21 (0.87, 1.69)
Renal failure			0.99 (0.70, 1.39)
Implantable cardiac devices			1.25 (0.91, 1.72)
Stroke			0.74 (0.45, 1.24)

High AFEQT is referent group. Impairment = depression, anxiety or cognitive impairment; AF = Atrial Fibrillation; AFEQT = Atrial Fibrillation Effect on Quality of Life.

Bold indicates statistical significance p < 0.05.

[a] Based on AFEQT: Low AFEQT = score ≤69.8; High AFEQT = score > 69.8.

[b] Some college or less = high school or less; some college. College graduate or more = college graduate; graduate degree.

practice as there is evidence of discordance between provider and patient HRQoL ratings in AF patients and that this discordance is mediated by depression. (von Eisenhart Rothe et al., 2013) More research in cognitive and psychosocial multimorbidity is needed to further explore how multimorbidity relates to other important clinical outcomes such as medication adherence, bleeding outcomes and mortality. Given that the prevalence of psychosocial and cognitive multimorbidity and its impact on HRQoL and potential impact on health outcomes, clinicians might consider incorporating psychosocial and cognitive screens into routine patient care.

4.1. Strengths and limitations

The present study has several strengths. Our study population is comprised of geographically diverse older adults with a high degree of comorbidity consistent with contemporary "real world" AF patients. Further, our study included a comprehensive assessment of clinical and patient reported factors utilizing validated and publicly available instruments. Our study is not without limitations. Though results from

Table 4

Unadjusted and Adjusted Odds Ratios (95 % Confidence Intervals) for High Symptom Burden in Relation to Cohort Characteristics and Burden of Psychosocial or Cognitive Impairment: The SAGE-AF Study (N = 1244)[a,b].

	High Symptom Burden		
	High Symptom Burden N (%)	Unadjusted OR (95 % CI)	Adjusted OR (95 % CI)
Number of Impairments			
0 Impairments	32 (7)	(Reference)	(Reference)
1 Impairment	33 (8)	1.15 (0.70, 1.91)	1.25 (0.74, 2.13)
2 Impairments	44 (21)	**3.80 (2.33, 6.20)**	**3.69 (2.22, 6.13)**
3 Impairments	25 (24)	**4.57 2.57,8.12**	**5.41 (2.85, 10.26)**
Demographic Covariates			
Age			**0.95 (0.93, 0.98)**
Female			**1.71 (1.16, 2.52)**
Race/ethnicity other than non-Hispanic White			0.90 (0.52, 1.57)
Education[b]			1.12 (0.74, 1.68)
Some college or less			
College graduate or more			
Clinical Covariates			
Heart failure			0.75 (0.48, 1.16)
Coronary artery disease			0.82 (0.42, 1.59)
Hypertension			0.97 (0.50, 1.88)
Diabetes			0.97 (0.62, 1.51)
Renal failure			1.31 (0.84, 2.04)
Implantable cardiac devices			1.25 (0.81, 1.91)
Stroke			0.81 (0.41, 1.59)

High AFEQT is referent group. Impairment = depression, anxiety or cognitive impairment; AF = Atrial Fibrillation;
Bold indicates statistical significance p < 0.05.

[a] High Symptom Burden = bothered by ≥ 1 AF symptom(s) in the past 4 weeks (symptoms include how bothered participants have been by palpitations, irregular heartbeats, pauses in heart activity and lightheadedness/dizziness).

[b] Some college or less = high school or less; some college. College graduate or more = college graduate; graduate degree.

this study showed race/ethnicity was an important predictor in impairment, 86 % of the SAGE-AF cohort is non-Hispanic White and therefore we were unable to explore differences in impairment in specific racial/ethnic groups (e.g., Black/African-American, Hispanic/Latinx) due to small cell sizes. Additionally, due to the cross-sectional nature of our analysis, we are unable to assess the temporality of observed associations, for example whether psychosocial and cognitive impairments precede declines in HRQOL and increased AF symptom burden, or whether worsening physical health leads to the development of psychosocial and cognitive impairments. Longitudinal research is needed to further explore these relationships. Lastly, there may be other unmeasured confounding factors that affect associations between psychosocial and cognitive multimorbidity and HRQoL and symptom burden including social determinants of health like neighborhood and physical environment or access to health care.

5. Conclusions

Psychosocial and cognitive multimorbidity is common among older adults with AF and older, less educated, racial/ethnic minority adults with medical comorbidities are more likely to have psychosocial and cognitive multimorbidity. Psychosocial and cognitive multimorbidity was associated with poor HRQoL and high symptom burden when compared to individual psychosocial and cognitive impairments. Given evidence that poor HRQoL and high symptom burden are associated with poorer outcomes, our findings suggest that incorporating psychosocial and cognitive screens into routine patient care may be necessary to identify a vulnerable group of patients who may benefit from closer follow-up and tailored interventions.

Author Contributions

BAB: Conceptualization, Methodology, Validation, Investigation, writing, visualization. SRS: writing- original draft, writing & editing DDM: conceptualization, methodology, writing- review and editing, supervision, funding acquisition. DL: software, validation, formal analysis, writing- review & editing, MEW: conceptualization, methodology, writing- review & editing SF: methodology, writing- review and editing, ISPL: data curation, writing- review & editing, visualization, JSS: conceptualization, methodology, validation, writing- original draft & review and editing, supervision, funding acquisition.

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Appendix A. Supplementary data

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