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Burden of Psychosocial and Cognitive Impairment in Patients With Atrial Fibrillation

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Background: Impairments in psychosocial status and cognition relate to poor clinical outcomes in patients with atrial fibrillation (AF). However, how often these conditions co-occur and associations between burden of psychosocial and cognitive impairment and quality of life (QoL) have not been systematically examined in patients with AF.

Methods: A total of 218 patients with symptomatic AF were enrolled in a prospective study of AF and psychosocial factors between May 2013 and October 2014 at the University of Massachusetts Medical Center. Cognitive function, depression, and anxiety were assessed at baseline and AF-specific QoL was assessed 6 months after enrollment using validated instruments. Demographic and clinical information were obtained from a structured interview and medical record review.

Results: The mean age of the study participants was 63.5±10.2 years, 35% were male, and 81% had paroxysmal AF. Prevalences of impairment in 1, 2, and 3 psychosocial/cognitive domains (eg, depression, anxiety, or cognition) were 75 (34.4%), 51 (23.4%), and 16 (7.3%), respectively. Patients with co-occurring psychosocial/cognitive impairments (eg, >1 domain) were older, more likely to smoke, had less education, and were more likely to have heart failure (all $P < 0.05$). Compared with participants with no psychosocial/cognitive impairments, AF-specific QoL at 6 months was significantly poorer among participants with baseline impairment in 2 ($B = -13.6$, 95% CI: −21.7 to −5.4) or 3 ($B = -15.1$, 95% CI: −28.0 to −2.2) psychosocial/cognitive domains.

Conclusion: Depression, anxiety, and impaired cognition were common in our cohort of patients with symptomatic AF and often co-occurred. Higher burden of psychosocial/cognitive impairment was associated with poorer AF-specific QoL.

Key Words: atrial fibrillation, psychosocial impairment, cognitive impairment, multimorbidity, quality of life

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Atrial fibrillation (AF) is the most common sustained heart rhythm abnormality, affecting approximately 3–6 million US adults, including almost 1 in 20 people over age 60.[1,2] Owing to the aging of the US population, the number of people diagnosed with AF is expected to more than double by the year 2050.[1,3] The increasing prevalence of AF has significant personal, clinical, and socioeconomic implications,[4] in part due to the fact that patients with AF often also have anxiety, depression, and cognitive impairment (CI) or dementia, even in the absence of ischemic stroke.[5,6]

Impairments in mood or cognition exert powerful and negative impacts on the prognosis of AF patients.[6–9] Specifically, depression and anxiety are associated with poorer AF outcomes, including higher AF recurrence rates, higher mortality rates, worse symptom severity, and greater health care utilization.[6–9] Patients with AF who are affected by CI have poorer anticoagulation adherence, more frequent adverse cardiovascular events, and show greater functional impairment compared with nonimpaired AF patients.[10]

Although individually harmful, psychosocial and/or CIs may in fact confer even poorer outcomes when they occur together, and evidence suggests that these impairments frequently cluster.[11] For example, anxiety and depression often co-occur in the general population,[11] and their combined presence negatively impacts important health outcomes, including somatic symptomatology, treatment response, and suicidality.[11,12] Studies also show that patients with even mild CI are vulnerable to mood disorders, including depression.[13] Data also show that psychosocial and CIs cluster in patients with coronary artery disease, in whom anxiety and depression occur together commonly,[14–16] and in whom the combination of anxiety and depression confers a higher risk for worse cardiovascular outcomes than either anxiety or depression alone.[15,16]

Despite work highlighting the profound impact of depression, anxiety, or CI individually on the long-term prognosis of patients with AF and data showing clustering of psychosocial and cognitive comorbidities in patients with other forms of cardiovascular disease,[6–9,14,16] we know little about patterns of co-occurrence in AF patients, their joint influence on AF-related quality of life (QoL), or patient factors associated with a greater burden of psychosocial and CIs. To address these knowledge gaps, we conducted the present analysis using data from InRhythm, a prospective study of psychosocial and cognitive factors in AF.

METHODS

Study Sample

The InRhythm study is a prospective study of AF and its relationship to psychosocial and CI. Participants with symptomatic AF were recruited and followed at 1 of 3 ambulatory clinics associated with the University of Massachusetts Medical Center AF Treatment Clinic (Heywood Hospital, Marlborough Hospital, and the University of Massachusetts Medical Center University Campus). The present analysis includes 218 InRhythm participants with symptomatic AF

and available clinical, psychosocial, cognitive, and QoL data. All participants gave informed consent, and all InRhythm protocols were approved by the University of Massachusetts Medical School Review Board.

Data Abstraction

All InRhythm study participants underwent a history, physical examination, and laboratory evaluation as part of their routine clinical evaluation for AF. The demographic, clinical, and treatment characteristics of InRhythm participants were abstracted from the electronic medical record by trained study staff. Information abstracted from the medical record included information about participant's age, sex, race, type of AF, cardiovascular comorbidities (eg, myocardial infarction, diabetes, hypertension, and heart failure), noncardiovascular comorbidities (eg, anemia, renal failure), and prior antiarrhythmic drug exposure status. Participants were classified as having AF if the arrhythmia was present on a 12-lead electrocardiogram obtained during an AF Treatment Center clinic visit or an encounter with an outside health care provider, on a Holter or cardiac event monitor, or if AF was noted in any hospital record.

Cognitive Function

Global cognitive function was assessed using the Montreal Cognitive Assessment Battery (MoCA).[17] The MoCA is a 10-minute, 30-item screening tool that was designed to assist physicians in detecting mild CI. The MoCA is the currently recommended screening test for CI in patients with cardiovascular disease by the National Institute for Neurologic Disorders and Stroke and the Canadian Stroke Institute.[18] A cutoff score of 27 (range, 0–30) has been shown to have a high sensitivity (0.90) and specificity (0.87) for detecting mild CI, and was used as a cutoff to define CI (scores of 26 and below were considered as "impaired").[17]

Depression

Depression was assessed using the 9-item version of the Patient Health Questionnaire (PHQ-9).[19] Using a cut-point range of ≥10 (range, 0–27), the PHQ-9 has high sensitivity (0.88) and specificity (0.88) for detecting major depression.[20]

Anxiety

Anxiety was assessed using the Generalized Anxiety Disorder-7 scale, a revised version of the anxiety module from the PHQ that consists of Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria for generalized anxiety disorder over the past 2 weeks.[19] The Generalized Anxiety Disorder-7 scale score ranges from 0 to 27 with a score ≥10 having high sensitivity (0.89) and specificity (0.82) for psychiatrist-diagnosed anxiety disorder.[21]

Atrial Fibrillation-related Quality of Life

Disease-specific QoL was measured during a clinic visit using the Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) Questionnaire, which includes subscales for symptom severity, global well-being, AF burden, and impact on health care utilization.[22] The AFEQT questionnaire consists of 20 questions separated into 4 domains: symptoms, treatment concerns, daily activities, and treatment satisfaction. Each question is graded on a 1- to 7-point scale, and the total raw score is transformed to a 0–100 scale, with 100 points indicating the best possible AF-related QoL and 0 points indicating the poorest possible AF-related QoL. AFEQT scores correlate to severity of physical symptoms from AF[22] and health care utilization.[23]

Statistical Analyses

We compared the characteristics of InRhythm participants according to number of psychosocial and cognitive comorbidities (count of anxiety, depression, and CI; range, 0–3) and compared baseline patient characteristics by number of comorbidities using analysis of variance for continuous variables and the χ^2 test for categorical variables. We used a linear regression model to examine associations between baseline burden of psychosocial/cognitive comorbidity and AF-specific QoL score at 6 months, adjusting for all factors associated with psychosocial/cognitive comorbidity ($P \leq 0.2$) in univariate analyses. Covariates included in multivariable models included age, sex, white race, education, smoking status, heart failure, prior stroke, anemia, renal failure, and total number of cardiac comorbidities.

RESULTS

A total of 218 adults with symptomatic AF who were willing to complete a study assessment of psychosocial factors and cognition comprised our study sample. The cohort was comprised mostly of middle-aged and older adults with a modest burden of cardiovascular and noncardiovascular risk factors. The cohort was predominantly female (64.9%) and white (93.9%) with an average age of 64 years. The majority of participants had paroxysmal AF (81%) and 68% had a college degree. Most patients carried a diagnosis of hypertension (77%) and the majority were taking an antiarrhythmic medication for rhythm control (82%). Just over one-half of participants used an antiplatelet agent (56%) and 3 out of 4 were prescribed an oral anticoagulation (56% on warfarin, 24% on a target-specific oral anticoagulant).

Burden of Psychosocial and Cognitive Comorbidities

Depression was the most commonly observed psychosocial or CI among InRhythm participants, noted in almost half of patients (45%). Nearly one-third (30%) of participants were cognitively impaired and 29% were noted to have anxiety (Fig. 1). Only 35% of

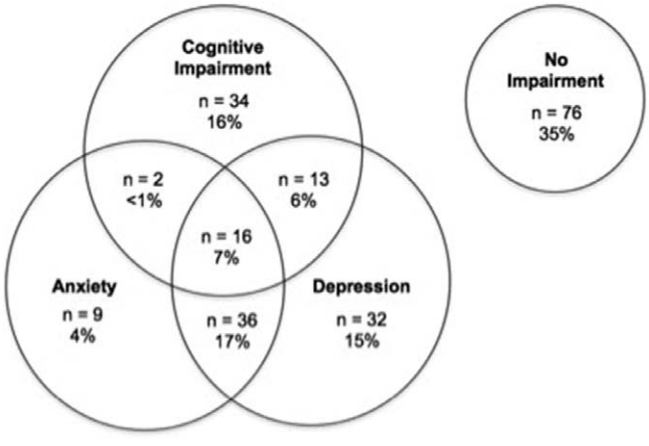

FIGURE 1. InRhythm participants categorized by impairment in psychosocial and cognitive domains. Percentage values refer to the percent of the total study population (n = 218).

participants were free from any psychosocial or CI. Psychosocial and cognitive comorbidities clustered frequently. Approximately one-third (34%) of the participants had a single psychosocial or CI, one-quarter (23%) had 2 impairments, and 7% were affected by all 3 impairments (Fig. 1).

Certain groupings of psychosocial/cognitive comorbidities were more common than others (Fig. 1). For example, almost one-fifth (17%) of all participants experienced both depression and anxiety. Anxiety more often co-occurred with depression and/or CI rather than in isolation. CI was most likely to occur on its own, but nevertheless almost half of participants with CI also had impairment in another domain (48%). Seven percent of participants were impaired in all 3 domains.

Patient Characteristics Associated With Increased Burden of Impairment

Participants with 1 or more psychosocial or CIs were older ($P < 0.001$), had less formal education ($P < 0.001$), and were more likely to be current smokers ($P = 0.01$). With the exception of heart failure, which was more prevalent among patients with multiple psychosocial and CIs ($P = 0.03$), the prevalence of comorbidities, such as hypertension, diabetes, stroke, etc., did not vary by level of psychosocial comorbidity (Table 1). Women were less likely than men to have multiple impairments ($P = 0.02$).

Baseline Burden of Psychosocial and Cognitive Impairment in Relation to AF-specific Quality of Life

Out of the 218 patients who completed baseline interviews, 180 (82.5%) completed the AFEQT questionnaire 6 months after enrolment. Based on their responses, greater burden of psychosocial and CI at baseline was associated with poorer AF-specific QoL at 6 months. In multivariable models adjusting for potential confounders (referent group = 0 impairments), there was a dose–response relationship between number of impairments and QoL score (Table 2). Impairment in 1 domain was associated with a 5-point ($P = 0.236$) lower score on the 100-point AFEQT, impairment in 2 domains with a 14-point ($P < 0.001$) lower score, and impairment in 3 domains was associated with a 15-point lower AFEQT score ($P = 0.02$).

DISCUSSION

In our study of 218 middle-aged and older adults with symptomatic AF, we observed that anxiety, depression, and CI were common comorbid illnesses and frequently co-occurred. Certain patterns of psychosocial and cognitive comorbidity were noted, with

TABLE 1. Characteristics of Participants by Burden of Psychosocial (Depression, Anxiety) or Cognitive Impairments

	Number of Factors Impaired				
	0	1	2	3	
Characteristic	**N = 76**	**N = 75**	**N = 51**	**N = 16**	***P***
Age, yrs, mean (SD)	65 (13)	70 (13)	75 (12)	77 (11)	<0.001
Age, yrs, N (%)					
<65	31 (41)	26 (35)	9 (18)	2 (12)	
65–74	23 (30)	16 (22)	12 (24)	3 (19)	
75–84	17 (22)	23 (30)	19 (37)	7 (44)	
≥85	5 (7)	10 (13)	11 (21)	4 (25)	<0.001
Female, N (%)	41 (54)	34 (46)	22 (44)	6 (35)	0.02
White race, N (%)	66 (87)	68 (91)	45 (88)	13 (82)	0.11
Education, N (%)					
<High school	7 (9)	12 (16)	17 (33)	7 (43)	
High school/some college	24 (32)	33 (44)	19 (37)	6 (38)	
≥College graduate	46 (60)	30 (40)	15 (30)	3 (19)	<0.001
Current smoker, N (%)	8 (11)	13 (17)	4 (7)	2 (11)	0.01
Medical history, N (%)					
Heart failure	50 (66)	53 (70)	36 (71)	13 (81)	0.03
Coronary artery disease	27 (36)	23 (30)	16 (32)	5 (30)	0.61
Peripheral vascular disease	13 (17)	16 (21)	9 (17)	3 (21)	0.49
Hypertension	60 (79)	58 (77)	42 (83)	13 (79)	0.44
Diabetes	27 (36)	24 (32)	18 (36)	6 (38)	0.61
Stroke	6 (8)	8 (10)	8 (16)	3 (19)	0.15
Alcohol abuse/dependency	5 (7)	2 (3)	3 (6)	1 (8)	0.69
Anemia	14 (18)	14 (18)	13 (25)	3 (19)	0.18
Asthma/COPD	17 (23)	27 (36)	14 (28)	5 (31)	0.06
Renal failure	21 (27)	26 (34)	19 (38)	6 (39)	0.11
Implantable cardiac device	10 (13)	6 (8)	6 (12)	2 (15)	0.25
Total cardiac comorbid conditions, mean (SD)*	3.4 (1.5)	3.4 (1.6)	3.6 (1.5)	3.7 (1.6)	0.06

*Cardiac comorbidities include heart failure, coronary artery disease, hypertension, diabetes, stroke, and peripheral vascular disease.
COPD indicates chronic obstructive pulmonary disease.

TABLE 2. Linear Regression of AFEQT Score Compared With Psychosocial or Cognitive Burden Reported as Adjusted *B* Coefficient*

Number of Impairments	Adjusted *B* Coefficient (95% CI)	*P*
0 (ref)	—	—
1	−4.6 (−12.5 to 3.4)	0.257
2	−13.6 (−21.7 to −5.4)	0.001
3	−15.1 (−28.0 to −2.2)	0.022

**B* adjusted for age, sex, white race, education, smoking status, heart failure, prior stroke, anemia, renal failure, and total number of cardiac comorbidities.

anxiety and depression frequently being observed together. Finally, we showed that impairment in 2 or more cognitive or psychosocial domains was associated with lower AF-specific QoL at 6 months in adjusted regression models.

Depression or anxiety have been shown to affect up to one-half of patients with AF,[6] and patients with AF are at a 2-fold higher risk of CI than same-aged patients without AF.[24] Thus, the rates of anxiety, depression, and CI observed in our study were high, but remarkably similar to those reported in prior, albeit smaller studies of patients with AF.[6,25] The current study validates these findings in a larger sample of well-characterized ambulatory patients with symptomatic AF and extends current knowledge by illustrating that these psychosocial and/or CIs frequently co-occurred in individual patients (Fig. 1). Furthermore, impairment in multiple domains was associated with poorer AF-specific QoL at 6 months.

Importantly, we observed that psychosocial and cognitive multimorbidity exerts a powerful and negative effect on AF-specific QoL. Differences in QoL scores between participants with multiple impairments as compared with participants with CI, anxiety, and depression alone were clinically meaningful[26] and statistically significant. Our finding that AF patients with an increasing burden of psychosocial or cognitive comorbidities also reported that lower QoL scores reflects greater symptom severity and likely relates to the fact that depressed and anxious AF patients utilize health resources at higher rates than do patients free from these mood disorders (eg, greater number of clinic and emergency room visits).[6,9] Indeed, several previous studies have examined the negative impact of individual psychosocial impairments on QoL in patients with AF.[6,9,27] However, only one of these prior studies assessed AF-specific QoL,[9] and none examined how the co-occurrence of multiple impairments collectively affected AF-specific QoL.

As mentioned above, depression, anxiety, and CI are common in patients with AF[6,24]; they are also common in other chronic cardiovascular pathologies. As illustrated by the 2008 statement of the American Heart Association's Council on Clinical Cardiology, mood and cognition are becoming increasingly recognized for their role in the risk, management, and prognosis of cardiovascular disease, including in the context of stable coronary artery disease, heart failure, AF, and myocardial infarction.[28–32] Impairments in mood and cognition have myriad adverse effects, including higher rates of morbidity, symptom severity, health care utilization, and even mortality.[30]

Although there is a growing appreciation for the importance of mood and CIs in the natural history of AF, no prior studies have examined their co-occurrence in AF patients. Especially in light of the fact that anxiety and depression so frequently co-occur in individuals with other chronic medical conditions,[33] and given their negative effects on cognitive performance,[13] it is not surprising, but nonetheless significant, that we observed a high rate of multimorbidity across distinct psychosocial and cognitive domains in patients with symptomatic AF. Our findings point to the profound impact of disease clusters on symptom severity, suggesting that assessments of mood and cognition should be performed in concert to best characterize AF patients at the greatest risk for complications.

Despite the increasing recognition of the importance of cognitive and psychosocial characteristics as determinants of response to cardiovascular treatments, including rhythm control for AF, contemporary AF Treatment Guidelines do not recommend routine assessment for CI, depression, or anxiety.[34] Our findings would suggest that such assessments might be useful in patients with symptomatic AF given their close relations with AF-specific QoL, symptom burden, and rehospitalization, which are major targets for contemporary rhythm control therapies, especially catheter ablation.[35]

Strengths and Limitations

The strengths of the present investigation include its prospective design, the enrollment of AF patients recruited from 3 different academic and community ambulatory clinics, the indepth characterization of participants' AF history, as well as the use of validated instruments to characterize each participant's psychosocial status, cognitive function, and QoL. Our study has several limitations, however, that should be considered when interpreting our results. First, all InRhythm study participants had symptomatic AF and were identified from cardiology clinics, so our findings may not be generalizable to older asymptomatic AF patients[1] who are evaluated in other settings. Also, the InRhythm cohort was comprised mostly of white individuals of European descent and those with paroxysmal AF, thereby limiting generalizability of our primary findings to other racial and ethnic groups or those with different types of AF. Finally, we did not adjust for factors that may have confounded or mediated relations between psychosocial and cognitive predictors and AF-specific QoL (eg, adherence to medications, cardioversions, emergency department visits, or baseline symptom severity).

CONCLUSIONS

Our findings suggest that cognitive and psychosocial impairments are common among patients with symptomatic AF and often co-occur, imparting risk for poorer AF-specific QoL. Knowledge of psychosocial and CIs may help guide patients, families, and physicians in appropriate screening and making informed AF treatment decisions.

DISCLOSURES

Nothing to declare.

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