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Frailty, Cognitive Impairment and Anticoagulation Among Older Adults with Non-Valvular Atrial Fibrillation

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Abstract

Background.—Oral anticoagulation (OAC) is challenging in older Non-Valvular Atrial Fibrillation (NVAF) patients who are often frail and have cognitive impairment (CI). We examine the characteristics of older NVAF patients associated with higher odds of physical and cognitive impairments. We also examined if these high-risk patients have different OAC prescribing patterns and their satisfaction with treatment, as it may impact optimal management of their NVAF.

Methods.—The SAGE-AF cohort (2016-2018) patients had NVAF, were ≥65 years, and eligible for the receipt of OAC. Measures included frailty (Fried Frailty scale), CI (Montreal Cognitive Assessment Battery), OAC prescribing and type (DOAC, VKA), depressive symptoms (PHQ9), bleeding, stroke risk and treatment benefit (Anti-Clot Treatment scale).

Results.—Patients (n=1244) were 49% female, aged 76 (SD: 7) years. 14% were frail and 42% had CI. Frailty and CI co-occurred in 9%. Odds of having both impairments versus none were higher with depression (OR=4.62, 95%CI: 2.59,8.26), older age (OR=1.56, 95%CI = 1.29,1.88), lower education (OR=3.81, 95%CI = 2.13,6.81), race/ethnicity other than non-Hispanic white (OR=7.94, 95%CI = 4.34,14.55), bleeding risk (OR=1.43, 95%CI = 1,12,1.81), and stroke risk (OR=1.35, 95%CI = 1.13,1.62). OAC prescribing was not associated with CI and frailty status. Among patients taking OACs (85%), those with both impairments were more likely to take DOAC than VKA (OR=1.69, 95%CI = 1.01, 2.80). Having both impairments (OR=1.87, 95%CI

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= 1.08,3.27) or CI (OR: 1.56, 95%CI = 1.09,2.24) was associated with higher odds of reporting lower treatment benefit.

Conclusion.—In a large cohort of older NVAF patients half were frail or cognitively impaired and 9% had both impairments. We highlight characteristics of patients who may benefit from cognitive and physical function screenings in order to maximize treatment and enhance prognosis. Finally, the co-occurrence of impairment was associated with low perceived benefit of treatment which may impede optimal management.

Keywords

non-valvular atrial fibrillation; frailty; cognitive impairment; Oral anticoagulation; burden of treatment; benefit of treatment

INTRODUCTION

Atrial fibrillation (AF), the most common cardiac arrhythmia, is associated with an increased risk for stroke, especially in older adults.[1-3] In addition to increasing stroke risk, AF is responsible for serious complications including decreased quality of life, frequent hospitalization, and an increased risk of dying.[4-6] Oral anticoagulation (OAC) treatment is the cornerstone of stroke prevention in patients with Non-Valvular Atrial Fibrillation (NVAF). [7-9] However, OAC is often not prescribed in eligible older patients due to a variety of reasons.[10] This is especially true for patients with geriatric impairments, such as physical frailty and cognitive impairment (CI), that may increase the risk of medication non-adherence and complications including falls.[10-13]

Older patients with AF are four times more likely to be frail and twice as likely to have cognitive impairment than older patients without AF.[14-16] Some studies suggest that older patients with AF who are frail or cognitively impaired are less likely to be prescribed an OAC than their non-impaired peers placing these patients at greater risk for stroke.[10, 11, 17-19] However, these studies often had an upper age limit of 80 years and had methodological limitations, including the use of data from medical records to determine cognitive or frailty status, potentially leading to underestimation of the prevalence of frailty and CI or their influence on OAC prescribing. [10, 12, 13] Moreover, data on the use of direct oral anticoagulant versus vitamin K antagonist medication in older patients who are frail and cognitively impaired, using validated and comprehensive assessments, are sparse. [10, 19, 20] Even less is known about how often frailty and cognitive impairment co-occur in patients with NVAF and whether these particularly high-risk patients have different OAC prescribing patterns and, among those prescribed, the type of OAC. [10]

Another factor in OAC treatment that is increasingly important to AF providers, patients, and their families is satisfaction with treatment, so much so that measures of treatment satisfaction are increasingly included as important patient-related outcomes in clinical trials. [21] Treatment satisfaction, which includes the perceived burden and benefit that a patient attributes to their treatment, has been associated with better treatment adherence among older patients with AF. [22, 23] Patient satisfaction of AF treatment is therefore central in achieving the target therapeutic goal for treatment.

Using data from the Systematic Assessment of Geriatric Elements in Atrial Fibrillation (SAGE-AF) Study we describe the separate and combined prevalence of frailty and cognitive impairment in a cohort of older adults with NVAF and examine characteristics associated with higher odds of impairment. Among these high-risk patients, we also examine whether OAC treatment patterns vary according to cognitive and frailty status; and (3) examine whether patient reported burden and benefits of OAC treatment vary by cognitive and frailty status.

METHODS

Study design and population

The ongoing SAGE-AF cohort enrolled a total of 1244 older patients between 2016 and 2018 from 5 practice sites in Massachusetts and 2 in Central Georgia. [24] Eligibility criteria included age ≥65 years, NVAF (if the arrhythmia was present on an electrocardiogram or Holter monitor or if it was noted in any clinic note or hospital record), had a CHA2DS2-VASc ≥2 and no contraindications to the receipt of OAC. Participants were not eligible for enrollment if they had an indication for OAC other than NVAF (i.e., mechanical heart valve requiring OAC), had a medical record diagnosis of dementia, did not speak English, had a planned invasive high bleeding risk procedure, were in prison, or if they were unwilling or unable to participate in planned one- and two-year follow-up visits. In addition, if our trained staff were concerned about a patient's ability to provide informed consent, a standardized Capacity for Informed Consent Instrument that combines capacity assessment questions with interviewer observation was used to determine ability to provide consent. [25]

All study participants received an invitation to participate one week before their scheduled clinic visit. All SAGE-AF participants have given informed written consent. Study protocols were approved by the University of Massachusetts Medical School, Boston University, and Mercer University Institutional Review Boards.

Data collection

All SAGE-AF study participants had a medical history obtained and a physical examination performed in the context of their routine care, typically on the day of study enrollment. All participants underwent a 60-minute interviewer-administered, computer-assisted interview with standardized measures, including assessments of mood, frailty, cognition, social support, and other patient-reported measures.

Study Outcomes and Predictor Variables

Frailty was assessed using the Fried Frailty scale [26], a biological model of frailty based on five components: weight loss/shrinking; exhaustion; low physical activity (assessed using the Minnesota Leisure Time Activity questionnaire[27]; slow gait speed (assessed using a 15-foot timed walk); and weakness (assessed using grip strength). Each element receives a single point and the frailty index ranges from 0-5. Patients were rated as frail if 3 or more criteria were present. [26]

Cognitive impairment (CI) was assessed using the Montreal Cognitive Assessment Battery (MoCA), scored 0-30 with higher scores representing better cognitive performance. [28] A cut-point of 23 was used to classify CI. [29] MoCA correlates well (.89) with the widely used Mini Mental State Exam (MMSE), but outperforms the MMSE in the detection of mild CI (sensitivity .90 vs. .18). [28-31] MoCA is the recommended screening test for CI in patients with CVD by the NINDS and the Canadian Stroke Institute and has 4 versions available to reduce practice effects. [32, 33]

OAC medication prescribing (yes/no) and the type of OAC medication (vitamin-K antagonist [VKA] vs or direct oral anticoagulants [DOAC]) were abstracted from patients' medical records and confirmed with patients during the baseline interview. Participants completed the Anti-Clot Treatment Scale (ACTS), a validated 15-item survey designed to assess OAC satisfaction. [34, 35] Treatment burden was measured on a 12-item scale, with scores ranging from 12 to 60, with higher scores indicating lower perceived burden. Treatment benefit is measured with 3 items, with scores ranging from 3 to 15, with higher scores indicating greater perceived benefit.

Demographic, clinical, treatment, and laboratory characteristics were abstracted from the medical record including participants' age and sex, smoking status, type of NVAF, and comorbidities relevant to stroke and bleeding risk (AMI, diabetes type II, hyperlipidemia, stroke, anemia, asthma). CHA_2DS_2VASC (congestive heart failure; hypertension; aged ≥75 y [doubled]; diabetes mellitus; prior stroke, transient ischemic attack, or thromboembolism [doubled]; vascular disease; age 65-74; female sex) and HAS-BLED scores were calculated. Participants self-reported education, marital status, living situation, race and ethnicity during the interview.

In addition to the in-person assessment of cognitive function and frailty, other geriatric elements were measured and included visual and auditory impairment (self-reported), social isolation, social support, depression, anxiety, and occurrence of falls in the past 6 months. Social support was measured using the 5-item modified version of the Social Support Scale and the 6-item Social Network scale to assess the breadth and depth of social support.[36] A cut-point of <12 was used to define social isolation. [37, 38] Depression was measured using the Patient Health Questionnaire. [39] The PHQ-9 incorporates the 9 criteria on which DSM-IV depressive disorders are based. Using a cut-point of ≥10 (range = 0-27), the PHQ-9 has high sensitivity (0.88) and specificity (0.88) for major depression in CVD patients. [40, 41] Anxiety was assessed using the Generalized Anxiety Disorder-7 [42] scale. A cut-point of 5 was used to indicate the presence of these psychosocial disorders on both scales.

Statistical Analysis

Patients were categorized into four groups according to cognitive function and frailty: cognitively impaired only, frail only, both impairments, and neither impairment.

Sociodemographic and clinical characteristics of patients in each group were reported using descriptive statistics (percentages and means ± standard deviation) and between group differences were compared using analysis of variance for continuous variables and the chi-square test for categorical variables.

Multinomial logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals for frailty, CI, or both impairments in relation to no impairment. We included geriatric elements as factors in the models in addition to factors that differed significantly between the cognitive function and frailty groups at $p< 0.05$. We controlled for the CHA2DS2VASC score in all models and thus did not control for factors that contributed to that score. The only exception was age because the CHA2DS2VASC score only accounts for ages 65-74 (1 point) and ≥75 (2 points), thus not accounting for the influence across the age spectrum.

Logistic regression was used to examine whether the prescribing of OACs, type of OAC, high perceived burden, and low benefit differed in the four CI and frailty groups. For these models, high burden was defined as being in the bottom quartile of the ACTS Burden sub-scale while low benefit was defined as being in the top quartile of the ACTS Benefit sub-scale. For each regression analysis, three models were computed. The first model was unadjusted for other potential covariates, the second was adjusted for the CHA_2DS_2VASC score and age and the third model was adjusted for other geriatric elements and factors that differed significantly between the cognitive function and frailty groups at a p value of < 0.05. Statistical analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

Patient characteristics and prevalence of frailty and cognitive impairment

Among the 1244 SAGE-AF participants with NVAF the average age was 76 years (Standard Deviation [SD] = 7), 49% were women and 86% were non-Hispanic white. The mean of the MoCA was 23.55 and the median was 24.0. Scores ranged from 6-30 with less than 5% of the scores under 15. Fourteen percent of the cohort were frail and 42% had cognitive impairment. Five percent (n=64, 5.1%) of the sample had frailty only, 33.8% (n=420) had CI only, and 8.7% (n=108) had both frailty and CI (Table 1). The overlap of cognitive impairment and frailty at more severe levels of cognitive impairment (lower MoCA cutpoints) are presented in Table S1.

More than one half of the cohort had paroxysmal atrial fibrillation and the mean CHA_2DS_2VASC and HAS-BLED scores were 4 (SD = 1.5) and 3 (SD = 1), respectively. With regards to the geriatric elements, one third of patients had vision or hearing impairment, 13% were socially isolated, 28% had elevated symptoms of depression, 24% had elevated symptoms of anxiety, and 22% reported the occurrence of falls in the past 6 months.

Characteristics associated with presence of frailty and cognitive impairment

Social isolation was associated with higher likelihood of having cognitive impairment alone (OR = 1.66, 95% CI = 1.10, 2.50) compared to having no impairments (Table 2). Patients who were depressed were more likely to have frailty (OR = 10.16, 95% CI = 5.17, 19.96) and both frailty and cognitive impairment (OR = 4.62, 95% CI = 2.59, 8.26), but were not more likely to have cognitive impairment alone. Patients reporting a fall in the last 6 months were more likely to be frail (OR = 2.11, 95% CI = 1.15, 3.87) than to have no impairments.

Every 5 year increment in age increased the likelihood of being cognitively impaired (OR = 1.48, 95% CI = 1.32, 1.66) and both frail and cognitively impaired (OR = 1.56, 95% CI = 1.29, 1.88). Patients with less than a college education were twice as likely to be cognitively impaired (OR = 2.03, 95% CI = 1.52, 2.70) and four times as likely to be both frail and cognitively impaired (OR = 3.81, 95% CI = 2.13, 6.81) than to have no impairment. Patients of races/ethnicities other than non-Hispanic white had 5 times the odds of CI only (OR = 5.26, 95% CI = 3.43, 8.07) and 8 times the odds of having both impairments (OR = 7.94, 95% CI = 4.34, 14.55) than to have no impairments. Higher bleeding risk score (HAS-BLED) was associated with higher likelihood of CI (OR=1.19, 95% CI = 1.04, 1.37) and of being both frail and cognitively impaired (OR = 1.43, 95% CI = 1.12, 1.81). Finally, higher CHA_2DS_2VASC score was associated with higher likelihood of being frail (OR = 1.32, 95% CI = 1.06, 1.64) and of being both frail and cognitively impaired (OR = 1.35, 95% CI = 1.13, 1.62), while a medical history of AMI was associated with higher likelihood of being frail (Table 2).

OAC Treatment

Overall, about 85% of study participants were taking an OAC and OAC prescribing did not differ according to cognitive or frailty status (Table 3). Participants with both impairments were nearly two times more likely to be prescribed a DOAC compared with VKA in the adjusted models (OR = 1.71, 95% CI = 1.02, 2.88; Table 3). We also examined OAC prescribing and type in a subsample restricted to those with paroxysmal AF (N=741). Overall, the direction of results in this subgroup analysis are similar to those from the full cohort model although fail to reach statistical significance due to the reduced sample size. (Table S2)

Perceived Burden and Benefit of Treatment

One third of patients with frailty or with both impairments reported high burden, whereas this was true for only 23% of patients with CI or no impairment (Table 4). Participant-reported treatment burden did not differ in our four cognition and frailty comparison groups (Table 4). Compared to participants without any impairment, those with CI alone were 50% more likely to report low benefit of treatment (OR: 1.57; 95%CI: 1.10, 2.24), while patients who were both cognitively impaired and frail were two times more likely to report low benefit (OR: 1.97; 95%CI: 1.12, 3.47).

DISCUSSION

In a large cohort of older patients with NVAF, approximately one half were frail or cognitively impaired and 9% were both frail *and* cognitively impaired. Depression, older age, lower education, being non-White, and higher bleeding and stroke risk scores were associated with being both frail and cognitively impaired. Among patients taking an OAC, participants with CI alone were less likely to be prescribed a DOAC, while participants who were frail and cognitively impaired were more likely to be prescribed a DOAC than a VKA. Participants who were cognitively impaired and those who were both cognitively impaired and frail were significantly more likely to report low benefits associated with AF treatment.

The proportion of patients with both frailty and cognitive impairment observed in this cohort was higher than observed in a previous study. Less than one percent of patients in the ORBIT-AF registry were classified as being both frail and cognitively impaired. [19] Assessments of frailty and cognition differed between the ORBIT-AF and the SAGE-AF cohorts, however. The ORBIT-AF cohort used the American Geriatric Society's Geriatric Evaluation and Management Tool to assess frailty and cognitive impairment was assessed by medical record review. In the SAGE-AF study, frailty was assessed using the Cardiovascular Health Survey frailty scale and cognitive impairment was objectively assessed using the Montreal Cognitive Assessment Battery. The ORBIT-AF registry included patients aged 18 years and older, while our cohort included only older patients. The proportion of frail patients in our cohort was similar to that reported in the ORBIT-AF cohort, but we observed a markedly higher proportion of cognitively impaired patients than was observed in the ORBIT-AF study. The proportion of cognitively impaired patients might have been underestimated in the ORBIT-AF study since no formal neurocognitive testing of patients was performed.

Few studies have examined factors associated with the presence of frailty and cognitive impairment in older patients with NVAF. Our results are consistent with previous findings that older age, lower education and heavier medical history are associated with either frailty or cognitive impairment in patients with AF. [15, 19] In addition to these predictors, we identified social isolation, depression, and reporting falls in the past 6 months as strong predictors of physical or cognitive impairments. Also, we observed that non-white participants were five times as likely to be cognitively impaired and were eight times as likely to be both frail and cognitively impaired than white participants. These results are consistent with previous studies in which older patients of races/ethnicities other than non-Hispanic white were at increased risk of cognitive impairment. [43] Several hypotheses have been proposed to explain racial disparities in the risk of cognitive impairment. The etiology and severity of cognitive impairment may differ, and differences may exist between these groups in the prevalence of chronic conditions, environmental, and sociodemographic factors.[44, 45] These findings merit further investigation in the AF population since non-Caucasians are at increased risk for OAC related complications when compared to Caucasians. [46, 47]

Contrary to previous studies of frailty and OAC prescribing in patients with AF, we found that OAC prescribing did not differ according to patient's cognitive or frailty status suggesting that prescribers are following current guidelines that underscore the benefit of anticoagulation treatment even in frail older adults. [8] However, we found that patients with both frailty and cognitive impairment were more often treated with DOACs than VKA and that those who were cognitively impaired were more likely to be treated with VKA. Current guidelines, released after collection of these data, highlight the benefits of using DOACs. [8] It has been previously reported that the relative safety of DOACs compared to VKA is maintained among older adults with NVAF who also may be frail or cognitively impaired. [20, 48]

In the SAGE-AF cohort, patients with CI alone or with both frailty and CI were more likely to report low treatment benefit. They also had socio-demographic characteristics that may

challenge the optimal management of AF, such as low social support, living alone with low levels of education. These characteristics can increase the challenges of maintaining therapeutic targets and may lower satisfaction with AF treatment. [49-52] Previous studies have highlighted that higher treatment satisfaction may translate into improved treatment adherence, which is critical for the long-term prevention of stroke among AF patients. [53, 54] It has also been shown that reduced burden of treatment will translate to greater patient adherence to their treatment plans and a positive effect on clinical outcomes. [55] Therefore, satisfaction with the AF treatment is closely related to adherence of treatment and better chances of achieving the therapeutic goal. [54, 56] Future studies could examine role of type of OAC in perceived treatment burden and benefit among patients in relation to frailty and CI status.

We observed that a large proportion of older patients with AF also present with cognitive and/or physical impairment. These results emphasize that addressing only AF symptoms and stroke prevention without managing other comorbidities is unlikely to result in long-term successful management of AF. Therefore, a holistic management of AF that considers the frailty and CI status of older patients with AF is key to maximizing the success of AF management and to improving clinical outcomes. Integrated care pathways have been shown to reduce poor clinical outcomes among patients with AF and other conditions [57, 58]. Our results identify key patient characteristics associated with cognitive and physical impairment and who would benefit from a more holistic management of their AF. With increasing interest in smart technology, a holistic care approach could incorporate App-based management to allow for remote care. [58]

This study has several strengths. Frailty and cognitive function were measured using validated tools via standardized in-person interviews, and we studied a large contemporary cohort of patients with documented NVAF. Several limitations of this study need to be considered in the interpretation of our study findings. Patients with diagnosed dementia were excluded, thereby limiting the generalizability of the results for this patient population. In addition, there is the potential for differential misclassification in cognitively impaired participants so results should be interpreted with caution. However, while cognitive impairment may impact a participant's ability to self-report some factors such as medication adherence, food diaries, etc, 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. [59-61] We could not assess causal/temporal relationships between the impairments under study and OAC prescribing or satisfaction with AF treatment because of the cross-sectional nature of this analysis.

CONCLUSION

In a large cohort of older adults with NVAF, the co-occurrence of cognitive impairment and frailty is common and is associated with low perceived benefit of treatment which may impede optimal NVAF management. We observed that half of patients were frail or cognitively impaired and 9% had both impairments. Social isolation, depression, falls in the past 6 months, older age, lower level of education, race/ethnicity, and clinical risk scores

were associated with a higher risk of having both impairments, suggesting that patients with these characteristics may benefit from cognitive and physical function screenings in order to maximize treatment planning and enhance the long-term prognosis of these patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Sociodemographic and clinical characteristics of older patients with atrial fibrillation, in relation to presence of cognitive impairment (CI) and frailty, SAGE-AF 2016-2018

	No impairment N=652 (52.4%)	Frailty only N=64 (5.1)	CI only N=420 (33.8)	Frailty and CI N=108 (8.7)	*P*-value
Sociodemographic					
Age, *mean years (SD)*	73.8 (6.3)	75.8 (7.1)	77.5 (7.4)	78.2 (7.6)	<.0001
Female	311 (47.7)	44 (68.8)	185 (44.0)	67 (62.0)	<.0001
Non-Hispanic white	616 (94.5)	61 (95.3)	324 (77.1)	68 (63.0)	<.0001
Education [a]					
College Graduate	350 (54.0)	23 (36.5)	135 (33.3)	19 (18.5)	<.0001
Marital Status[b], *married*	401 (62.0)	29 (45.3)	217 (53.2)	47 (44.8)	0.0003
Living Situation[c], *alone*	177 (27.4)	21 (32.8)	117 (28.6)	35 (33.3)	0.53
Clinical					
Type of AF					
Paroxysmal	388 (59.5)	40 (62.5)	255 (60.7)	58 (53.7)	0.66
Persistent	158 (24.2)	13 (20.3)	104 (24.8)	34 (31.5)	
Permanent	36 (5.5)	3 (4.7)	28 (6.7)	6 (5.6)	
CHA_2DS_2VASC, *mean (SD)*	4.01 (1.50)	5.31 (1.68)	4.65 (1.59)	5.57 (1.49)	<.0001
HAS-BLED, *mean (SD)*	3.08 (1.02)	3.38 (0.92)	3.34 (1.12)	3.73 (1.12)	<.0001
MoCA, *mean (SD)*	26.33 (1.70)	26.20 (1.72)	20.02 (3.02)	18.96 (4.26)	<.0001
Medical History					
AMI	109 (16.7)	28 (43.8)	78 (18.6)	27 (25.0)	<.0001
Diabetes type II	145 (22.4)	26 (40.6)	122 (29.1)	53 (49.1)	<.0001
Hyperlipidemia	521 (79.9)	54 (84.4)	336 (80.0)	85 (78.7)	0.82
Stroke	49 (7.5)	8 (12.5)	44 (10.5)	21 (19.4)	0.0011
Asthma/COPD	146 (22.4)	24 (37.5)	106 (25.2)	40 (37.0)	0.0013
Smoking Status					
Former smoker	325 (49.9)	32 (50.0)	205 (48.8)	53 (49.1)	0.99
Current smoker	19 (2.9)	1 (1.6)	12 (2.9)	3 (2.8)	
Other geriatric impairment					
Vision impairment	188 (28.8)	31 (48.4)	154 (36.7)	55 (50.9)	<.0001
Hearing impairment	209 (32.1)	17 (26.6)	179 (42.6)	46 (42.6)	0.0007
Social Isolation	67 (10.3)	9 (14.1)	66 (15.7)	14 (13.0)	0.07
Depression	132 (20.3)	45 (70.3)	108 (25.7)	68 (63.0)	<.0001
Anxiety	126 (19.3)	24 (37.5)	92 (21.9)	49 (45.4)	<.0001
Fall in the past 6 months	119 (18.2)	25 (39.1)	94 (22.4)	32 (29.6)	0.0002

Note.

[a] N=1220

[b] N=1224

[c] N=1225

SD: Standard Deviation.

Table 2.

Presence of cognitive impairment and frailty in relation to other geriatric impairments and demographic and clinical characteristics among older patients with atrial fibrillation, SAGE-AF 2016-2018, OR (95% confidence interval)*

	Frailty only N=419 (33.7)	CI only N=64 (5.1)	Frailty and CI N=108 (8.7)
Other geriatric impairment			
Vision impairment	1.42 (0.79, 2.58)	1.07 (0.79, 1.45)	1.17 (0.71, 1.93)
Hearing impairment	0.44 (0.23, 0.84)	1.32 (0.99, 1.76)	0.96 (0.58, 1.60)
Social isolation	1.30 (0.56, 3.04)	1.66 (1.10, 2.50)	1.01 (0.47, 2.17)
Elevated symptoms of depression	10.16(5.17, 19.96)	1.11 (0.76, 1.62)	4.62 (2.59, 8.26)
Elevated symptoms of anxiety	0.69 (0.35, 1.34)	1.19 (0.81, 1.75)	1.68 (0.94, 3.00)
Any fall in the past 6 months	2.11 (1.15, 3.87)	0.99 (0.71, 1.40)	1.14 (0.66, 1.98)
Demographic characteristics			
Age (5 year increments)	1.20 (0.97, 1.50)	1.48 (1.32, 1.66)	1.56 (1.29, 1.88)
Less than college graduate	1.33 (0.73, 2.43)	2.03 (1.52, 2.70)	3.81 (2.13, 6.81)
Non-Hispanic white	0.75 (0.26, 2.15)	5.26 (3.43, 8.07)	7.94 (4.34, 14.55)
Not married	1.30 (0.72, 2.34)	0.93 (0.70, 1.25)	0.96 (0.58, 1.58)
Clinical characteristics			
CHA_2DS_2VASC	1.32 (1.06, 1.64)	1.07 (0.96, 1.19)	1.35 (1.13, 1.62)
HAS-BLED	0.99 (0.75, 1.32)	1.19 (1.04, 1.37)	1.43 (1.12, 1.81)
AMI	2.79 (1.46, 5.35)	0.90 (0.61, 1.31)	0.88 (0.48, 1.62)
Asthma/COPD	1.51 (0.83, 2.77)	0.99 (0.72, 1.37)	1.33 (0.80, 2.24)

*Referent group is those who are not impaired (n=653).

Table 3.

Odds of OAC treatment and receiving DOAC in relation to frailty and cognitive impairment among older patients with atrial fibrillation, SAGE-AF 2016-2018

		Odds ratio (95% confidence interval)		
		Unadjusted	Model 1	Model 2
	On OAC *n (%)*	Odds of not receiving OAC treatment (N=1244)		
No impairment	561 (85.9)	referent	referent	referent
Frailty	54 (84.4)	1.14 (0.56, 2.32)	1.55 (0.75, 3.22)	1.51 (0.70, 3.27)
CI	354 (84.5)	1.15 (0.82, 1.62)	1.34 (0.94, 1.91)	1.39 (0.94, 2.05)
Both frailty and CI	95 (88.-)	0.84 (0.45, 1.56)	1.23 (0.64, 2.35)	1.35 (0.66, 2.77)
	On DOAC *n (%)*	Odds of receiving a DOAC among those on OAC (n=1064)		
No impairment	256 (45.6)	referent	referent	referent
Frailty	21 (38.9)	0.76 (0.43, 1.34)	0.92 (0.51, 1.64)	0.89 (0.49, 1.67)
CI	138 (39.-)	0.76 (0.58, 0.99)	0.84 (0.63, 1.10)	0.91 (0.67, 1.23)
Both frailty and CI	51 (53.7)	1.38 (0.89, 2.14)	1.73 (1.10, 2.73)	1.71 (1.02, 2.88)

Note. OAC: Oral anticoagulation; DOAC: Direct-Acting Oral Anticoagulants

Model 1 is adjusted for CHA_2DS_2VASC score, Model 2 is adjusted for Model 1 + age, education, race, marital status, has-bled score, AMI, asthma/COPD, vision impairment, hearing impairment, social support, depression, anxiety, fall in the past 6 months.

Table 4.

Odds of high treatment burden and low treatment benefit in relation to frailty and cognitive impairment among older patients with atrial fibrillation, SAGE-AF 2016-2018

	Burden and Benefit results		Odds ratio (95% confidence interval)		
			Unadjusted	Model 1	Model 2
	Burden *mean score (SD)*	High burden *n (%)*	Odds of reporting high burden		
No impairment	16.6 (5.2)	132 (23.5)	referent	referent	referent
Frailty	18.1 (5.6)	19 (35.2)	1.77 (0.98, 3.19)	1.74 (0.95, 3.18)	1.05 (0.54, 2.08)
CI	16.5 (6.4)	80 (22.6)	0.95 (0.69, 1.30)	0.94 (0.68, 1.30)	0.87 (0.60, 1.26)
Both frailty and CI	17.9 (6.5)	31 (32.6)	1.50 (0.93, 2.41)	1.47 (0.90, 2.42)	0.76 (0.42, 1.37)
	Benefit *mean score (SD)*	**Low benefit *n (%)***	**Odds of reporting low benefit**		
No impairment	11.3 (3.5)	98 (17.5)	referent	referent	referent
Frailty	10.2 (3.4)	15 (27.8)	1.67 (0.89, 3.20)	1.63 (0.85, 3.16)	1.22 (0.59, 2.50)
CI	10.4 (4.3)	100 (28.3)	1.88 (1.37, 2.59)	1.86 (1.35, 2.57)	1.57 (1.10, 2.24)
Both frailty and CI	9.6 (3.6)	34 (35.8)	2.67 (1.66, 4.28)	2.59 (1.58, 4.25)	1.97 (1.12, 3.47)

Note. SD: Standard Deviation,

High burden was defined as being the bottom quartile of the Anti-clot Treatment Burden Scale while low benefit was defined as being the Top quartile of the Anti-clot Treatment Benefit Scale.

Model 1 is adjusted for CHA_2DS_2VASC score, Model 2 is adjusted for Model 1 + age, education, race, marital status, has-bled score, AMI, asthma/COPD, vision impairment, hearing impairment, social support, depression, anxiety, fall in the past 6 months