



Clinical Research

Effect of Mental Health Status on Arrhythmia Recurrence After Catheter Ablation of Atrial Fibrillation

Zhaoxu Jia, MD,^a Xin Du, MD,^a Shangxin Lu, MD,^a Xiaoyi Yang, MS,^b Sanshuai Chang, MD,^a Jiapeng Liu, MD,^a Jingye Li, MD,^a Yingchun Zhou, MS,^b Laurent Macle, MD,^c Jianzeng Dong, MD,^a and Changsheng Ma, MD^a

^aDepartment of Cardiology, Beijing Anzhen Hospital, Capital Medical University and National Clinical Research Center for Cardiovascular Diseases, Beijing, China

^bFaculty of Economics and Management, East China Normal University, Shanghai, China

^cMontreal Heart Institute, Université de Montréal, Montréal, Québec, Canada

ABSTRACT

Background: Patients diagnosed with atrial fibrillation suffer more from anxiety and depression than the general population. This study sought to evaluate the association between mental health status and recurrence of atrial tachyarrhythmia (AT) after catheter ablation.

Methods: A total of 448 patients who underwent catheter ablation for atrial fibrillation were enrolled in this single-centre prospective cohort study. Mental Health Inventory-5 (MHI-5) was used to assess the mental health status at the end of the blanking period after ablation and lower scores indicated poorer mental health status. Patients with no early recurrence of AT during the blanking period were included for analyses. Multivariate logistic regression was used to examine the association between mental health status and risk of arrhythmia recurrence in the following 3 months.

RÉSUMÉ

Contexte : Les patients ayant reçu un diagnostic de fibrillation auriculaire souffrent davantage d'anxiété et de dépression que la population générale. Cette étude avait pour objectif d'évaluer l'association entre l'état de santé mentale et la récurrence de la tachyarythmie auriculaire (TA) après une ablation par cathéter.

Méthodologie : Au total, 448 patients ayant subi une ablation par cathéter pour traiter leur fibrillation auriculaire ont été recrutés dans cette étude de cohorte prospective unicentrique. Le questionnaire Mental Health Inventory-5 (MHI-5) a été utilisé pour évaluer l'état de santé mentale à la fin de la période de suppression suivant l'ablation; plus ce score est faible, moins l'état de santé mentale est satisfaisant. Des analyses ont été effectuées chez les patients n'ayant pas présenté de récurrence précoce de TA durant la période de suppression. Une

Atrial fibrillation (AF) is one of the most common arrhythmias encountered in clinical practice. AF is associated with a higher risk of stroke, heart failure, mortality,¹⁻³ and impaired quality of life (QoL).^{4,5} Patients with AF suffer more from anxiety and depression than patients without AF or patients with other types of arrhythmia.⁶⁻¹⁰ Although anxiety and sadness are associated with a 4- to 6-fold higher risk of AF, happiness could be a protective factor.^{11,12} Ablation therapy is now widely used for the treatment of AF, but recurrence rates remain high with the need for repeat procedures.¹³ Recent guidelines have recommended an integrated management

targeting modifiable risk factors to prevent recurrence of the arrhythmia.¹⁴ However, previous studies that examined predictors of atrial tachyarrhythmia (AT) recurrence after catheter ablation largely ignored the mental health status.¹⁵ Thus, we sought to determine the impact of mental health status of patients on the risk of arrhythmia recurrence after catheter ablation of AF.

Methods

Patient cohort and definitions

Our study is a single-centre prospective cohort study. Between October 2015 and February 2016, consecutive patients with paroxysmal or persistent AF who underwent catheter ablation in Beijing Anzhen Hospital and signed a written informed consent were recruited. To avoid potential bias induced by early recurrence (ER) of AT, we only included patients without ER during blanking period in the mental health status analyses. Paroxysmal AF was defined as AF that

Received for publication October 3, 2018. Accepted February 12, 2019.

Corresponding authors: Dr Xin Du or Dr Changsheng Ma, Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, No.2 Anzhen Rd, Chaoyang District, Beijing 100029, China. Tel.: +86-13-370103558 (X. Du) or +86-13-901357404 (C. Ma); fax: +86-10-84005363.

E-mail: duxinheart@sina.com; chshma@vip.sina.com

See page 837 for disclosure information.

Results: Among 335 patients without early recurrence during the blanking period, 36 patients (10.7%) experienced AT recurrence in the 3 months after the mental health status evaluation. Recurrence rates were 35.7%, 13.5%, 10.6%, and 4.6% in patients with an MHI-5 score of 0-52, 53-75, 76-85, and 86-100, respectively (overall $P = 0.004$). A significant association between low MHI-5 scores and AT recurrence was observed after multivariate adjustment (odds ratio: 8.81 [1.93-40.22], $P = 0.005$ for the MHI-5 score of 0-52 and 3.61 [1.05-12.35], $P = 0.041$ for the MHI-5 score of 53-75, compared with an MHI-5 score of 86-100).

Conclusions: A poorer mental health status is associated with AT recurrence after catheter ablation. Intervention studies are warranted to evaluate the efficacy of counselling and psychological support after ablation in improving success rates in these patients.

terminates spontaneously or with intervention within 7 days of onset. Persistent AF was defined as AF that persists over 7 days.¹⁶ This study was approved by the Institutional Committee on Human Research of our hospital.

Baseline data collection

Data were prospectively collected by trained staff members. Baseline demographic and clinical factors included age, sex, body mass index, smoking status, alcohol consumption, systolic blood pressure, education level, health insurance coverage, AF type, time of the first AF diagnosed, history of hypertension, diabetes mellitus, hyperlipidemia, congestive heart failure, vascular disease (coronary artery disease or peripheral artery disease), previous stroke/transient ischemic attack/thromboembolism, and bleeding. Active medical treatment and echocardiographic data were also collected. Congestive Heart Failure, Hypertension, Age (≥ 75 years), Diabetes, Stroke/Transient Ischemic Attack, Vascular Disease, Age (65-74 years), Sex (Female) score (CHA₂DS₂-VASc) was calculated by assigning 2 points for a history of stroke/transient ischemic attack/thromboembolism and age ≥ 75 years, 1 point for age between 65 and 74 years, a history of hypertension, diabetes mellitus, congestive heart failure, vascular disease, and female sex.¹⁷

Catheter ablation and periprocedure management

Antiarrhythmic drugs (AADs) were discontinued before ablation. Patients were treated with new oral anticoagulants or warfarin with an international normalized ratio in the target range (2.0-3.0) before ablation. Transesophageal echocardiography was performed before operation to exclude the presence of thrombus in left atrial appendage.

The ablation strategy in our centre has been previously reported.¹⁸⁻²⁰ Briefly, circumferential pulmonary vein isolation (with the endpoint of entrance block) was performed for patients with paroxysmal AF. For patients with persistent AF, linear ablation across the left atrial roof, mitral isthmus, and

analyse de régression logistique multivariée a été effectuée pour évaluer l'association entre l'état de santé mentale et le risque de récurrence de l'arythmie au cours des 3 mois suivants.

Résultats : Parmi les 335 patients n'ayant pas présenté une récurrence précoce durant la période de suppression, 36 (10,7 %) ont eu une récurrence de TA au cours des 3 mois suivant l'évaluation de leur état de santé mentale. Les taux de récurrence étaient respectivement de 35,7 %, 13,5 %, 10,6 % et 4,6 % chez les patients ayant obtenu un score au MHI-5 de 0 à 52, de 53 à 75, de 76 à 85 et de 86 à 100 (p pour l'ensemble = 0,004). Une association significative entre un score peu élevé au MHI-5 et la récurrence de la TA a été observée après ajustement multivarié (rapport de cotes : 8,81 [1,93-40,22], $p = 0,005$ pour un score au MHI-5 de 0 à 52 et 3,61 [1,05-12,35], $p = 0,041$ pour un score au MHI-5 de 53 à 75, comparativement à un score au MHI-5 de 86 à 100).

Conclusions : Un état de santé mentale moins satisfaisant est associé à une récurrence de la TA après une ablation par cathéter. Il est nécessaire de réaliser des études interventionnelles pour évaluer l'efficacité avec laquelle le counseling et le soutien psychologique après l'ablation permettent d'augmenter les taux de succès chez ces patients.

cavotricuspid isthmus (all lines with the endpoint of bidirectional block) was performed in addition to circumferential pulmonary vein ablation.

A blanking period of 3 months after ablation was observed. AADs were allowed during the blanking period. New oral anticoagulants (dabigatran 110/150 mg twice a day or rivaroxaban 10/15/20 mg once daily) or warfarin with a target international normalized ratio between 2.0 and 3.0 was administered for at least 3 months after catheter ablation.

AT recurrence

All patients had a 12-lead electrocardiogram (ECG) and 24-hour Holter recordings at 1, 2, 3, and 6 months after ablation. Additional ECGs or Holvers were performed whenever the patients felt palpitations. All the ECGs and Holter results were forwarded to the coordinating centre and blindly adjudicated by cardiologists of the Anzhen Hospital. Recurrence of AT was defined as any documented atrial arrhythmia (symptomatic or asymptomatic), including AF, atrial flutter, and atrial tachycardia lasting 30 seconds or more after the blanking period of 3 months after ablation.²¹ AT recurrence at 6 months' follow-up was used to assess its association with mental health status.

QoL measurement

QoL data were measured by the Atrial Fibrillation Effect on Quality-of-life (AFEQT) questionnaire at the 6 months' follow-up.²² The AFEQT questionnaire consists of 20 items from 4 individual domains, including symptoms (4 items), daily activities (8 items), treatment concern (6 items), and treatment satisfaction (2 items). The global health status is determined based on the sum of scores of the first 3 domains. The raw scores of 1 to 7 are transformed to a 0 to 100 scale, where a score of 0 indicates the most severe symptoms or disability and a score of 100 indicates no limitation or disability. Thus, higher scores on the AFEQT questionnaire represent a better health status.

Table 1. Sociodemographic and clinical characteristics of patients at different levels of MHI-5 score

Variables	MHI-5 category				P value
	0-52, N = 14	53-75, N = 74	76-85, N = 160	86-100, N = 87	
Age, N (%)					0.082
< 65	12 (85.7%)	52 (70.3%)	109 (68.1%)	51 (58.6%)	
65-75	2 (14.3%)	17 (23.0%)	40 (25.0%)	21 (24.1%)	
≥ 75	0	5 (6.8%)	11 (6.9%)	15 (17.2%)	
Sex, N (%)					0.423
Male	7 (50.0%)	52 (70.3%)	113 (70.6%)	58 (66.7%)	
Female	7 (50.0%)	22 (29.7%)	47 (29.4%)	29 (33.3%)	
BMI, N (%)					0.367
< 24	5 (35.7%)	20 (27.0%)	38 (23.8%)	21 (24.1%)	
24-28	9 (64.3%)	38 (51.4%)	82 (51.2%)	40 (46.0%)	
≥ 28	0	16 (21.6%)	40 (25.0%)	26 (29.9%)	
Smoking, N (%)					0.323
No	9 (64.3%)	61 (82.4%)	117 (73.1%)	67 (77.0%)	
Yes	5 (35.7%)	13 (17.6%)	43 (26.9%)	20 (23.0%)	
Alcohol, N (%)					0.477
No	9 (64.3%)	47 (63.5%)	96 (60.0%)	61 (70.1%)	
Yes	5 (35.7%)	27 (36.5%)	64 (40.0%)	26 (29.9%)	
SBP (mm Hg), N (%)					0.433
< 140	12 (85.7%)	51 (68.9%)	105 (65.6%)	56 (64.4%)	
≥ 140	2 (14.3%)	23 (31.1%)	55 (34.4%)	31 (35.6%)	
Educational level, N (%)					0.334
Under high school education	10 (71.4%)	39 (52.7%)	91 (56.9%)	56 (64.4%)	
Other	4 (28.6%)	35 (47.3%)	69 (43.1%)	31 (35.6%)	
Health insurance coverage, N (%)					0.104
All	0	13 (17.6%)	32 (20.3%)	15 (17.2%)	
Partially	14 (100%)	61 (82.4%)	115 (72.8%)	67 (77.0%)	
None	0	0	11 (7.0%)	5 (5.7%)	
Unavailable	0	0	2	0	
Type of AF, N (%)					0.886
Paroxysmal	9 (64.3%)	48 (64.9%)	96 (60.0%)	52 (59.8%)	
Persistent	5 (35.7%)	26 (35.1%)	64 (40.0%)	35 (40.2%)	
History of AF duration (y), N (%)					0.327
< 5	11 (78.6%)	46 (66.7%)	118 (75.2%)	58 (69.9%)	
5-10	2 (14.3%)	15 (21.7%)	29 (18.5%)	12 (14.5%)	
≥ 10	1 (7.1%)	8 (11.6%)	10 (6.4%)	13 (15.7%)	
Unavailable	0	5	3	4	
Hypertension, N (%)					0.658
No	7 (50.0%)	24 (32.4%)	58 (36.3%)	31 (35.6%)	
Yes	7 (50.0%)	50 (67.6%)	102 (63.7%)	56 (62.4%)	
DM, N (%)					0.099
No	13 (92.9%)	56 (75.7%)	132 (82.5%)	62 (71.3%)	
Yes	1 (7.1%)	18 (24.3%)	28 (17.5%)	25 (28.7%)	
Hyperlipidemia, N (%)					0.662
No	8 (57.1%)	41 (55.4%)	87 (54.4%)	41 (47.1%)	
Yes	6 (42.9%)	33 (44.6%)	73 (45.6%)	46 (52.9%)	
Congestive heart failure, N (%)					0.924
No	13 (92.9%)	66 (89.2%)	143 (89.4%)	76 (87.4%)	
Yes	1 (7.1%)	8 (10.8%)	17 (10.6%)	11 (12.6%)	
Prior stroke/TIA/TE, N (%)					0.893
No	13 (92.9%)	63 (85.1%)	137 (85.6%)	75 (86.2%)	
Yes	1 (7.1%)	11 (14.9%)	23 (14.4%)	12 (13.8%)	
Vascular disease, N (%)					0.038
No	11 (78.6%)	66 (89.2%)	143 (89.4%)	67 (77.0%)	
Yes	3 (21.4%)	8 (10.8%)	17 (10.6%)	20 (23.0%)	
Prior bleeding, N (%)					0.855
No	11 (78.6%)	58 (78.4%)	129 (80.6%)	66 (75.9%)	
Yes	3 (21.4%)	16 (21.6%)	31 (19.4%)	21 (24.1%)	
Medical treatment, N (%)					0.281
Drug for rhythm control					
No	0	6 (8.1%)	17 (10.6%)	13 (14.9%)	
Yes	14 (100%)	68 (91.9%)	143 (89.4%)	74 (85.1%)	
Drug for rate control					0.670
No	12 (85.7%)	56 (75.7%)	121 (75.6%)	62 (71.3%)	
Yes	2 (14.3%)	18 (24.3%)	39 (24.4%)	25 (28.7%)	
ACEIs/ARBs					0.204
No	12 (85.7%)	42 (56.8%)	104 (65.0%)	55 (63.2%)	
Yes	2 (14.3%)	32 (43.2%)	56 (35.0%)	32 (36.8%)	

Continued

Table 1. Continued.

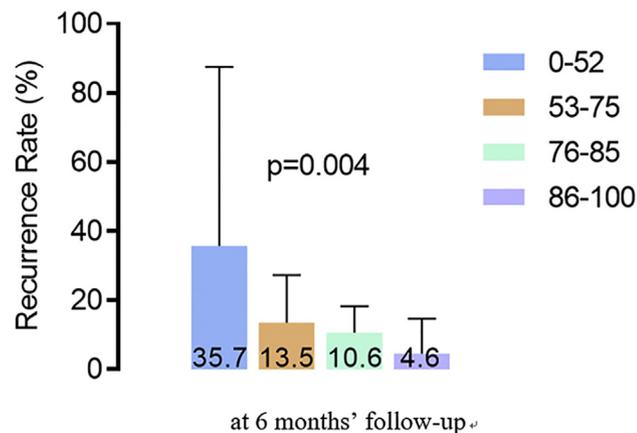
Variables	MHI-5 category				P value
	0-52, N = 14	53-75, N = 74	76-85, N = 160	86-100, N = 87	
Echocardiographic measures					
LAD, mean ± SD	40.54 ± 5.74	40.49 ± 5.03	40.89 ± 6.13	41.92 ± 4.95	0.383
LVEDD, mean ± SD	48.85 ± 3.13	47.92 ± 5.65	47.85 ± 4.79	48.03 ± 5.22	0.920
CHA ₂ DS ₂ -VASc, N (%)					
< 2	7 (50.0%)	30 (40.5%)	73 (45.6%)	26 (29.9%)	0.097
≥ 2	7 (50.0%)	44 (59.5%)	87 (54.4%)	61 (70.1%)	
Number of comorbidities, N (%)					
0-1	7 (50.0%)	20 (27.0%)	49 (30.6%)	20 (23.0%)	0.145
2-3	4 (28.6%)	33 (44.6%)	77 (48.1%)	36 (41.4%)	
≥ 4	3 (21.4%)	21 (28.4%)	34 (21.3%)	31 (35.6%)	
Length of hospital stay, median (range)	5.00 (3.00, 6.25)	4.00 (3.00, 5.25)	4.00 (3.00, 6.00)	5.00 (4.00, 6.00)	0.418

Comorbidities indicate patients had a history of one of the following diseases: hypertension, DM, congestive heart failure, vascular disease, stroke/TIA/TE, bleeding, hyperlipidemia, hypertrophic cardiomyopathy, dilated cardiomyopathy, paroxysmal supraventricular tachycardia, pacemaker implantation, respiratory diseases, peptic ulcer, or thyroid disease.

ACEIs, angiotensin-converting enzyme inhibitors; AF, atrial fibrillation; ARBs, angiotensin receptor blockers; BMI, body mass index; CHA₂DS₂-VASc, Congestive Heart Failure, Hypertension, Age (≥ 75 years), Diabetes, Stroke/Transient Ischemic Attack, Vascular Disease, Age (65-74 years), Sex (Female); DM, diabetes mellitus; LAD, left atrial diameter; LVEDD, left ventricular end diastolic diameter; MHI-5, Mental Health Inventory-5; SBP, systolic blood pressure; SD, standard deviation; TE, thromboembolism; TIA, transient ischemic attack.

Mental health status measurement

Mental health status and the presence and severity of depressive symptom were assessed using the Mental Health Inventory-5 (MHI-5) score at 3 months (±2 weeks) after catheter ablation. The MHI-5 score is a 5-item subscale of the short-form 36 health status survey that has been validated in large population cohorts.^{23,24} The Chinese version of short-form 36 has been developed through strict procedures including forward and backward translations, and has been psychometrically tested. It showed satisfactory validity and reliability in Chinese population and has been widely used.^{25,26}



MHI-5 score	6 month's follow-up
0-52	5/14 (35.7%)
53-75	10/74 (13.5%)
76-85	17/160 (10.6%)
86-100	4/87 (4.6%)

Figure 1. Incidence of atrial tachyarrhythmia recurrence at different levels of Mental Health Inventory-5 (MHI-5) score during the 6-month follow-up.

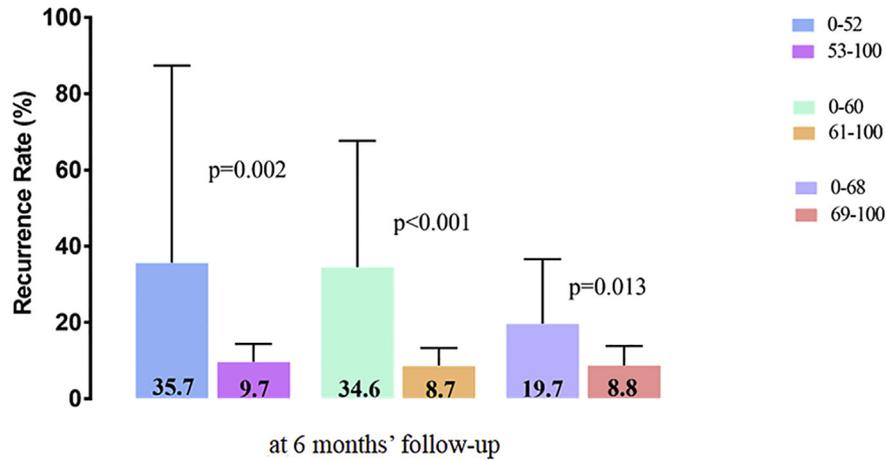
Each item records the number of times over the past month (all, most, a good bit, some, little, or none) that a patient felt nervous, so down that nothing could cheer them up, calm and peaceful, down and blue, or happy. The answers are scored on a 0 to 100 numerical scale with lower scores indicating poorer mental health status. In accordance with previous studies,^{12,27} patients were classified into 4 groups based on their MHI-5 score: 86-100, 76-85, 53-75, and 0-52. Patients with scores of 86-100 were used as the reference group. In addition, specific cutoffs of MHI-5 scores may be used to grade the severity of depressive symptoms.²⁸ A cutoff of 52 is used to indicate the presence of severe depressive symptoms only; a cutoff of 60 is used to indicate the presence of moderate or severe depressive symptoms; and a cutoff of 68 is used to indicate the presence of mild or moderate or severe depressive symptoms.²⁸ Further sensitivity analyses were performed based on these cutoffs.

Statistical analysis

All statistical analysis was performed using SPSS 22.0. Continuous data were presented as mean ± standard deviation or median (range), and differences between groups were assessed by the 1-way analysis of variance or the Kruskal-Wallis H rank sum test. The χ^2 test was used for categorical variables. Univariate logistic regression analysis was performed to assess the association of each variable with AT recurrence at 6 months' follow-up. Variables with a P value of < 0.2 in univariate analysis and of clinical importance were included in the multivariate logistic regression analysis, including smoking status, under high school education, medical treatment of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, CHA₂DS₂-VASc score, and the MHI-5 score. A P value of < 0.05 was considered statistically significant.

Results

During the study period, 448 patients underwent catheter ablation for AF at Anzhen Hospital and were followed up in the study. A total of 113 ablated patients experienced ER during the blanking period and were excluded from the analyses. Therefore, 335 patients without ER in the blanking



MHI-5 score	6 month's follow-up	MHI-5 score	6 month's follow-up	MHI-5 score	6 month's follow-up
0-52	5/14 (35.7%)	0-60	9/26(34.6%)	0-68	12/61 (19.7%)
53-100	31/321 (9.7%)	61-100	27/309 (8.7%)	69-100	24/274 (8.8%)

Figure 2. Incidence of atrial tachyarrhythmia recurrence for the different cutoffs of Mental Health Inventory-5 (MHI-5) score used for diagnosing depressive symptoms during the 6-month follow-up.

period were included in the analyses and 36 (10.7%) reported AT recurrence between 3 and 6 months. The MHI-5 score was performed at 90 ± 10 days (range: 80-115 days) after ablation (end of the blanking period) and was used for patient classification. Baseline characteristics of patients according to their MHI-5 score are summarized in Table 1. Although there was no statistical difference, higher proportions of younger aged, female and smoking patients and lower proportions of patients with body mass index ≥ 28 , systolic blood pressure ≥ 140 mm Hg, history of hypertension, diabetes, hyperlipidemia, congestive heart failure, and stroke were observed in patients with an MHI-5 score of 0-52.

Among the 335 patients, 8 procedure-related complications were observed, including 5 vascular complications and 3 pericardial tamponade/pericardial effusion. Three patients experienced oral anticoagulant-related side effects (including 2 bleeding events). In addition, 6 patients reported amiodarone-related side effects (including 4 abnormal thyroid function, 1 gastrointestinal, and 1 respiratory side effects).

Among the 335 patients, 14 (4.2%) had an MHI-5 score of 0-52, and 74 (22.1%), 160 (47.8%), and 87 (26.0%) had an MHI-5 score of 53-75, 76-85, and 86-100, respectively. The incidence of AT recurrence at 6 months after ablation amongst patients classified by MHI-5 scores is shown in Figure 1. Arrhythmia recurrence rates were 35.7%, 13.5%, 10.6%, and 4.6% in patients with an MHI-5 score of 0-52, 53-75, 76-85, and 86-100, respectively (overall P value = 0.004). Of the 36 patients with AT recurrence, arrhythmia recurrence was documented by ECG in 23 patients (63.9%) and by routine Holter in 13 (36.1%). When the routine Holter data were analysed alone, the AT recurrence rates were 14.3%, 4.1%, 4.4%, and 1.1% in patients with an MHI-5 score of 0-52, 53-75, 76-85, and 86-100, respectively.

Analyses of recurrence rates according to the different reported cutoffs of the MHI-5 score were also performed.

Patients with depressive symptoms had a significantly higher arrhythmia recurrence rate than patients without depressive symptoms (Fig. 2).

In univariate logistic regression analysis, the MHI-5 score was significantly associated with AT recurrence (Table 2). After adjusting for the difference in patient characteristics collected at baseline, including smoking status, under high school education, medical treatment of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and CHA₂DS₂-VASc score, education below a high school level and poorer mental health status were significantly associated with a higher risk of AT recurrence. Odds ratio (OR) of AT recurrence in the group with an MHI-5 score of 0-52 was 8.81 (95% confidence interval [CI]: 1.93-40.22, $P = 0.005$), compared with patients with an MHI-5 score of 86-100 (Table 2). Patients with an MHI-5 score of 53-75 also had a significantly increased risk of AT recurrence vs patients with an MHI-5 score of 86-100 (OR: 3.61, 95% CI: 1.05-12.35, $P = 0.041$). The trend was consistent although not statistically significant for the MHI-5 score of 76-85 (OR: 2.34, 95% CI: 0.75-7.31, $P = 0.145$).

When the different cutoffs of MHI-5 scores were analysed, depressive symptoms were also significantly associated with arrhythmia recurrence (Table 3). OR for AT recurrence in the group with an MHI-5 score of 0-52 was 4.04 (95% CI: 1.23-13.33, $P = 0.022$), compared with patients with an MHI-5 score of 53-100. When cutoffs of the MHI-5 score of 60 or 68 were used, the depressive symptoms were also associated with higher AT recurrence rates (OR: 5.86 [2.27-15.11], $P < 0.001$ and 2.56 [1.17-5.59], $P = 0.018$, respectively).

In addition to AT recurrence, a lower MHI-5 score was also associated with a lower score on the AFEQT questionnaire. This was observed for each domain of the AFEQT questionnaire, including symptoms, daily activities, treatment concern, and treatment satisfaction (all $P < 0.05$); see Table 4.

Table 2. Univariate and multivariate logistic regression analysis for AT recurrence

Variables	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (y)				
65-75 vs < 65	0.73 (0.30-1.76)	0.482		
≥ 75 vs <65	0.82 (0.23-2.87)	0.751		
Female	1.11 (0.53-2.31)	0.785		
BMI				
< 24 vs ≥ 28	1.57 (0.66-3.72)	0.310		
24-28 vs ≥ 28	0.50 (0.20-1.23)	0.133		
Smoking	1.92 (0.92-3.99)	0.081	1.61 (0.74-3.52)	0.233
Alcohol	1.28 (0.63-2.59)	0.489		
SBP ≥ 140 mm Hg	1.16 (0.56-2.39)	0.688		
Under high school education vs higher education	1.97 (0.92-4.24)	0.081	2.31 (1.03-5.19)	0.042
Health insurance coverage				
Partially vs all covered	1.10 (0.43-2.79)	0.840		
None vs all covered	1.29 (0.23-7.07)	0.773		
Type of AF: persistent vs paroxysmal	1.14 (0.57-2.31)	0.709		
History of AF duration (y)				
5-10 vs < 5	0.57 (0.19-1.68)	0.306		
≥ 10 vs < 5	1.09 (0.36-3.35)	0.880		
Hypertension	0.99 (0.48-2.03)	0.969		
DM	0.56 (0.21-1.49)	0.245		
Hyperlipidemia	0.89 (0.44-1.77)	0.729		
Congestive heart failure	0.71 (0.21-2.44)	0.584		
Prior stroke/TIA/TE	0.99 (0.36-2.68)	0.979		
Vascular disease	0.51 (0.15-1.74)	0.285		
Prior bleeding	1.27 (0.57-2.85)	0.555		
Medical treatment				
Drug for rhythm control	0.96 (0.32-2.89)	0.940		
Drug for rate control	0.84 (0.37-1.92)	0.676		
ACEIs/ARBs	0.46 (0.20-1.05)	0.066	0.51 (0.21-1.24)	0.136
Echocardiographic measures				
LAD	1.00 (0.94-1.07)	0.921		
LVEDD	0.98 (0.91-1.05)	0.500		
CHA ₂ DS ₂ -VASC				
< 2 vs ≥ 2	1.97 (0.98-3.96)	0.056	1.67 (0.77-3.63)	0.198
MHI-5 score*				
86-100	1.00		1.00	
76-85	2.47 (0.80-7.58)	0.115	2.34 (0.75-7.31)	0.145
53-75	3.24 (0.97-10.81)	0.056	3.61 (1.05-12.35)	0.041
0-52	11.53 (2.61-50.84)	0.001	8.81 (1.93-40.22)	0.005

ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; AT, atrial tachyarrhythmia; BMI, body mass index; CHA₂DS₂-VASC, Congestive Heart Failure, Hypertension, Age (≥ 75 years), Diabetes, Stroke/Transient Ischemic Attack, Vascular Disease, Age (65-74 years), Sex (Female); CI, confidence interval; DM, diabetes mellitus; LAD, left atrial diameter; LVEDD, left ventricular end diastolic diameter; MHI-5, Mental Health Inventory-5; OR, odds ratio; SBP, systolic blood pressure; TE, thromboembolism; TIA, transient ischemic attack.

*The MHI-5 score at the 3 months' follow-up was used.

Discussion

In this single-centre prospective cohort study, we found that patients with depressive symptoms detected by the MHI-5 score or poorer mental health status as indicated by a lower MHI-5 score experienced an increased risk of AT recurrence. A significant association between poor mental health status and AT recurrence was found using the

different classifications (0-52, 53-75, 76-85) as well as the different cutoffs (52, 60, 68) of the MHI-5 score for diagnosing depressive symptoms. Our results may have important implications for clinical management and are consistent with the existing literature reporting the role of psychological status in the AT recurrence after catheter ablation.

Table 3. Univariate and multivariate logistic regression analysis for AT recurrence using different cutoffs of MHI-5 score for diagnosing depressive symptoms

MHI-5 cutoff points	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
52	5.20 (1.64-16.48)	0.005	4.04 (1.23-13.33)	0.022
60	5.53 (2.25-13.59)	< 0.001	5.86 (2.27-15.11)	< 0.001
68	2.55 (1.20-5.44)	0.015	2.56 (1.17-5.59)	0.018

AT, atrial tachyarrhythmia; CI, confidence interval; MHI-5, Mental Health Inventory-5; OR, odds ratio.

Table 4. The AFEQT outcomes

Variables	MHI-5 category				P value
	0-52, N = 14	53-75, N = 74	76-85, N = 160	86-100, N = 87	
AFEQT					
Symptoms	70.24 ± 16.57	81.08 ± 12.36	83.91 ± 12.50	82.61 ± 9.32	0.001
DA	64.29 ± 16.03	66.27 ± 14.60	70.61 ± 11.91	70.61 ± 12.88	0.037
TC	74.40 ± 15.64	77.40 ± 13.26	81.54 ± 10.05	80.43 ± 8.10	0.009
GS	68.98 ± 12.10	73.27 ± 10.57	77.19 ± 9.02	76.54 ± 8.34	0.001
TS	69.05 ± 17.12	75.34 ± 14.50	78.90 ± 12.40	80.27 ± 10.33	0.003

Values are shown as the mean ± standard deviation.

AFEQT, Atrial Fibrillation Effect on Quality-of life questionnaire; DA, daily activities; GS, global score; MHI-5, Mental Health Inventory-5; TC, treatment concern; TS, treatment satisfaction.

Catheter ablation is an effective method of treating AF, but recurrence is not uncommon and the use of AADs and/or repeat ablation procedures may be required.¹³ Lange and Herrmann-Lingen²⁹ demonstrated that depressive mood is a major risk factor for recurrence of AF after electrical cardioversion. In 2 small studies, anxiety and depression were independently associated with an increased risk of AF recurrence after pulmonary vein ablation in patients with both paroxysmal and persistent AF.^{30,31} Another small study of 57 patients from Efremidis et al.³² suggested that baseline anxiety and depression metrics were associated with AF recurrence after pulmonary vein isolation.

Currently, the mechanisms of the association between depressive symptoms and AF are unclear. Recently, some studies have demonstrated possible mechanisms that could be taken into consideration. First, depressive symptoms could increase the levels of interleukin-6 and C-reactive protein,³³⁻³⁵ and these 2 inflammatory mediators are associated with the initiation and maintenance of AF,^{36,37} and hence increase the recurrence rate after cardioversion and ablation.^{38,39} Second, depression could increase the level of circulating plasma norepinephrine, caused by increased sympathetic activity.⁴⁰ The sympathetic activation and parasympathetic stimulation may then contribute to the initiation and maintenance of AF.^{41,42} Some studies also demonstrated that abnormal autonomic modulation (increased sympathetic and decreased vagal modulation), evaluated by heart rate variability, had been found in patients who experienced recurrence of AF after cardioversion.^{43,44} Third, depressed patients had a higher level of serum aldosterone,⁴⁵ and it promotes atrial fibrosis, which is an important component of the arrhythmogenic substrate of AF through mineralocorticoid receptor signalling. Some studies have shown that mineralocorticoid receptor antagonists (spironolactone and eplerenone) could reduce AF recurrence after cardioversion.^{46,47}

Previous studies have shown conflicting data on whether cardiac rehabilitation (including psychosocial support) could improve the mental health status in patients with AF.⁴⁸ Thus, more research is further needed to thoroughly examine the impact of psychological support in adults with AF to potentially reduce AT recurrence after catheter ablation.

Limitations

The limitations of our study are as follows. Data on pre-existing history of depression, other psychiatric diseases, or the use of psychoactive medications were not collected. Only the MHI-5 score measured at 3 months after ablation was

used to evaluate the outcomes at the 6 months' follow-up, to reduce the impact of long-term confounders. As the inherent shortage of the observational study, we could not draw any causal relation between psychological status and AT recurrence. It remains possible that a poorer mental health status does not increase the risk of arrhythmia recurrence after AF ablation, but that there are some other "upstream" factors that may cause both conditions. In addition, patients with depressive symptoms may be more likely to over-report symptoms and therefore have their arrhythmia documented. However, when only the routine follow-up Holters were used to analyse AT recurrence, the trend was consistent with the overall results. Lastly, this is a single-centre study with a small sample size. These results need to be confirmed in large multicentre clinical studies.

Conclusions

A poorer mental health status is associated with AT recurrence after catheter ablation. An integrated and holistic management of patients with AF after ablation therapy may have a positive impact. The assessment of the mental health status of patients with AF undergoing ablation may allow for a postablation intervention trial of psychological support and counselling to potentially reduce AT recurrence.

Acknowledgements

This study was based in part on data from the Chinese Atrial Fibrillation Registry (CAFR). We would like to thank the CAFR investigators for assistance in the data collection. We thank Prof. John Sanderson for editing this manuscript.

Funding Sources

This work was supported by the National Key Research and Development Program of China (2016YFC0900901), grant from the National Science Foundation of China (81530016), and grants from Beijing Municipal Commission of Science and Technology (D151100002215003). The construction of the CAFR was also supported by grants from Bristol-Myers Squibb, Pfizer, Johnson & Johnson, Boehringer-Ingelheim, and Bayer.

Disclosures

Changsheng Ma has received honoraria from Bristol-Myers Squibb, Pfizer, Johnson & Johnson, Boehringer-Ingelheim, and Bayer for giving lectures. Jianzeng Dong has received

honoraria from Johnson & Johnson for giving lectures. The rest of the authors have no conflicts of interest to disclose.

References

- Benjamin EJ, Wolf PA, D'Agostino RB, et al. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation* 1998;98:946-52.
- Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *Am J Cardiol* 1998;82:2N-9N.
- Wang TJ, Larson MG, Levy D, et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. *Circulation* 2003;107:2920-5.
- Dorian P, Jung W, Newman D, et al. The impairment of health-related quality of life in patients with intermittent atrial fibrillation: implications for the assessment of investigational therapy. *J Am Coll Cardiol* 2000;36:1303-9.
- Reed JL, Clarke AE, Faraz AM, et al. The impact of cardiac rehabilitation on mental and physical health in patients with atrial fibrillation: a matched case-control study. *Can J Cardiol* 2018;34:1512-21.
- McCabe PJ. Psychological distress in patients diagnosed with atrial fibrillation: the state of the science. *J Cardiovasc Nurs* 2010;25:40-51.
- Schnabel RB, Michal M, Wilde S, et al. Depression in atrial fibrillation in the general population. *PLoS One* 2013;8:e79109.
- Dąbrowski R, Smolis-Bąk E, Kowalik I, et al. Quality of life and depression in patients with different patterns of atrial fibrillation. *Kardiologia Pol* 2010;68:1133-9.
- Lioni L, Vlachos K, Letsas KP, et al. Differences in quality of life, anxiety and depression in patients with paroxysmal atrial fibrillation and common forms of atrioventricular reentry supraventricular tachycardias. *Indian Pacing Electrophysiol J* 2014;14:250-7.
- Thrall G, Lip GY, Carroll D, Lane D. Depression, anxiety, and quality of life in patients with atrial fibrillation. *Chest* 2007;132:1259-64.
- Lampert R, Jamner L, Burg M, et al. Triggering of symptomatic atrial fibrillation by negative emotion. *J Am Coll Cardiol* 2014;64:1533-4.
- Whang W, Davidson KW, Conen D, et al. Global psychological distress and risk of atrial fibrillation among women: the women's health study. *J Am Heart Assoc* 2012;1:e001107.
- Ganesan AN, Shipp NJ, Brooks AG, et al. Long-term outcomes of catheter ablation of atrial fibrillation: a systematic review and meta-analysis. *J Am Heart Assoc* 2013;2:e004549.
- Andrade JG, Verma A, Mitchell LB, et al. 2018 Focused update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. *Can J Cardiol* 2018;34:1371-92.
- Balk EM, Garlitski AC, Alsheikh-Ali AA, et al. Predictors of atrial fibrillation recurrence after radiofrequency catheter ablation: a systematic review. *J Cardiovasc Electrophysiol* 2010;21:1208-16.
- January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol* 2014;64:e1-76.
- Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. *Chest* 2010;137:263-72.
- Sang C, Jiang C, Dong J, et al. A new method to evaluate linear block at the left atrial roof: is it reliable without pacing. *J Cardiovasc Electrophysiol* 2010;21:741-6.
- Dong J, Liu X, Long D, et al. Single-catheter technique for pulmonary vein antrum isolation: is it sufficient to identify and close the residual gaps without a circular mapping catheter. *J Cardiovasc Electrophysiol* 2009;20:273-9.
- Dong JZ, Sang CH, Yu RH, et al. Prospective randomized comparison between a fixed '2C3L' approach vs. stepwise approach for catheter ablation of persistent atrial fibrillation. *Europace* 2015;17:1798-806.
- Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Europace* 2018;20:e1-160.
- Spertus J, Dorian P, Bubien R, et al. Development and validation of the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) Questionnaire in patients with atrial fibrillation. *Circ Arrhythm Electrophysiol* 2011;4:15-25.
- Rumpf HJ, Meyer C, Hapke U, John U. Screening for mental health: validity of the MHI-5 using DSM-IV Axis I psychiatric disorders as gold standard. *Psychiatry Res* 2001;105:243-53.
- Cuijpers P, Smits N, Donker T, ten HM, de Graaf R. Screening for mood and anxiety disorders with the five-item, the three-item, and the two-item Mental Health Inventory. *Psychiatry Res* 2009;168:250-5.
- Li L, Wang HM, Shen Y. Chinese SF-36 Health Survey: translation, cultural adaptation, validation, and normalisation. *J Epidemiol Community Health* 2003;57:259-63.
- Yang Z, Li W, Tu X, et al. Validation and psychometric properties of Chinese version of SF-36 in patients with hypertension, coronary heart diseases, chronic gastritis and peptic ulcer. *Int J Clin Pract* 2012;66:991-8.
- Whang W, Kubzansky LD, Kawachi I, et al. Depression and risk of sudden cardiac death and coronary heart disease in women: results from the Nurses' Health Study. *J Am Coll Cardiol* 2009;53:950-8.
- Yamazaki S, Fukuhara S, Green J. Usefulness of five-item and three-item Mental Health Inventories to screen for depressive symptoms in the general population of Japan. *Health Qual Life Outcomes* 2005;3:48.
- Lange HW, Herrmann-Lingen C. Depressive symptoms predict recurrence of atrial fibrillation after cardioversion. *J Psychosom Res* 2007;63:509-13.
- Yu S, Zhao Q, Wu P, et al. Effect of anxiety and depression on the recurrence of paroxysmal atrial fibrillation after circumferential pulmonary vein ablation. *J Cardiovasc Electrophysiol* 2012;23(suppl 1):S17-23.
- Yu SB, Hu W, Zhao QY, et al. Effect of anxiety and depression on the recurrence of persistent atrial fibrillation after circumferential pulmonary vein ablation. *Chin Med J (Engl)* 2012;125:4368-72.
- Efremidis M, Letsas KP, Lioni L, et al. Association of quality of life, anxiety, and depression with left atrial ablation outcomes. *Pacing Clin Electrophysiol* 2014;37:703-11.
- Stewart JC, Janicki-Deverts D, Muldoon MF, Kamarck TW. Depressive symptoms moderate the influence of hostility on serum interleukin-6 and C-reactive protein. *Psychosom Med* 2008;70:197-204.
- Danner M, Kasl SV, Abramson JL, Vaccarino V. Association between depression and elevated C-reactive protein. *Psychosom Med* 2003;65:347-56.

35. Jeenger J, Sharma M, Mathur DM, Amandeep. Associations of number and severity of depressive episodes with C-reactive protein and Interleukin-6. *Asian J Psychiatr* 2017;27:71-5.
36. Issac TT, Dokainish H, Lakkis NM. Role of inflammation in initiation and perpetuation of atrial fibrillation: a systematic review of the published data. *J Am Coll Cardiol* 2007;50:2021-8.
37. Aviles RJ, Martin DO, Apperson-Hansen C, et al. Inflammation as a risk factor for atrial fibrillation. *Circulation* 2003;108:3006-10.
38. Malouf JF, Kanagala R, Al AFO, et al. High sensitivity C-reactive protein: a novel predictor for recurrence of atrial fibrillation after successful cardioversion. *J Am Coll Cardiol* 2005;46:1284-7.
39. Jiang H, Wang W, Wang C, Xie X, Hou Y. Association of pre-ablation level of potential blood markers with atrial fibrillation recurrence after catheter ablation: a meta-analysis. *Europace* 2017;19:392-400.
40. Veith RC, Lewis N, Linares OA, et al. Sympathetic nervous system activity in major depression. Basal and desipramine-induced alterations in plasma norepinephrine kinetics. *Arch Gen Psychiatry* 1994;51:411-22.
41. Arora R. Recent insights into the role of the autonomic nervous system in the creation of substrate for atrial fibrillation: implications for therapies targeting the atrial autonomic nervous system. *Circ Arrhythm Electrophysiol* 2012;5:850-9.
42. Shen MJ, Choi EK, Tan AY, et al. Neural mechanisms of atrial arrhythmias. *Nat Rev Cardiol* 2011;9:30-9.
43. Lombardi F, Colombo A, Basilio B, et al. Heart rate variability and early recurrence of atrial fibrillation after electrical cardioversion. *J Am Coll Cardiol* 2001;37:157-62.
44. Akyürek O, Diker E, Güldal M, Oral D. Predictive value of heart rate variability for the recurrence of chronic atrial fibrillation after electrical cardioversion. *Clin Cardiol* 2003;26:196-200.
45. Murck H, Held K, Ziegenbein M, et al. The renin-angiotensin-aldosterone system in patients with depression compared to controls—a sleep endocrine study. *BMC Psychiatry* 2003;3:15.
46. Lavall D, Selzer C, Schuster P, et al. The mineralocorticoid receptor promotes fibrotic remodeling in atrial fibrillation. *J Biol Chem* 2014;289:6656-68.
47. Neefs J, van den Berg NW, Limpens J, et al. Aldosterone pathway blockade to prevent atrial fibrillation: a systematic review and meta-analysis. *Int J Cardiol* 2017;231:155-61.
48. Reed JL, Terada T, Chirico D, Prince SA, Pipe AL. The effects of cardiac rehabilitation in patients with atrial fibrillation: a systematic review. *Can J Cardiol* 2018;34:S284-95.