Cardiovascular Topics

Obesity is associated with long-term outcome of catheter ablation of atrial fibrillation in patients with dilated cardiomyopathy

Jiaqi Yang, Tienan Sun, Xunxun Feng, Yuchao Zhang, Biyang Zhang, Yang Liu, Qianyun Guo

Abstract

Background: Patients with atrial fibrillation (AF) and dilated cardiomyopathy (DCM) often exhibit cardiac dysfunction and a poor prognosis. However, the specific reasons are unclear. This study aimed to describe the impact of obesity in patients with AF and DCM.

Methods: Seventy-four consecutive patients with AF and DCM were enrolled and classified by body mass index. We measured primary endpoints, including cardiac death, recurrent AF, recurrent atrial tachyarrhythmia and stroke, as well as secondary endpoints.

Results: In multivariate analysis, compared to the normal-weight group, the overweight and obese groups had greater incidences of recurrent AF (0.0 vs 30.3 vs 40.0%, respectively, log-rank $p = 0.048$) and rehospitalisation (9.1 vs 36.4 vs 45.0%, respectively, log-rank $p = 0.035$). Compared to the normal-weight group, five-year outcomes for primary endpoints were inferior in the overweight and obese groups (18.2 vs 30.3 vs 50.0%, respectively, log-rank $p = 0.042$). Overweight patients exhibited more benefit in recovery of left ventricular ejection fraction after ablation (from 39.1 to 50.0%, $p = 0.005$) than the normal-weight group (from 43.1 to 52.3%, $p = 0.199$) and obese group (from 44.9 to 51.2%, $p = 0.216$).

Conclusion: Patients with AF and DCM with overweight or obesity exhibited worse long-term outcomes in recurrent AF than normal-weight patients. However, overweight patients showed the most benefit in cardiac function after ablation.

Keywords: obesity, atrial fibrillation, dilated cardiomyopathy, heart failure, body mass index

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Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice, affecting one to 4% of the general population, and is responsible for considerable morbidity and mortality rates, primarily because of an increased risk of stroke and heart failure.[1] As one of the most common causes of deterioration in cardiac function in the setting of dilated cardiomyopathy (DCM),[2] AF often complicates the course of DCM and, in some cases, may be the presenting feature.[3]

As an effective method for the treatment of AF, ablation is widely used for improving heart function and quality of life in patients with AF complicated with heart failure.[4] For patients with AF and DCM, ablation for AF has also been shown to be an effective means of improving left ventricular ejection fraction (LVEF) and reducing the incidence of secondary endpoints, including a reduction in left ventricular (LV) and left atrial (LA) dimensions, B-type natriuretic peptide levels and New York Heart Association (NYHA) functional class.[5,6]

Studies have shown that obesity is a risk factor for the incidence and recurrence of AF after catheter ablation and leads to significant atrial remodelling. For each one-point increase in body mass index (BMI), the incidence of AF increased by three to 7% and the recurrence rate of catheter ablation increased by 3.1%.[7] However, there are few studies focused on prognostic factors in patients with DCM and AF after ablation. In this study, we aimed to show the impact of obesity on long-term outcomes in patients with DCM with AF after ablation.

Methods

Enrolled patients were searched for co-diagnoses of DCM and AF, according to electronic medical records at the Beijing Anzhen Hospital between 2008 and 2015. The diagnosis of DCM included the presence of the following: (1) cardiac enlargement and reduced LV systolic function, with or without clinical congestive heart failure; or (2) X-ray and echocardiographic evidence of LV end-diastolic diameter > 55 mm, LVEF ≤ 50% and decreased wall motion.

Patients with the following were excluded from this study: (1) severe valvular diseases, peripartum cardiomyopathy, coronary heart disease (coronary angiography found one or more stenoses

> 50%); and (2) history of acute myocardial infarction, systemic hypertension or drug abuse. These standards conformed to American Heart Association/European Society of Cardiology criteria.[8,9]

AF was detected by 12-lead electrocardiography and dynamic electrocardiography combined with a medical history and was confirmed by a physician. All diagnostic criteria for AF came from the American Heart Association/American College of Cardiology/European Society of Cardiology guidelines.[10] BMI was calculated by weight/height^2 and is expressed as kg/m^2. Patients were classified as having normal weight (18.5 < BMI < 24 kg/m^2), overweight (24 ≤ BMI < 28 kg/m^2) or obesity (≥ 28 kg/m^2), following guidelines by the Working Group on Obesity in China.[11]

All baseline characteristics were collected by physicians through the electronic medical record system, and information on radiofrequency ablation procedures was obtained from surgery records. Baseline information included age, gender, BMI, NYHA class, admission times, AF heart rate, smoking status and alcohol intake. Past medical histories included hypertension, hyperlipidaemia, diabetes, stroke, heart failure, chronic obstructive pulmonary disease, electrical cardioversion and other arrhythmias.

Echocardiography was used to record cardiac indices, including LA diameter, LV end-diastolic diameter, LV end-systolic diameter, LVEF and LV posterior wall motion range (LVPMR), as well as the status of the mitral and aortic valves, and the presence of pulmonary hypertension.

Laboratory tests included creatinine, C-reactive protein, troponin, B-type brain natriuretic peptide and the international normalised ratio. All medication treatments during hospitalisation were recorded, including the use of antiplatelet and anticoagulant agents, β-blockers, calcium channel blockers (CCB), amiodarone and various diuretics. A total of 74 consecutive patients with DCM and AF met the inclusion criteria and were enrolled.

Catheter ablation was guided by a three-dimensional mapping system (Carto, Biosense Webster, Diamond Bar, CA, USA). The SMARTABLATE system (STOCKERT GmbH, USA) was used to perform radiofrequency ablation. First, patients with AF and DCM underwent circumferential pulmonary vein ablation (CPVA) to obtain pulmonary vein isolation (PVI). Second, some of those patients underwent three-line ablation, including (1) the mitral isthmus line, between the mitral annulus and the left inferior pulmonary vein; (2) the cavotricuspid isthmus (CTI) line, if atrial tachycardia was consistent with CTI-dependent AF; and (3) the roof line, which is located between two pulmonary veins.

Complex fractionated atrial electrograms (CFAEs) were used for long-term persistent AF. The coronary sinus was ablated if necessary. If AF still existed, electrical cardioversion was used to restore sinus rhythm. Under sinus rhythm, PVI was reconfirmed and additional linear ablations were performed, if necessary, to sustain a bidirectional block of lines.

The endpoints in our study were divided into primary and secondary endpoints. Primary endpoints included cardiac death, recurrent AF, recurrent atrial tachyarrhythmia (ATa), stroke and major bleeding. Secondary endpoints included rehospitalisation, pacemaker implantation, mild bleeding and the emergence of new arrhythmias.

The follow-up period began on the day of the first admission and continued until the occurrence of the first cardiac event, cardiac death or the date of the five-year follow-up deadline. Information on the endpoints was ascertained via re-admission records, clinical visits, telephone contact and text messages. For deceased patients, death certificates were obtained and the next of kin was interviewed to confirm the date and cause of death. To collect accurate information reflecting the current situation during follow up, echocardiography was collected within three months from the day of follow up, and NYHA class was determined by clinical staff by phone call.

This study conformed to the principles of the Declaration of Helsinki and approval of the local ethical committee was obtained. All patients provided informed consent prior to their inclusion in the study.

A total number of 74 patients who met the inclusion were initially selected in our study. Among them, the ablation failed in two patients and they remained in AF status. Another eight patients were lost to follow up due to either loss of contact or unwillingness to be followed up. Patients lost to follow up were excluded from further analysis.

Statistical analysis

All analyses were performed using SPSS statistical software, version 21.0 (SPSS Inc, Chicago, USA). All tests were two-sided, and a p-value < 0.05 was considered statistically significant. Continuous data are presented as mean ± standard deviation or as medians and interquartile ranges. Categorical variables

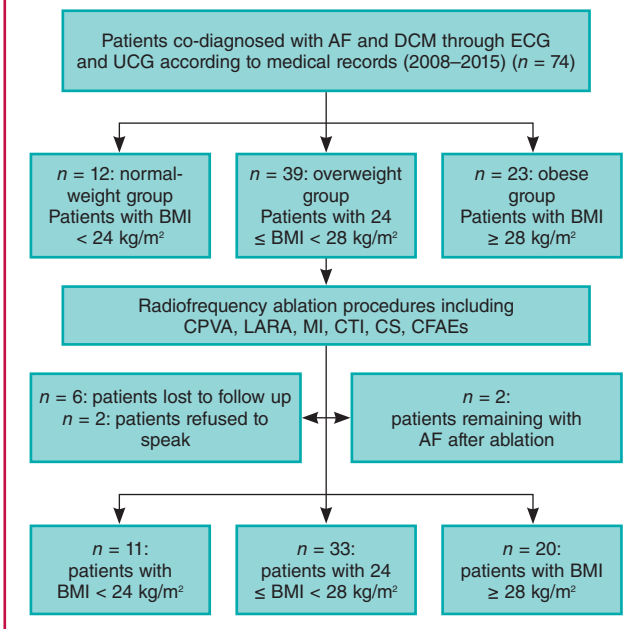

Fig. 1. Flow chart of our study. A total of 74 patients with AF and DCM were enrolled in our study, and 64 of them remained after follow up. AF, atrial fibrillation; DCM, dilated cardiomyopathy; ECG, electrocardiography; UCG, echocardiography; CPVA, circumferential pulmonary vein ablation; LARA, left atrial roof line ablation; MI, mitral isthmus; CTI, cavotricuspid isthmus; CS, coronary sinus; CFAEs, complex fractionated atrial electrograms.

Table 1. Baseline characteristics of the study participants

Variables	*Total* (n = *74*)	*Normal* (n = *12*)	*Overweight* (n = *39*)	*Obese* (n = *23*)	p-*value*
Age, years	52.203 ± 10.825	56.583 ± 7.960	52.410 ± 11.078	49.565 ± 11.285	0.198
Male, *n* (%)	66 (89.2)	10 (83.3)	34 (87.2)	22 (95.7)	0.463
BMI, kg/m²	26.805 ± 3.241	22.518 ± 1.283	25.862 ± 1.109	30.640 ± 2.218	0.000*
NYHA, *n* (%)					0.580
I	18 (24.3)	2 (16.7)	9 (23.1)	7 (30.4)	
II	35 (47.3)	4 (33.3)	19 (48.7)	12 (52.2)	
III	18 (24.3)	5 (41.7)	10 (25.6)	3 (13.0)	
IV	3 (4.1)	1 (2.9)	1 (2.6)	1 (4.4)	
Admission times, *n* (%)	1.297 ± 0.735	1.250 ± 0.622	1.359 ± 0.903	1.217 ± 0.422	0.748
Persistent AF, *n* (%)	58 (78.4)	12 (100.0)	30 (76.9)	16 (69.6)	0.113
Premature AF, *n* (%)	47 (5.4)	6 (50.0)	28 (71.8)	13 (56.5)	0.319
AFHR, bpm	84.500 (70.000–102.500)	75.000 (62.250–93.250)	88.000 (76.000–111.000)	78.000 (66.000–100.000)	0.114
HTN, *n* (%)	26 (35.1)	5 (41.7)	13 (33.3)	8 (34.8)	0.873
Diabetes, *n* (%)	7 (9.5)	2 (16.7)	2 (5.1)	3 (13.0)	0.392
Hyperlipidaemia, *n* (%)	11 (14.9)	3 (25.0)	3 (7.7)	5 (21.7)	0.022*
Stroke, *n* (%)	2 (2.7)	0 (0.0)	1 (2.6)	1 (4.3)	0.759
Other arrhythmias, *n* (%)	5 (6.8)	2 (16.7)	2 (5.1)	1 (4.3)	0.335
Heart failure, *n* (%)	6 (8.3)	1 (8.3)	2 (5.1)	3 (13.0)	0.555
COPD, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.000
Electrical cardioversion, *n* (%)	4 (5.4)	1 (8.3)	3 (7.7)	0 (0.0)	0.394
Smoking, *n* (%)	49 (66.2)	9 (75.0)	23 (59.0)	17 (73.9)	0.390
Alcohol, *n* (%)	34 (45.9)	6 (50.0)	19 (48.7)	9 (39.1)	0.738
LA diameter, mm	56.368 ± 1.637	55.000 ± 3.000	57.222 ± 2.402	55.200 ± 4.461	0.880
LVEDd, mm	60.737 ± 1.806	58.500 ± 7.500	62.667 ± 3.210	60.800 ± 1.744	0.079
LVESd, mm	47.263 ± 2.079	42.500 ± 6.500	50.111 ± 3.931	46.800 ± 1.281	0.070
LVEF, %	41.248 ± 1.308	53.000 ± 4.000	38.111 ± 4.367	39.000 ± 3.688	0.357
LVPMR, mm	8.737 ± 0.582	9.000 ± 2.000	8.111 ± 1.033	10.200 ± 0.200	0.020*
MR, *n* (%)					0.122
non	13 (17.6)	2 (16.7)	3 (7.7)	8 (34.8)	
mild	39 (52.7)	6 (50.0)	23 (59.0)	10 (43.5)	
≥ moderate	22 (29.7)	4 (33.3)	13 (33.3)	5 (21.7)	
AR, *n* (%)					0.184
non	52 (70.3)	7 (58.3)	25 (64.1)	20 (87.0)	
mild	16 (21.6)	3 (25.0)	10 (25.6)	3 (13.0)	
≥ moderate	6 (8.1)	2 (16.7)	4 (10.3)	0 (0.0)	
Pulmonary hypertension, *n* (%)					0.579
non	62 (83.8)	9 (75.0)	33 (84.6)	20 (87.0)	
mild	12 (16.2)	3 (25.0)	6 (15.4)	3 (13.0)	
≥ moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Cr, µmol/l	79.700 (72.600–90.000)	77.650 (63.325–87.875)	82.600 (74.275–98.250)	79.600 (72.400–84.150)	0.100
CRP, µmol/l	0.785 (0.433–2.403)	2.090 (0.230–3.560)	0.630 (0.405–1.220)	1.060(0.520–4.160)	0.019*
cTNI	0.010 (0.010–0.272)	0.170 (0.010–4.650)	0.296 ± 0.262	3.464 ± 1.880	0.097
BNP	229.000 (92.175–449.500)	142.500 (89.425–339.175)	241.000 (64.800–445.000)	243.000 (152.000–523.000)	0.992
INR	1.095 (0.983–1.513)	1.110 (0.990–1.540)	1.090 (0.985–1.613)	1.080 (0.965–1.150)	0.226
Rate-control, *n* (%)					
β-blocker	40 (54.1)	4 (33.3)	21 (53.8)	15 (65.2)	0.205
Digoxin	5 (6.8)	1 (8.3)	3 (7.7)	1 (4.3)	0.860
CCB	9 (12.2)	4 (33.3)	3 (7.7)	2 (8.7)	0.049*
Rhythm-control, *n* (%)					
Amiodarone	48 (63.5)	9 (75.0)	24 (61.5)	15 (65.2)	0.703
Sotalol	34 (45.9)	5 (31.3)	20 (51.3)	9 (39.1)	0.457
Antiplatelet, *n* (%)					
Aspirin	3 (4.1)	0 (0.0)	1 (2.6)	2 (8.7)	0.377
Clopidogrel	1 (1.4)	0 (0.0)	0 (0.0)	1 (4.3)	0.335
Ticagrelor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.000
Anticoagulation, *n* (%)					
Warfarin	41 (56.9)	7 (58.3)	25 (64.1)	9 (39.1)	0.162
Dabigatran	17 (23.0)	4 (33.3)	6 (15.4)	7 (30.4)	0.265
Rivaroxiban	13 (17.6)	1 (8.3)	7 (17.9)	5 (21.7)	0.621
Statin	16 (21.6)	2 (16.7)	6 (15.4)	8 (34.8)	0.186
BAN	26 (36.1)	4 (33.3)	15 (38.5)	7 (30.4)	0.770
Spironolactone	39 (52.7)	5 (41.7)	23 (59.0)	11 (47.8)	0.502
Hydrochlorothiazide	7 (9.5)	0 (0.0)	6 (15.4)	1 (4.3)	0.174
ACEI/ARB	55 (74.3)	8 (66.7)	31 (79.5)	16 (69.6)	0.563

BMI, body mass index; NYHA: New York Heart Association; AFHR: atrial fibrillation heart rate; HTN: hypertension; COPD: chronic obstructive pulmonary disease; LVEDd: left ventricular end-diastolic diameter; LVESd, left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; LVPMR, left ventricular posterior wall motion range; MR, mitral valves; AR, aortic valves; Cr, creatinine; CRP, C-reactive protein; cTNI, troponin; BNP, B-type brain natriuretic peptide; INR, international normalised ratio; CCB, calcium channel blockers; BAN, furosemide; ACEI/ARB, angiotension converting enzyme inhibitors/angiotensin receptor blockers.

are summarised as percentages and were compared using the chi-squared test where appropriate.

Multivariate binary logistic regression was used to analyse the risk factors for patients with obesity and AF and DCM. Univariate and multivariate Cox proportional hazards models were used to identify study endpoint predictors. Variables with univariate *p*-values < 0.10 were selected for multivariate analysis and are expressed as hazard ratios with 95% confidence intervals. Multivariate Cox regression analysis was performed using an enter method. Survival was graphically represented using Kaplan–Meier curves. Differences in survival rates were compared using the log-rank test.

Results

A total of 74 patients (66 males and eight females) who had concomitant diagnoses of AF and DCM were enrolled from Beijing Anzhen Hospital between 2008 and 2015 (Fig. 1). Baseline characteristics are summarised in Table 1. The 74 patients had a mean BMI of 26.8 ± 3.2 kg/m^2, among whom 39 patients (52.7%) were overweight (24 ≤ BMI < 28 kg/m^2; mean 25.9 ± 1.1 kg/m^2) and 23 patients (31.1%) were obese (BMI ≥ 28 kg/m^2; mean 30.6 ± 2.2 kg/m^2).

There were no significant differences in ages among the normal-weight, overweight and obese groups (56.6 ± 8.0 vs 52.4 ± 11.1 vs 49.6 ± 11.3 years, respectively, $p = 0.198$), number of males (10 vs 34 vs 22, respectively, $p = 0.463$), laboratory examinations and past medical histories, except hyperlipidaemia ($n = 3$ vs 3 vs 5, respectively, $p = 0.022$) and C-reactive protein (2.1, 0.2–3.6 vs 0.6, 0.4–1.2 vs 1.1, 0.5–4.2 µmol/l, respectively, $p = 0.019$). The normal-weight, overweight and obese groups were otherwise well matched in NYHA classes (NYHA ≥ 2; $n = 10$ vs 30 vs 16, respectively, $p = 0.580$), admission times (1.3 ± 0.6 vs 1.4 ± 0.9 vs 1.2 ± 0.4 days, respectively, $p = 0.748$), types of AF (persistent AF; 12 vs 30 vs 16, respectively, $p = 0.089$) and heart rate during AF episodes (84.5, 70.0–102.5 vs 76.0, 88.0–111.0 vs 66.0, 78.0–100.0 bpm, respectively, $p = 0.113$).

Use of medications for rate control, rhythm control, anticoagulation therapy and heart failure treatment tended to be consistent in all patients except for the usage of CCB (4 vs 3 vs 2, respectively, $p = 0.049$). The results of ultrasound cardiography showed a significant difference in LVPMR among the three groups (9.0 ± 2.0 vs 8.1 ± 1.0 vs 10.2 ± 0.2 mm, respectively, $p = 0.020$).

All procedural characteristics are summarised in Table 2. A total of 74 patients completed successful CPVA, and other procedures among the normal-weight, overweight and obese groups showed no significant differences except CFAEs (2 vs 1 vs 4, respectively, $p = 0.036$). The normal-weight group underwent a longer procedural duration than the overweight and obese groups (190.0, 166.3–300.0 vs 120.0, 100.0–180.0 vs 135.0, 120–187.5 h, respectively, $p = 0.004$); however, there was no difference in radiation duration among the three groups (19.0, 10.0– 67.5 vs 14.5, 6.0– 20.5 vs 8.0, 5.5– 21.0 h, respectively, $p = 0.216$). After ablation, 12 patients (100%) in the normal-weight group presented with immediate sinus rhythm, a larger number

Table 2. Procedural characteristics of the study participants

Variables	*Total (n = 74)*	*Normal (n = 12)*	*Overweight (n = 39)*	*Obese (n = 23)*	p-*value*
Procedure duration, h	150 (120–183)	190 (166.25–300)	120 (100–180)	135 (120–187.5)	0.004*
Radiation duration, h	10 (6–21.75)	19 (10–67.5)	14.5 (6–20.25)	8 (5.5–21)	0.216
CPVA, *n* (%)	74 (100.0)	12 (100.0)	39 (100.0)	23 (100.0)	1.000
LARA, *n* (%)	54 (73.0)	9 (75.0)	28 (71.8)	17 (73.9)	0.382
MAI, *n* (%)	53 (71.6)	8 (66.7)	29 (74.4)	16 (69.6)	0.907
CTI, *n* (%)	53 (71.6)	8 (66.7)	29 (74.4)	16 (69.6)	0.907
CS, *n* (%)	34 (45.9)	5 (41.7)	17 (43.6)	12 (52.2)	0.791
CFAEs, *n* (%)	7 (9.5)	2 (16.7)	1 (2.6)	4 (17.4)	0.036*
CV, *n* (%)	44 (59.5)	7 (58.3)	23 (59.0)	14 (60.9)	0.986
Immediate sinus rhythm	68 (91.9)	12 (100.0)	38 (97.4)	22 (95.7)	0.775

CPVA, circumferential pulmonary vein ablation; LARA, left atrial roof line ablation, MAI, mitral isthmus; CTI, cavotricuspid isthmus; CS, coronary sinus; CFAEs, complex fractionated atrial electrograms; CV: cardioversion.

Table 3. Five-year outcomes of the study participants

Outcomes	*Total (n = 64)*	*Normal (n = 11)*	*Overweight (n = 33)*	*Obese (n = 20)*	p_1	p_2	p_3
Follow up, days	874.5 (270.0–1825.0)	1825.0	1007.0 (288.0–1825.0)	270.0 (78.3–1558.0)	0.002*	0.020*	0.000*
Major endpoints	21 (32.8)	1 (9.1)	10 (30.3)	10 (50.0)	0.042*	0.174	0.026*
Cardiac death	2 (3.1)	1 (9.1)	0 (0.0)	1 (5.0)	0.271	0.083	0.642
Recurrent AF	19 (29.7)	0 (0.0)	11 (33.3)	8 (40.0)	0.064	0.037*	0.020*
Recurrent ATa	21 (32.8)	0 (0.0)	11 (33.3)	10 (50.0)	0.014*	0.037*	0.007*
Stroke	1 (1.6)	0 (0.0)	0 (0.0)	1 75 (5.0)	0.333	–	0.458
Major bleeding	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0	0	0
Secondary endpoints	28 (43.8)	1 (9.1)	16 (48.5)	11 (55.0)	0.029*	0.026*	0.012*
Re-hospitalisation	22 (34.4)	1 (9.1)	12 (36.4)	9 (45.0)	0.104	0.101	0.042*
New arrhythmia	13 (20.3)	1 (9.1)	5 (15.2)	7 (35.0)	0.095	0.612	0.115
Mild bleeding	6 (9.4)	0 (0.0)	3 (9.1)	3 (15.0)	0.386	0.310	0.187
Pacemaker implanting	4 (6.3)	1 (9.1)	1 (3.0)	2 (10.0)	0.554	0.421	0.936

p_1, compound log-rank *p*-value for overweight and obese groups compared to the normal-weight group; p_2, log-rank *p*-value for overweight group compared to normal-weight group; p_3, log-rank *p*-value for obese group compared to normal-weight group.
Ata, atrial tachyarrhythmia.

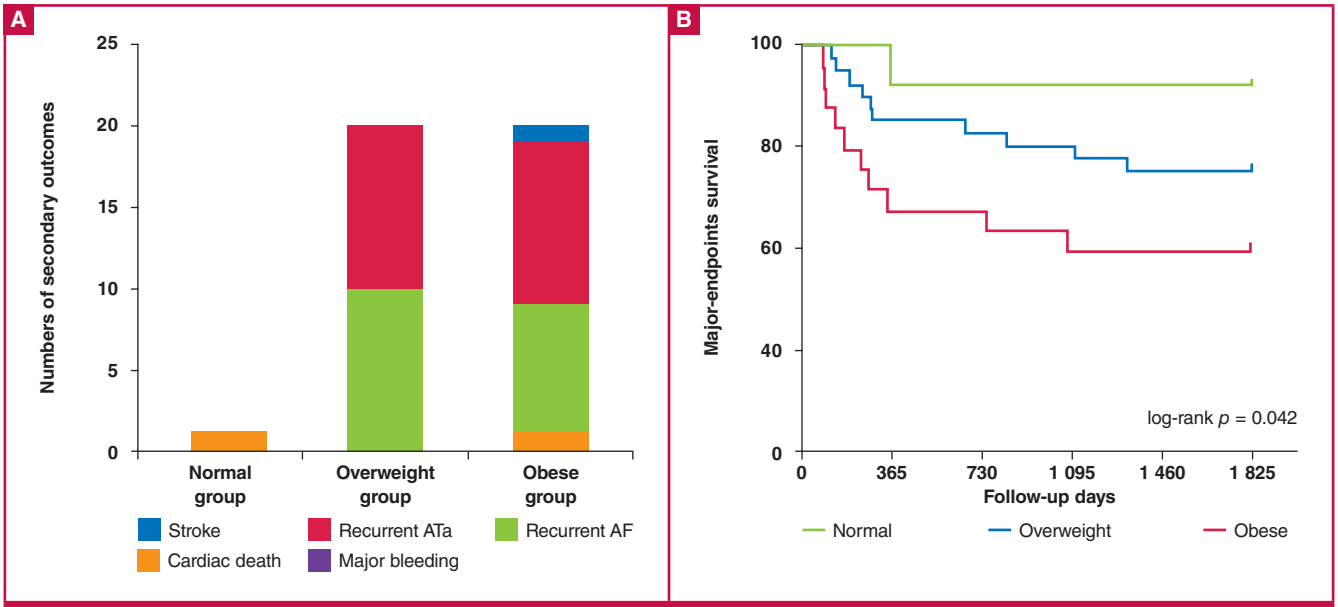

Fig. 2. Major outcomes in 64 AF and DCM patients after ablation. A: Major endpoints in the three groups. B: Kaplan–Meier curves for major endpoints. ATa, atrial tachyarrhythmia; AF, atrial fibrillation.

than in the overweight group (38 patients, 97.4%) and obese group (22 patients, 96.7%), although this difference was not significant ($p = 0.775$).

The long-term outcomes of patients with DCM and AF are summarised in Table 3. After a median follow up of 2.5 years (range 0.75–5 years), major adverse cardiac events occurred in 21 patients (32.8%), and the obese group exhibited more major outcomes than the normal-weight group ($n = 1$ vs 10 vs 10, respectively, log-rank $p = 0.042$). Among these, two patients (3.1%) had cardiac death ($n = 1$ vs 0 vs 1, respectively, log-rank $p = 0.271$) (Fig. 2).

The cumulative incidence of recurrent AF after multiple procedures was 29.7%. The survival of recurrent AF patients compared to the normal-weight group was inferior in the overweight and obese groups ($n = 0$ vs 11, $p = 0.037$ and 0 vs 8, respectively, log-rank $p = 0.02$), and recurrent ATa outcomes among the three groups were similar ($n = 0$ vs 11 vs 10, respectively, $p = 0.014$, Fig. 3A, B), whereas the incidence of stroke ($n = 0$ vs 0 vs 1, respectively, log-rank $p = 0.333$) showed no significant difference in all enrolled patients. Major bleeding events were not observed during follow up.

A total of 28 patients (43.8%) in the normal-weight, overweight and obese groups met secondary endpoints (1 vs 16 vs 11, respectively, log-rank $p = 0.029$, Fig. 4A). Patients in the obese group were re-admitted more frequently than those in the normal-weight group due to cardiac factors ($n = 1$ vs 9, log-rank $p = 0.042$, Fig. 4C). Thirteen of 64 patients (20.3%) had new arrhythmias, including 10 patients with atrial flutter and three with supraventricular tachycardia. However, there was no significant difference among the three groups (1 vs 5 vs 7,

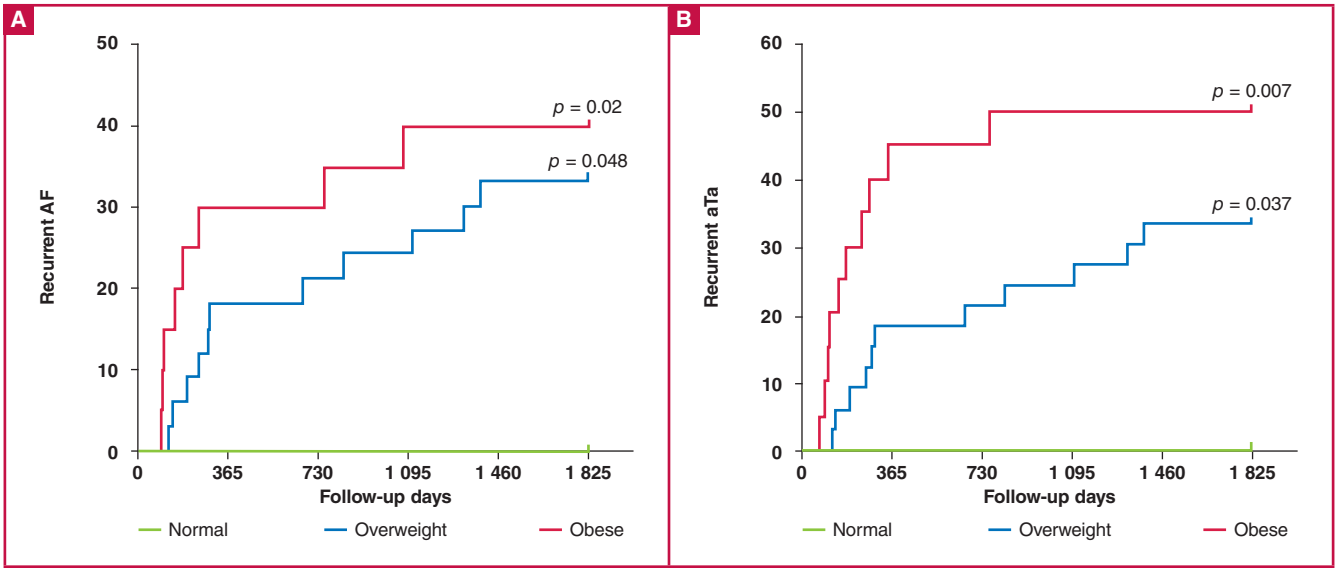

Fig. 3. A: Incidence of recurrent AF in the three groups. B: Incidence of recurrent ATa in the three groups. ATa, atrial tachyarrhythmia; AF, atrial fibrillation.

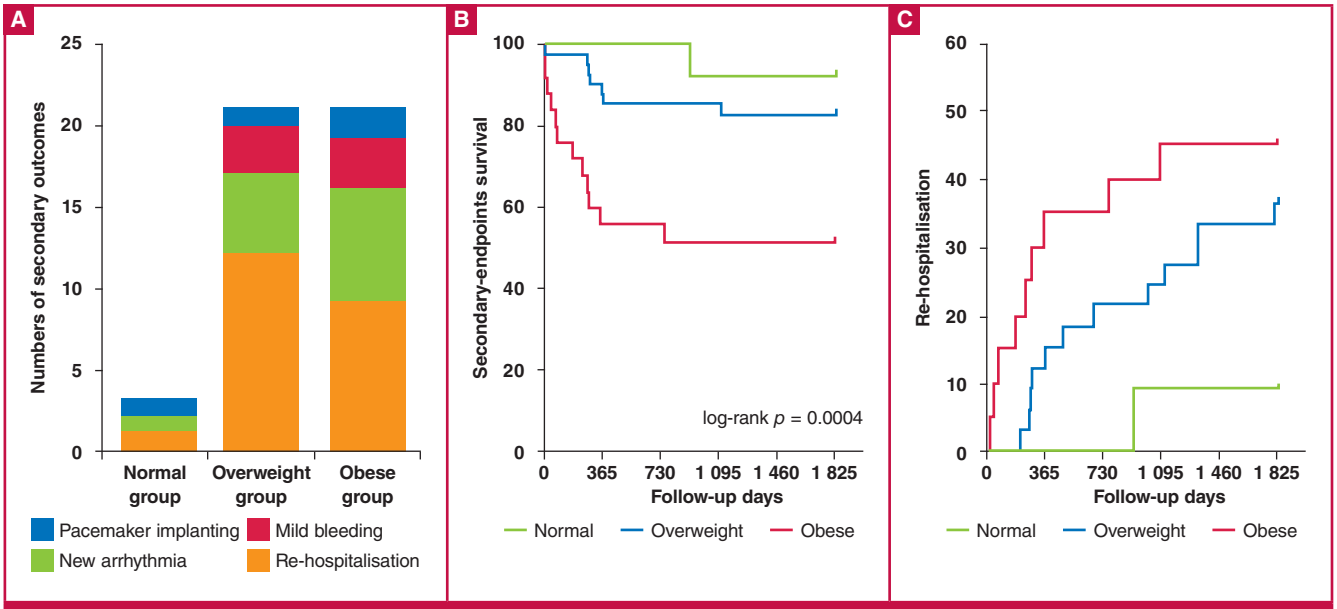

Fig. 4. Secondary outcomes in 64 AF and DCM patients after ablation. A: Secondary endpoints in the three groups. B: Kaplan–Meier curves for major endpoints. C: Incidence of recurrent rehospitalisation among the three groups.

respectively, log-rank $p = 0.095$). Mild bleeding events were only observed in three (9.1%) of the overweight and three (15.0%) of the obese patients. During follow up, four patients (6.3%) underwent pacemaker implantation and presented no significant difference among the normal-weight, overweight and obese groups (1 vs 1 vs 2, respectively, log-rank $p = 0.554$, Fig. 4B).

LVEF and NYHA classes were used to evaluate heart failure among these three groups. After ablation, the LVEF value of each group was increased to varying degrees (Fig. 1), with overweight patients achieving a significant increase in LVEF (normal-weight group: 43.1 ± 11.8 vs 53.3 ± 9.8%, overweight group: 39.1 ± 9.8 vs 50.0 ± 12.3% and obese group: 45.0 ± 11.9 vs 51.2 ± 12.5%). NYHA improved at the same time (normal-weight group: 2.5 ± 0.9 vs 1.7 ± 1.0, overweight group: 2.1 ± 0.7 vs 1.5 ± 0.7 and obese group: 2.0 ± 0.8 vs 1.5 ± 0.8). In the overweight and obese groups, NYHA scores exhibited significant improvement after ablation (Fig. 5A, B).

Discussion

The main finding of our study is that among patients with AF and DCM, obesity was associated with a worse prognosis after radiofrequency ablation of AF. The main findings are as follows: (1) the overweight and obese groups exhibited worse outcomes, including major and secondary cardiac events, than the normal-weight group; and (2) postoperative cardiac function was improved in all three groups, and the overweight group seemed to benefit the most.

BMI is not only an independent factor associated with a long-term increased risk of AF but is also a predictor of AF recurrence after ablation.[12] According to a meta-analysis,[13] for every five-unit increase in BMI, the risk of AF recurrence post-ablation increased by 13%. Another study showed similar results in that when BMI rose above 35 kg/m^2, the risk of AF recurrence increased significantly.[14] The LEGACY study also demonstrated that a body weight increase of more than 5% had

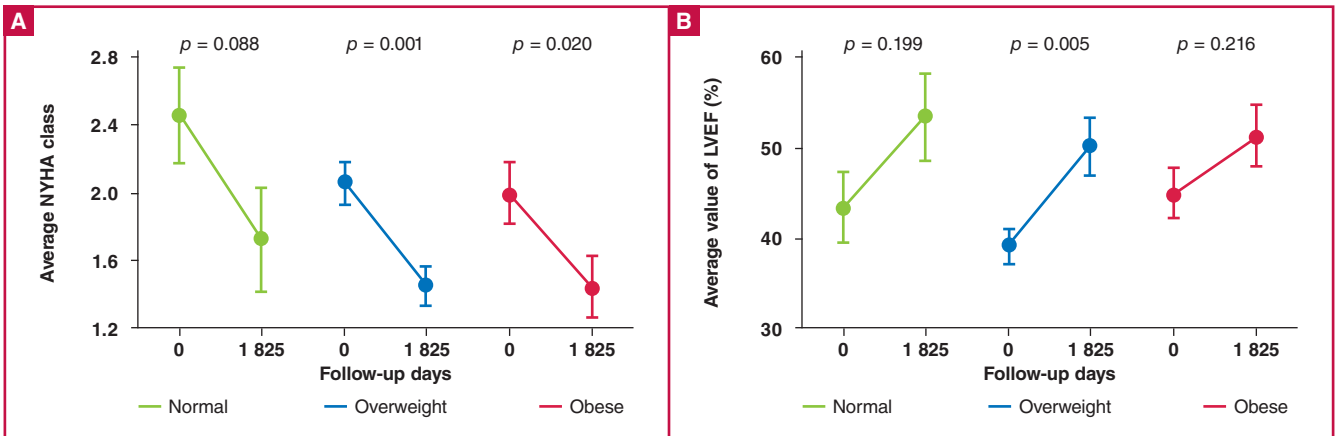

Fig. 5. Improvement of NYHA class and LVEF in patients with AF and DCM. A: The average decreasing number of NYHA classes among the three groups. B: Improvement in LVEF among the three groups. NYHA, New York Heart Association; LVEF, left ventricular ejection fraction.

an adverse effect on overall freedom from AF, with a two-fold greater likelihood of recurrent arrhythmia.[15] Therefore, body weight management is necessary for freedom from AF (FFAF) after ablation.

Based on the multiple clinical studies mentioned above, it is recommended that when discussing the risks, benefits and outcomes of AF ablation with patients, BMI should be considered and weight loss may be needed (Class IIa, level of evidence B).[14] Furthermore, several pieces of evidence have implied that body weight control prior to ablation also benefits the patients for FFAF. The ARREST-AF prospective cohort study indicated a synthetic risk factor management, including control of body weight, glycaemic and lipid profiles, before ablation significantly decreased the incidence of recurrent AF.[16] However, there is no categorised analysis regarding body weight reduction-dependent FFAF in this study.

In 2021, a retrospective study with a larger number of 747 patients showed the benefits of FFAF from body weight reduction. In this study, obesity increased the incidence of recurrent AF within 15 months of ablation. On the other hand, weight loss before ablation improved rates of FFAF in patients both with and without obesity.[17]

Several studies have found that obesity is responsible for the new onset of AF, and that for every unit increase in BMI, the incidence of AF increases by 4%, which may be caused by LA dilation.[18] Recent studies indicate that obesity and its associated co-morbidities such as hypertension, diabetes mellitus and sleep apnoea also lead to a high incidence of AF. Although most study results have shown that obesity is an independent risk factor for cardiac diseases, other studies have shown a favourable prognosis in patients with obesity suffering from coronary artery disease, hypertension and heart failure, which is called the obesity paradox.[19]

The obesity paradox also exists in diseases including cancer, osteoporosis and chronic obstructive pulmonary disease. The explanation of the obesity paradox is that nearly 2% of slim patients may have illnesses accompanied by worse conditions, such as heart failure, multiple organ dysfunction, malignancies and malnutrition, which lead to a poor prognosis. Additionally, slim patients tend to be older than patients with overweight and obesity, which is also an underlying risk factor for the incidence of adverse cardiac events, even after therapy.

Obesity may induce the production of serum lipoproteins, which are responsible for neutralising bacterial toxins and circulating cytokines. Additionally, lower levels of adiponectin and a reduced catecholamine response in patients with obesity may increase the chances of survival.[20]

One randomised, controlled trial (RCT) showed that weight management for patients with obesity (BMI > 27 kg/m^2) was able to reduce the symptom burden and severity of AF, as well as the cumulative duration. Another observational study demonstrated better outcomes in AF catheter ablation in patients with obesity who participated in a weight-management programme. The 2019 update of the American Heart Association/American College of Cardiology/ Heart Rhythm Society guidelines for the management of patients with AF suggested that weight loss in patients with obesity is helpful for improving the symptoms and type of AF.[21]

Few studies have examined the potential risk factors in patients with AF combined with DCM. In our study of patients with AF and DCM, compared to the normal-weight group, the rates of recurrent AF and ATa were significantly higher in the overweight and obese groups. In addition, patients with obesity were re-admitted more frequently than those in the normal-weight group, mostly due to the obese group having higher rates of recurrent AF and more severely compromised cardiac function. In addition, the presentation of new arrhythmias after ablation increased as BMI increased, but this did not achieve statistical significance. This result indicated that obesity is associated with the incidence of adverse cardiac events, which may be related to a series of electrophysiological and structural changes induced by obesity.

Patients with AF and DCM tend to have a more complicated clinical presentation, poorer prognoses and are more likely to relapse than patients with only AF. Sustained obesity has proven to be related to global endocardial remodelling, characterised by LA enlargement, conduction abnormalities, fractionated electrograms and interstitial atrial fibrosis. Additionally, obesity tends to bring a heavy burden of heart failure and reduced posterior LA endocardial voltage and the infiltration of epicardial fat into the adjacent posterior LA muscle; therefore, obesity is correlated with the enhancement of optimal conditions for the occurrence of AF.[22]

Additionally, the increase of atrial/ventricular septal tension and the overstretch of the myocardium, and the conduction system that accompanies DCM also play an important role in complicated disorders. As an effective and safe treatment for AF, catheter ablation can markedly improve cardiac function, symptoms and quality of life in patients with congestive heart failure. According to a meta-analysis, for patients with AF and LV systolic dysfunction, the ventricular function was improved significantly after ablation, especially when performed in the early stages of AF and heart failure.

For patients with DCM and AF, some studies have reached similar conclusions.[23] Prabhu found that effective ablation resulted in improvement in LV volumes, LVEF and NYHA class.[5] Our study came to the same conclusion, as in all three groups, LVEF and NYHA class were improved to varying degrees, and the ablation effectively improved cardiac function in patients with DCM. Interestingly, we found that the improvement of LVEF and NYHA in the normal-weight group was not statistically significant, but in the overweight group, improvement of these outcomes was highly significant. In the obese group, there was also an obvious improvement in the NYHA score. This may have been because obesity itself puts a heavy burden on the heart. These results indicate that obesity may reduce the benefit of catheter ablation and have an adverse influence on the recovery of LVEF and improvement in quality of life.

Our study also suggests that ablation may be the first choice for patients with AF and DCM and that weight management should be considered during recovery after surgery. However, the non-randomised study by Zhao *et al.* with a small sample size showed that improvement in cardiac function after ablation was not sustained beyond three years.[6] The effect of ablation on cardiac function in patients with AF and DCM remains to be explored. Relevant large RCTs are needed.

Another dominant risk factor of AF induction is worth being discussed here. Binge alcohol intake is well investigated in clinical research, which shows that it can increase the incidence of new-onset AF in people with and without previous cardiac

diseases.[24,25] Chronic alcohol abuse causes a higher incidence of recurrent AF and worse outcomes after ablation.[26]

The probable mechanism investigated by Yan *et al*. is the activation of stress-activated c-Jun N-terminal kinase (JNK) and the downstream Ca^{2+} variations in the heart.[27] The convincing results verified from both human and animal hearts *ex vivo* showed that alcohol-exposed hearts had a higher incidence, a longer duration of AF after electrical stimulation, and a higher phosphorylation level of JNK. The pace-induced AF was abolished after inhibiting JNK, which could provide a new potential target against alcohol-induced AF in clinical treatment.

On the other hand, chronic alcohol abuse can also induce disorders of lipid metabolism and it is an independent risk factor for obesity.[28] Furthermore, alcohol abuse is one of the most important acquired factors of DCM.[29] Alcohol intake seems to interact with obesity and DCM, which induce occurrence of AF. In our data, obese patients seemed to have more alcohol intake (but not significantly) than the control group, which could also be a clue that the development of AF in obese patients with DCM is an interaction of various risk factors. To verify the effect of obesity on AF more clearly, our next study with more enrolled patients should eliminate the bias from confounding factors.

Limitations

This study was a retrospective cohort study with a relatively small sample size. Selection and recall bias may have affected the results. Therefore, we defined primary and secondary endpoints to reduce the bias arising from the retrospective study. All baseline characteristics and follow ups were performed by cardiac physicians to ensure the accuracy of the data. Several patients lost to follow up were excluded from further survival analysis (for example, changed phone numbers or address), as these could have been indications of adverse events and could have caused an underestimation of our outcomes.

Our study enrolled patients from one clinical centre, which led to the under-representation of patients with relative clinical stability and milder symptoms. We also did not collect six-minute walk test results to evaluate cardiac function because of the lack of such data in this retrospective cohort. However, patients with DCM represent a small proportion in those with AF. For example, Zhao *et al*. observed only 49 patients who met the appropriate inclusion criteria.[6] It is not feasible to enroll a large number of patients at one single clinical centre. We will address these limitations in our future studies.

Conclusion

Overweight or obese patients with AF and DCM exhibited worse long-term outcomes in recurrent AF than normal-weight patients. However, overweight patients showed the most benefit in cardiac function after ablation.

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