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Extreme Obesity is Associated with Low Success Rate of Atrial Fibrillation Catheter Ablation

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Abstract

Background: Catheter ablation (CA) is an established treatment for patients with symptomatic atrial fibrillation (AF). The purpose of this study was to evaluate the safety and efficacy of single CA in AF patients with extreme obesity (body mass index [BMI] ≥ 40 kg/m²) and its long-term impact on body weight.

Methods: Patients with BMI ≥40 kg/m² who underwent CA at the Ohio State University between 2012 and 2016 were included. The primary efficacy endpoint was no atrial arrhythmia lasting > 30 seconds without anti-arrhythmic drugs during 1-year follow-up after a single procedure.

Results: Out of 230 AF patients with BMI ≥ 40 kg/m² undergoing CA, pulmonary vein isolation was achieved in 226 (98%) patients. Seventeen patients (7.4%) experienced acute major complications, including pericardial effusion, vascular complications and respiratory failure. Patient characteristics for 135 patients with complete 1-year follow-up were as follows: mean age 58.6 ± 9.6 years, mean BMI 44.5± 4.7 kg/m², female 63 (47%), non-paroxysmal AF 100 (74%), median CHA_2DS_2-VASc score 2 (IQR:1-3). In this cohort, the primary efficacy endpoint was achieved in 44 (33%) patients. Paroxysmal AF was associated with higher CA success compared to non-paroxysmal (51 vs. 26% [p < 0.01]).There was no significant weight change even in patients with successful AF CA.

Conclusions: Extreme obesity is associated with low AF CA success, particularly in those with non-paroxysmal AF. Successful AF CA was not associated with long-term weight reduction. A better treatment strategy is needed in this population of AF and extreme obesity

Introduction

Atrial fibrillation (AF) remains the most common sustained arrhythmia and has been progressively increasing with the estimated prevalence of over >5 million in the United States and > 30 million globally.[1-3] Numerous risk factors for AF have been identified, including hypertension, diabetes, coronary artery disease, and sleep apnea.[4] Recently, obesity has been recognized as a critical AF risk factor due to its adverse structural, functional, electrophysiological, and neurohormonal effects in the human atria.[5,6] Conversely, sustained weight reduction has been shown to be associated with reduced AF burden.[7,8]

Catheter ablation (CA) is an established treatment strategy for patients with symptomatic AF, and associated with drug-free 1-year AF free survival of 60-80% and 50-60% in patients with paroxysmal AF and persistent AF, respectively.[9-12] Prior studies have demonstrated that obesity negatively impacts AF CA outcomes.[13-16] However, the number of patients with extreme obesity defined as body mass index (BMI) ≥ 40 kg/m² enrolled in these studies is relatively small.[17]

The purpose of this study was to evaluate the efficacy and safety of CA in AF patients with extreme obesity in a high-volume tertiary care electrophysiology program.

Key Words

Atrial fibrillation; Catheter ablation; Body mass index; Obesity.

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Methods

Patient population

Consecutive patients with BMI ≥ 40 kg/m² who underwent index AF CA at the Ohio State University Medical Center (OSUMC) between 1/2012 and 6/2016 were included. Baseline demographic, clinical, procedural, and follow-up data were collected. Patients who did not complete 1-year follow-up at OSUMC or through affiliated clinics were excluded from efficacy analysis (Figure 1). Baseline patient characteristics at the time of ablation included age, weight, height, gender, AF type (paroxysmal vs. non-paroxysmal), history of atrial flutter, electrical cardioversion, congestive heart failure, chronic kidney disease, diabetes mellitus, hypertension, coronary artery disease, peripheral vascular disease, stroke, thromboembolism,

prior Class I or III anti-arrhythmic drug (AAD) use, and echocardiographic parameters (left ventricular ejection fraction [EF] and left atrial size on trans-esophageal echocardiography [TEE]). The CHA_2DS_2-VASc scores were calculated for all patients. Patients who had undergone prior cardioversion and/or had at least one AF episode lasting > 7 days were classified as having "non-paroxysmal" AF. Transesophageal echocardiography performed at OSUMC 1-3 days prior to the AF CA was reviewed. Informed consent for inclusion in any retrospective study was obtained from the patients prior to CA. The Ohio State University Institutional Review Board approved the study.

Pre-Procedural Management

Patients underwent a TEE and cardiac computed tomography (CT) (or cardiac magnetic resonance imaging) 1-3 days prior to AF CA. Generally, warfarin was continued without interruption and direct oral anticoagulants (DOACs) were held 24 hours prior to the CA in accordance with local practice. Perioperative management of class I and III AAD was left to the discretion of the electrophysiologist and were generally discontinued after 1 month.

Echocardiographic Measures

Two-dimensional TEE images of the left atrium (LA) were obtained in the standard 2-, 3- and 4-chamber views. The anterior-posterior diameter, LA area and LA volume (using the Method of Discs) were measured in each view at the end of ventricular systole.[18] Estimated LA volume (ml) was calculated as a mean of 2-chamber and 4-chamber volume measurements using biplane Simpson method. All LA volumes were indexed by body surface area (BSA).

Ablation Procedure

Catheter ablation was performed using either radiofrequency (RF) or cryoballoon under general anesthesia. Trans-septal puncture was guided by intracardiac echocardiogram and fluoroscopy. An esophageal temperature probe was used for all patients. Active clotting time was maintained above 300 seconds. The procedural endpoint was electrical isolation of all pulmonary veins (PV). RF ablation procedures were performed using a 3.5-mm tip irrigation catheter (Thermocool or Thermocool Smarttouch, Biosense Webster Diamond Bar, CA, USA) to achieve wide area circumferential ablation. Additional ablation strategies were left to the discretion of the operator, including empiric linear lines, electrical isolation of superior vena cava, ablation of complex fractionated electrograms and mapping and ablation of rotors using a proprietary mapping algorithm.[19] Power was titrated to 20-25 watts in the left atrial posterior wall and 30-40 watts in other areas. A force-sensing

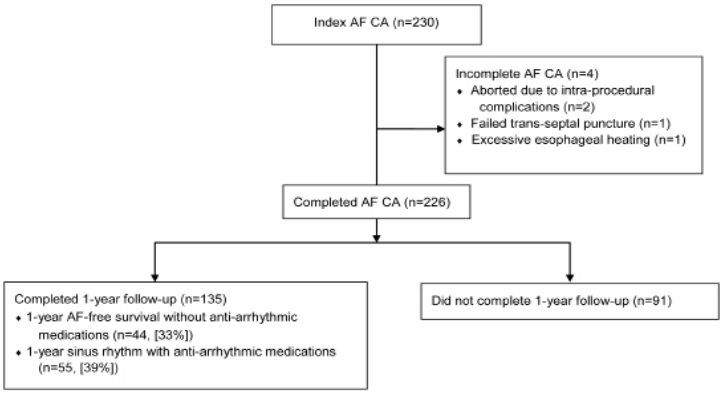

Figure 1: Patient flow diaphragm

Table 1: Baseline characteristics of the total patients, patients with complete 1-year follow-up, and patients who were lost to follow-up (total n= 226)

Characteristic	Completed Follow Up (n=135)	Lost to Follow Up (n=91)	P Value
Age-yr	58.5 ± 9.6	57.8 ± 9.9	0.60
Weight (kg)	135.9 ± 20.8	135.6 ± 18.7	0.90
BMI (kg/m²)	44.5 ± 4.7	45.1 ± 5	0.38
Female	63 (46.7)	40 (44)	0.69
AF Type			0.10
Paroxysmal	35 (25.9)	33 (36.3)	
Non-Paroxysmal	100 (74.1)	58 (63.7)	
Ablation Type			0.93
RFA	118 (87.4)	76 (83.5)	
Cryo	14 (10.4)	13 (14.3)	
Phased RFA	3 (2.2)	2 (2.2)	
Medical History			
Atrial flutter	23 (17)	18 (19.8)	0.60
CHF	25 (18.5)	22 (24.2)	0.30
CKD	6 (4.4)	6 (6.6)	0.48
Diabetes	51 (37.8)	28 (30.8)	0.28
Hypertension	115 (85.2)	78 (85.7)	0.91
CVA/TIA	6 (4.4)	4 (4.4)	1
CAD/PVD	17 (12.6)	22 (24.2)	0.06
Number of AAD use (Median [IQR])	1	1	0.36
0	13 (9.6)	9 (9.9)	
1	79 (58.5)	53 (58.2)	
2	34 (25.2)	17 (18.7)	
3	7 (5.2)	9 (9.9)	
4	1 (0.7)	3 (3.3)	
5	0 (0)	0 (0)	
6	1 (0.7)	0 (0)	
CHA_2DS_2-VASc score (Median [IQR])	2 (1-3)	2 (2-3)	0.64
0	2 (1.5)	4 (4.4)	
1	33 (24.4)	18 (19.8)	
2	45 (33.3)	26 (28.6)	
3	35 (25.9)	26 (28.6)	
4	13 (9.6)	10 (11)	
5	4 (3)	6 (6.6)	
6	2 (1.5)	1 (1.1)	
7	1 (0.7)	0 (0)	
Echocargiographic Parameters			
Ejection Fraction	60 (50-60)	55 (50-60)	0.27
Left atrial volume (ml/m²)	28.0 ± 9.7	29.6 ± 9.6	0.25

AAD = antiarrhythmic drug; AF = atrial fibrillation; BMI = body mass index; CAD= coronary artery disease; CHF= congestive heart failure; CKD=chronic kidney disease; CVA=cerebrovascular accident; IQR=interquartile range; RFA=radiofrequency ablation; PVD=peripheral vascular disease; TIA=transient ischemic attack

catheter (Thermocool Smarttouch, Biosense Webster, Diamond Bar, CA, USA) has been primarily used since 2014. A small number of patients (N=5) underwent phased RF ablation as part of VICTORY AF trial (ClinicalTrials.gov Identifier: NCT01693120. The study was terminated due to lower than expected enrollment rate).[20] Antral cryoballoon ablation was performed with 2nd generation 28 mm cryoballoon using standard two 3-minute freeze applications. (Arctic Front, Medtronic Inc., Minneapolis, MN, USA). During cryoballoon application to the right PVs, right phrenic nerve capture was monitored with abdominal palpation and diaphragmatic compound motor action potentials (CMAP).[21] A circular mapping catheter (Lasso: Biosense Webster; Achieve: Medtronic Inc.) or a multipolar mapping catheter (Pentaray: Biosense Webster) was used to confirm PV isolation. Warfarin was continued perioperatively and DOACs were resumed after venous hemostasis was confirmed; regardless of indication, anticoagulation was continued indefinitely. Aspirin and proton pump inhibitor were prescribed for minimum 1-month post ablation.

Outcomes

The primary efficacy endpoint of AF CA was no atrial arrhythmia recurrence lasting > 30 seconds off AAD (class I and class III drugs) during 1-year follow-up following a single CA procedure. Atrial arrhythmia recurrence was corroborated based on review of routine 30-day event monitors performed approximately 3 and 6 months after the index CA and any ECG performed during the 1-year months of follow up. In patients with implantable loop recorders and cardiac implantable devices, periodic device interrogation was used to assess for atrial arrhythmia recurrence.[22] Adjudication of atrial arrhythmias was performed by one of nine board-certified cardiac electrophysiologists. The secondary efficacy outcome was sinus rhythm maintenance after the index CA procedure with the aid of an AAD at 1-year follow-up. Safety endpoints include any major periprocedural adverse events, including myocardial infarction, stroke, pericardial effusion/tamponade, phrenic nerve paresis, atrial-esophageal fistula, acute respiratory failure, or vascular complications requiring a surgical or percutaneous intervention. Early arrhythmia recurrence within the first 3-month blanking period was not included in the efficacy endpoints. Patients' weights were recorded at baseline and at each follow-up visit.

Follow-up

Patients were routinely followed at 3, 6, and 12 months, including detailed history, exam, weight, EKG, and 30-day continuous rhythm monitor. Outpatient visits between 11 and 13 months were considered the 1-year follow-up for this study. AF/atrial tachycardia episodes were reviewed if patients had a cardiac implantable electronic device and implantable loop recorders. Patients were queried regarding any adverse complications or arrhythmia episodes that may have occurred at another health care center.

Statistical analysis

Statistical analysis: Continuous variables were compared using Student's t-test after normality was verified with histogram analysis or the Shapiro-Wilkins test; categorical variables were compared using the chi-square test or Fisher's Exact test as appropriate. Continuous variables are expressed as the mean ± SD and categorical variables are expressed n (%). The effect of incremental increase in BMI on AF CA outcome was assessed by grouping subjects with BMI ≤ 45 into one group and BMI > 45 into a second group. Student's t-test was used to compare subjects' weights on the day of AF CA and final day of follow-up. All analyses were considered significant if $p < 0.05$. Univariate predictors of AF CA success with $p < 0.20$ were included as candidate predictors in a multivariate model.

Table 2: Demographic and clinical characteristics of 135 patients with complete 1-year follow-up according to AF recurrence.

Characteristic		AF recurrence n = 91	No AF recurrence n = 44	P Value
Age-yr		58.7 ± 9.0	58.1 ± 10.7	0.76
Weight (kg)		138.1 ± 21.4	131.3 ± 19.0	0.07
BMI (kg/m^2)		44.7 ± 5.2	44.0 ± 3.6	0.35
Female		38 (60.3)	25 (39.7)	0.10
AF Type				0.01
Paroxysmal		17 (18.7)	18 (40.9)	
Non-Paroxysmal		74 (81.3)	26 (59.1)	
Ablation Type				0.95
RFA		80 (87.9)	38 (86.4)	
Cryo		9 (9.9)	5 (11.4)	
Phased RFA		2 (2.2)	1 (2.3)	
Medical History				
Atrial flutter		17 (18.7)	6 (13.6)	0.46
CHF		19 (20.9)	6 (13.6)	0.31
CKD		6 (6.6)	0 (0)	0.08
Diabetes		56 (61.5)	28 (63.6)	0.81
Hypertension		14 (15.4)	6 (13.6)	0.79
CVA/TIA		4 (4.4)	2 (4.5)	1
CAD/PVD		10 (11)	7 (15.9)	0.42
Number of AAD use (Median [IQR])		1 (1-2)	1 (1-2)	0.47
	0	7 (7.7)	6 (13.6)	
	1	54 (59.3)	25 (56.8)	
	2	25 (27.5)	9 (20.5)	
	3	3 (3.3)	4 (9.1)	
	4	1 (1.1)	0 (0)	
	5	0 (0)	0 (0)	
	6	1 (1.1)	0 (0)	
CHA_2DS_2-VASc score (Median [IQR])		2 (1-3)	2 (2-3)	0.60
	0	2 (2.2)	0 (0)	
	1	24 (26.4)	9 (20.5)	
	2	28 (30.8)	17 (38.6)	
	3	25 (27.5)	10 (22.7)	
	4	7 (7.7)	6 (13.6)	
	5	3 (3.3)	1 (2.3)	
	6	2 (2.2)	0 (0)	
	7	0 (0)	1 (2.3)	
Echocargiographic Parameters				
Ejection Fraction		60 (50-60)	60 (50-60)	0.27
Left atrial volume (ml/m^2)		29.6 ± 10.8	26.8 ± 7.6	0.13

AAD = antiarrhythmic drug; AF = atrial fibrillation; BMI = body mass index; CAD= coronary artery disease; CHF= congestive heart failure; CKD=chronic kidney disease; CVA=cerebrovascular accident; IQR=interquartile range; RFA=radiofrequency ablation; PVD=peripheral vascular disease; TIA=transient ischemic attack

Results

Patient population

Two hundred and thirty consecutive patients with BMI ≥ 40 kg/m^2 underwent attempted AF CA between 1/2012 and 6/2016. The mean weight was 135.8 ± 19.9 kg (299.4 ± 43.9 pounds) and the mean BMI was 44.8 ± 4.9 kg/m^2. PV isolation was acutely successful in 226 (98%) patients. Out of 226 patients with complete PVI, 135 patients completed 1-year follow-up at the OSUMC and were included in the efficacy analyses (Figure 2). There were no significant differences between 135 patients with complete 1-year follow-up and 91 patients with incomplete follow-up with regards to baseline demographics and clinical factors (Table 1).Baseline patient characteristics for 135 patients with one-year follow-up were as follows: mean age 58.5 ± 9.6 years, mean weight 135.9 ± 20.8 kg, mean BMI 44.5 ± 4.7 kg/m2, female 63 (47%), non-paroxysmal AF 100 (74%), median CHA2DS2-VASc score 2 (IQR:1-3), and median EF 60% (IQR: 50-60). Patients tried median 1 AAD (IQR:1-2) before AF CA. (Table 2)

Peri-procedural complications: AF CA was aborted in 2 patients due to intraprocedural complications (acute respiratory failure and cardiac tamponade) and could not be completed in 2 others due to failed trans-septal catheterization and excessive esophageal heating. Among the patients who completed PVI, there were 17 additional procedural complications in 15 patients. These complications included 5 cases of pericardial effusion requiring pericardiocentesis, 11 cases of groin pseudoaneurysm or AV fistula requiring a procedural intervention and one case of acute post-procedural respiratory failure requiring re-intubation and mechanical ventilation. In total, 17 out of 230 patients (7.4%) experienced acute major procedural complications.

Primary efficacy endpoint: Among the 135 obese patients included in this study, the primary efficacy endpoint of single AF CA success (no atrial arrhythmia recurrence lasting > 30 seconds off AAD during 1-year follow-up) was achieved in 44/135 patients (33%) (Table 2). Paroxysmal AF was associated with a higher CA success rate compared to non-paroxysmal AF (51% vs. 26%, p<0.01). The ablation technique (cryoablation versus radiofrequency ablation) did not impact AF CA success (Table 3) (p=0.95). Additionally, patients with paroxysmal AF had a longer median AF-free survival (300 days) than those with non-paroxysmal AF (278 days) (p < 0.01). By multivariate analysis, AF type (paroxysmal vs. non-paroxysmal) remained the only independent predictor of AF CA success. In this cohort of extremely obese patients, incremental increase in BMI above 40 kg/m^{2}did not impact AF CA outcomes (p=0.55). The secondary efficacy outcome (sinus rhythm maintenance with AF CA ± an AAD at 1-year follow-up) was observed in 53 (39%) patients, meaning the addition of AAD to CA increased sinus rhythm maintenance by 6%.

Impact of successful CA on weight: There was no significant weight change among all patients with 1-year follow-up (135.8 kg at AF CA vs.135.3 kg at last follow up, p = 0.39); this finding persisted when considering only the 53 patients maintaining sinus rhythm with CA ± AAD (131.8 kg at AF CA vs. 131.8 kg at last follow up, p = 0.96).

Discussion

Major findings

Major findings: In the present study of extremely obese patients (BMI ≥ 40 kg/m2) undergoing AF CA, sinus rhythm maintenance was only 39% at 1-year follow-up even with the use of class I or III AAD. Patients with non-paroxysmal AF had even lower success rate. Furthermore, there was no significant weight loss, with or without maintenance of sinus rhythm during the 1-year follow-up.

Overweight and obesity are generally defined as BMI 25-29.9, and ≥ 30 kg/m^2, respectively.[17] In Europe and North America, over 60% of adults are at least overweight, and of these 20-30% are obese.[23] In the Framingham Heart Study, every unit increase in BMI correlated with a 4-5 % increase in AF diagnosis.[24] The interplay between excess body weight and AF is complex. In addition to its close association with other cardiovascular risks and sleep disordered breathing (SDB), obesity appears to modulate underlying arrhythmogenic substrates,[25,26] exacerbating atrial dilatation,[27,28] diastolic dysfunction,[28-30] inflammation[31-33], fibrosis,[34] and conduction heterogeneity.[35] More recently, the pro-arrhythmic roles of pericardial fat and obesity-associated biomarkers (leptin, adiponection) have been implicated in the pathogenesis of AF.[6,23,36]

Excess body weight has been shown to negatively impact AF CA outcomes. Winkle et al evaluated AF CA outcomes in 2715 patients, including 129 patients with BMI > 40 kg/m2.15After multiple AF CA procedures, the reported 1-year AF free survival (no AAD) was 67% with an increase in the rate of complications. Sivasambu et al examined AF CA outcomes for 701 patients, including 84 patients with BMI > 40 kg/m^2.[14] In this subgroup with BMI > 40 kg/m^2, the 1-year AF free survival after CA was 42%, similar to the results of our current study. Compared to prior publications, the current study population was younger, and had a lower CHA_2DS_2-VASc score, yet the success of a single AF CA procedure was lower (33%) at 1-year follow-up. This may be due to the more intensive arrhythmia monitoring, the strict definition of single AF CA success, and higher rate of non-paroxysmal AF (74%) in our cohort. The relatively high rates of AF CA procedural complications observed in this study are consistent with complication rates observed by Winkle et al. in patients with BMI ≥ 4015.

Despite advances in mapping, imaging and ablation technologies, the success rates for AF CA remain rather constant for 60-80% and 50-60% in patients with paroxysmal AF and persistent AF, respectively.[9-12] Consequently, there has been a growing interest in comprehensive management of AF risk factors including body weight, SDB, and other cardiovascular comorbidities as therapeutic targets for AF management. In the ARREST-AF (Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation) and LEGACY (Long-Term Effect of Goal Directed Weight Management on an Atrial Fibrillation Cohort) studies, the investigators demonstrated that a structured, physician driven, and goal-directed weight and risk factor management strategy can lead to reduced AF burden and higher AF CA success rates.[7,8] In the LEGACY study, sustained > 10% weight loss was associated with lower AF recurrence, compared to those with < 3% weight loss, indicating a dose-dependent effect of weight loss on AF burden.[8]

In the sub-analysis of the LEGACY cohort, the investigators also observed regression of persistent AF to either paroxysmal or no AF among patients with more substantial weight loss and, 52% of patients with AF and > 10% weight loss achieved no AF after the mean 48-month follow-up.[37]

Lastly, the lack of weight loss even among patients with successful sinus rhythm maintenance is discouraging since one of the incentives for the patient and the physician to pursue AF CA in this cohort is that with long-term sinus rhythm maintenance, the patient will feel more motivated to pursue active lifestyle and to achieve sustained weight loss.

Given the incomplete understanding of AF pathogenesis, the increased risk of complications and the low success of AF CA in extreme obesity, electrophysiologists should incorporate other strategies for managing atrial arrhythmias before considering CA, such as enrollment and active participation in a monitored weight reduction program, and perhaps consideration of bariatric surgical options. Once the patient demonstrates successful lifestyle changes and sustained weight loss, then AF CA may be considered and would likely have greater success.

Limitations

Several limitations of this study should be noted. First, this is a single-center retrospective analysis. Second, 91 out of 230 patients did not complete follow-up through our system. Yet, the study population data show no significant differences between patients completing vs. not completing 1-year follow-up. Thus, it seems unlikely that the patients completing follow-up elsewhere would have significantly different outcomes. Third, diagnosis and treatment status of SDB were not captured in this study. The adverse impact of OSA on AF CA outcomes has been well described.[38,39] Fourth, continuous rhythm monitoring was not systematically utilized, yet monitoring and follow up was consistent with published guidelines. Fifth, we compared cohorts with BMI ≥ 40 and <45 against those with BMI ≥ 45 but did not include those with BMI ≤ 30 in this analysis. However, the single-procedure freedom from AF in this population has consistently been shown to be 60-70% in several large trials. Lastly, there may have been more AF episodes that were noted at outside hospitals without the knowledge of primary electrophysiologists.

Conclusions

Extreme obesity is associated with low AF CA success, particularly in those with non-paroxysmal AF. Successful sinus rhythm maintenance after AF CA was not associated with long-term weight reduction. A better treatment strategy is needed in this population of AF and extreme obesity.

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