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Success of Radiofrequency Catheter Ablation of Atrial Fibrillation: Does Obesity Influence the Outcomes?

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Abstract

Background

Catheter ablation of atrial fibrillation (AF) is an increasingly popular therapeutic option for symptomatic patients who have failed multiple antiarrhythmic drugs (AADs). Patients of higher body mass index often fail direct current cardioversion. The role of body mass index (BMI) on the success of AF ablation is not well understood.

Methods

We prospectively studied 511 patients who underwent AF ablation at the Cleveland Clinic Foundation between 2002 and 2005. Patients were divided into four classes based on their BMI: Class I (25); Class II (25.1-30); Class III (30.1-35) and Class IV (>35). These groups were compared for baseline demographic and clinical characteristics. Any recurrence of AF after 3 months of ablation was considered as failure. All classes were followed for at least 12 months and rates of failure were compared.

Results

Based on their BMI, 25% of patients were assigned to class I, 37% in class II, 21% in class III and 16% in class IV. Patients of higher classification (class III or IV) were more likely to be male (p<0.001), diabetic (p<0.001), smokers (p=0.002), with coronary artery disease (=0.018), left atrial enlargement (p=0.015) and longstanding AF (p=0.007). Severity of obesity as measured by BMI had a direct correlation to early (p=0.05) and late (p=0.01) recurrence of AF.

Conclusion

Obesity is significantly associated with long-term AF recurrence after catheter ablation. Higher incidence of smoking & left atrial enlargement may possibly contribute to higher failure rates in this subgroup of patients.

Key Words: **Atrial Fibrillation, Ablation, Obesity, Risk Factors, Arrhythmia**

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Introduction

Background

World Health Organization's latest projections for 2005 estimated that approximately 1.6 billion adults (age 15+) were overweight (Body Mass Index (BMI) 25) and at least 400 million adults were obese (BMI 30) among an estimated world population of 6.5 billion people.[1,2] Obesity has currently reached epidemic proportions in the United States with nearly 65% of the population being overweight and about 31% obese.[3] Atrial fibrillation (AF) is the most arrhythmia that is responsible for substantial worldwide morbidity, mortality and health care costs.[4-11] It affects approximately 1% of the general population and its prevalence appears to increase with age (0.1% among adults younger than 55 years to 9.0% in persons aged 80 years or older).[12] Obesity (Body Mass Index – BMI, used as the surrogate marker) has clearly been identified as an independent risk factor for AF in multiple studies.[13-18] The Framingham Heart Study clearly demonstrated that obesity was associated with a 50% increase in the risk of AF. In multivariable models adjusted for cardiovascular risk factors and interim myocardial infarction or heart failure, a 4% increase in AF risk per 1-unit increase in BMI was observed in both men and women.[13] The Danish Diet, Cancer and Health Study estimated the adjusted hazard rate ratio of AF or flutter to be 1.75 in overweight (BMI 25.0-30 kg/m2) men and 1.39 in overweight women and 2.35 in obese (BMI => 30.0 kg/m2) men and 1.99 in obese women, using the normal weight (BMI 18.5 to 25 kg/m2) as a reference.[15] These values underestimate the aggregate impact of obesity on AF risk, because they adjust for conditions such as hypertension, diabetes mellitus (DM), congestive heart disease (CHF) and coronary artery disease (CAD), which are common sequelae of obesity and well-known independent risk factors of AF.[18]

Current management of atrial fibrillation includes anticoagulation, rate-control or rhythm-control strategies.[19-23] Antiarrhythmic drugs and catheter ablation are the main methods of rhythm control. Arrhythmia does recur within one to two years in at least 50% of patients despite antiarrhythmic drug (AAD) therapy.[24-26] Percutaneous catheter ablation has been demonstrated to provide an effective, superior and safe curative therapy for atrial fibrillation.[27-30] There is limited data on the impact of obesity on the success of AF ablation.[31] In this multicenter study, we assess the effect of obesity on the success of AF ablation by using BMI as a surrogate marker.

Methods and Materials

Study Population

We prospectively studied 511 consecutive patients with symptomatic AF that was resistant to multiple antiarrhythmic drugs (AADs), who underwent first time radiofrequency (RF) ablation at the Cleveland Clinic, Ohio and Hôpital Cardiologique du Haut-Lévêque, Bordeaux-Pessac, FRANCE between 2002 and 2005. All AADs were withdrawn five half-lives before the ablation, with the exception of amiodarone, which was discontinued at least 5-6 months before the procedure. We used BMI calculated from the patients' weight and height as a surrogate marker of obesity. Based on BMI the entire study population was divided into class-I: BMI 25.0, class-II: BMI 25.1 to 30.0, class-III: BMI 30.1 to 35.0 and class-IV: BMI >35.0

AF Ablation

The AF ablation was performed with pulmonary vein antral isolation as described previously.[32] Patients were continuously anticoagulated before, during and after the ablation with warfarin and enoxaparin bridging during the periablation period. Patients who had known right atrial isthmus dependent flutter underwent additional cavo-tricuspid isthmus ablation. At the end of the procedure all 4 PVs were tested for complete electrical isolation. All patients who underwent ablation with a 8 mm-Biosense Webster Catheter were included in this study for consistency. Patients who had ablation with a 4 mm and open irrigated or close loop catheters were excluded from the study.

Follow-Up

After ablation, all patients were continued on oral anticoagulation with warfarin for a minimum of 3 months and restarted on their AADs on the day of PV isolation for a total of 8 weeks. Symptoms related to AF recurrence were verified during out-

patient visits at 1, 3, 6 and 12 months after ablation and by monthly telephonic interviews. Recurrence of AF was assessed during the follow-up period by an external loop recorder worn for the first 6 months by all patients. Computed tomography was done at 3 months and repeated at 6 months and 12 months if any evidence of PV narrowing was detected during the initial scan. Early recurrence is defined as any atrial arrhythmia (atrial fibrillation, atrial flutter and/or intraatrial reentry tachycardia) at three months and late recurrence at 12 months.

Results

Demographic characteristics of our study population are summarized in Table-1. A comparison of the various BMI classes reveals a significant difference (p 0.05) in the types of AF observed amongst them. Specifically, higher BMI classes (such as class III or IV) had a higher percentage of persistent or permanent than paroxysmal AF (p = 0.007). The incidence of diabetes, smoking, obstructive sleep apnea and coronary artery disease was directly proportional to the severity of obesity. Echocardiographic parameters, including left atrial (LA) size, left ventricular ejection fraction (LVEF), presence of mitral regurgitation, concomitant patent foramen ovale (PFO) and aortic valvular abnormality, were analyzed amongst the various BMI classes; only the left atrial enlargement significantly (p=0.015) correlated to the severity of obesity (Table-2). Prior to enrollment, patients were on multiple antiarrhythmic medications (AAD's). There was no signifi-

Table 1 **Differences in demographic variables amongst the four classes of patients. CAD-Coronary artery disease; CABG-Coronary artery bypass graft; VT-Ventricular tachycardia; CVACerebrovascular accident; COPD-Chronic obstructive pulmonary disease**

Clinical Variables	Class I BMI < 25 N = 113	Class II BMI 25.1 – 30 N = 201	Class III BMI 30.1 – 35 N = 115	Class IV BMI > 35 N = 82	p-value
Age	55.4±11.8	54.8±11.0	55.5±10.6	54.8±9.5	0.866
Gender (M/F)	139/61 (69.5%/30.5%)	287/44 (86.7%/13.3%)	143/40 (78.1%/21.9%)	107/33 (76.4%/23.6%)	**<0.001**
Presenting Rhythm					**0.396**
Sinus rhythm	116 (58.3%)	170 (52.1%)	92 (50.3%)	69 (50.4%)	
Atrial fibrillation	75 (37.7%)	142 (43.6%)	83 (45.4%)	65 (47.4%)	
Atrial flutter	6 (3.0%)	14 (4.3%)	6 (3.3%)	2 (1.5%)	
Other	2 (1.0%)	0	2 (1.1%)	1 (0.7%)	
Type of AF					**0.007**
Paroxysmal	125 (62.5%)	186 (56.7%)	97 (53.0%)	61 (44.2%)	
Persistent	20 (10.0%)	46 (14.0%)	23 (12.6%)	32 (23.2%)	
Permanent	55 (27.5%)	96 (29.3%)	63 (34.4%)	45 (32.6%)	
Smoking	4 (1.9%)	12 (3.5%)	15 (7.9%)	13 (9.0%)	**0.002**
Co morbidities					
Hypertension	41 (19.2%)	66 (19.1%)	43 (22.5%)	35 (24.3%)	0.510
LVEF < 45%	17 (8.0%)	27 (7.8%)	16 (8.4%)	10 (6.9%)	0.971
OSA	1 (0.9%)	13 (6.4%)	15 (13%)	18 (22%)	**<0.001**
DM	3 (1.4%)	9 (2.6%)	6 (3.1%)	14 (9.7%)	**<0.001**
CAD	13 (6.1%)	49 (14.2%)	28 (14.7%)	16 (11.1%)	**0.018**
CABG	5 (2.3%)	11 (3.2%)	13 (6.8%)	4 (2.8%)	0.076
Hyperthyroidism	4 (1.9%)	5 (1.4%)	2 (1.0%)	1 (0.7%)	0.784
Sick sinus	12 (5.6%)	18 (5.2%)	9 (4.7%)	2 (1.4%)	0.239
VT	5.(2.3%)	7 (2.0%)	4 (2.1%)	3 (2.1%)	0.995
Hypothyroidism	5 (2.3%)	10 (2.9%)	6 (3.1%)	6 (4.2%)	0.801
CVA	4 (1.9%)	11 (3.2%)	3 (1.6%)	7 (4.9%)	0.244
COPD	2 (0.9%)	1 (0.3%)	4 (2.1%)	2 (1.4%)	0.235

Table 2 Differences in echo parameters amongst various BMI classes. MR – mitral regurgitation; AR – aortic regurgitation; AS –aortic stenosis

Clinical Variable	Class I N = 113	Class II N = 201	Class III N = 115	Class IV N = 82	pvalue
LA size (cm)	4.27±0.61	4.43±1.79	4.48±0.61	5.34±5.96	0.015
LVEF	53.7±8.6	53.1±7.8	52.2±7.8	54.7±8.8	0.060
MR (1+ or more)	43 (20.2%)	61 (17.7%)	48 (25.1%)	31 (21.5%)	0.231
Concomitant PFO	6 (2.8%)	11 (3.2%)	10 (5.2%)	4 (2.8%)	0.506
AR/AS (1+ or more)	7 (3.3%)	10 (2.9%)	11 (5.8%)	8 (5.6%)	0.285

cant difference in the use of antiarrhythmic drugs amongst the four BMI classes (Table-3). Pulmonary vein activity was found in more than 90% of the veins. There was no significant difference in pulmonary vein activity amongst the various classes (Table-4). On multivariate analysis, severity of obesity as measured by BMI had a direct correlation to short- (p=0.05) and long-term (p=0.01) recurrence of AF. And smoking was found to be a significant predictor of only late recurrence (p=0.002) (Table-5). Interestingly, history of obstructive sleep apnea (OSA) was not an independent predictor of AF recurrence after RF ablation.

Discussion

Major Findings

This is a large study that assessed the impact of BMI (as a surrogate marker of obesity) on the success of RF ablation for AF using pulmonary vein isolation. Higher BMI was predictive of early and late recurrences after RF ablation. Contrary to prior studies, our series did not show any significant correlation between history of OSA and procedural success.[31] Our review of the current literature suggests that obesity is not just another physiologic parameter, rather a syndrome of anatomic, physiologic and metabolic abnormalities, all of which act synergistically to induce and maintain atrial ectopic activity. Catheter ablation in such an electrically unstable environment would then have its own limitations, as already indicated in our study by the lower success rates in permanently eliminating atrial fibrillation.

First of all, obese individuals are at a higher risk of having diabetes mellitus, hypertension, dislipidemia, coronary artery disease, heart failure and valvular heart disease, which were all shown to be significant predictors of atrial fibrillation.[15] Insulin resistance commonly observed in type 2 diabetes and obesity has been associated with molecular signaling abnormalities (such as enhanced expression of interleukin-6 (IL-6), vascular cellular adhesion molecule-1 (VCAM-1) and monocyte chemoattractant protein -1 (MCP-1)) and marked decrease in nitric oxide bioavailability via increased formation of advanced glycation end products (AGE), leading to endothelial dysfunction and chronic vascular inflammation.[33] Mechanical forces and shear stress

Table 3 Differences in drugs used by the various BMI classes

Clinical Variable	Class I N = 113	Class II N = 201	Class III N = 115	Class IV N = 82	pvalue
Beta blocker	77 (36.2%)	149 (43.2%)	83 (43.5%)	58 (40.3%)	0.354
Calcium CB	18 (8.5%)	39 (11.3%)	10 (5.2%)	9 (6.3%)	0.071
Digoxin	12 (5.6%)	23 (6.7%)	13 (6.8%)	10 (6.9%)	0.927
Propafenone	32 (15.0%)	58 (16.8%)	35 (18.3%)	32 (22.2%)	0.345
Sotalol	99 (46.5%)	178 (51.6%)	106 (55.5%)	76 (52.8%)	0.326
Flecainide	87 (40.8%)	124 (36.0%)	86 (45.0%)	64 (44.4%)	0.288
Amiodarone	89 (41.8%)	142 (41.2%)	101 (52.9%)	63 (43.8%)	0.054
Dofetilide	42 (19.7%)	58 (16.8%)	45 (23.6%)	38 (26.4%)	0.068

Table 4 Differences in PV activity amongst 4 classes

Clinical Variable	Class I N = 113	Class II N = 201	Class III N = 115	Class IV N = 82	pvalue
Right Upper	73 (34.3%)	134 (38.8%)	82 (42.9%)	56 (38.9%)	0.361
Right Lower	44 (20.7%)	82 (23.8%)	53 (27.7%)	43 (29.9%)	0.171
Left lower	95 (44.6%)	161 (46.7%)	84 (44.0%)	66 (45.8%)	0.931
Left lower	39 (18.3%)	74 (21.4%)	40 (20.9%)	38 (26.4%)	0.339

from disturbed blood flow present in hypertensive states and in atheromatous coronary artery disease are other causes of endothelial dysfunction and inflammation. On their own or in conjunction with each other, diabetes mellitus, hypertension, dyslipidemia and coronary artery disease affect cardiac structure and function by causing left ventricular hypertrophy and/or dilatation, diastolic and/or systolic dysfunction and valvular abnormalities, most prominently mitral regurgitation, increasing the wall tension and size of the left atrium, changing myocyte action potentials and inducing chaotic electrical activity, the hallmark of atrial fibrillation.

C-reactive protein (CRP) which is a marker of inflammation was found to correlate well with BMI and presence of AF and was an independent predictor of new onset AF.[34-38] In obese patients initial cardioversion success (but not AF recurrence) was shown to be inversely related to hsCRP levels.[39] Although, no clear correlation was found in our study, obese individuals appear to have an increased prevalence (40-60%) of depression which can stimulate neuroendocrine pathways leading to catecholamine and cortisol release sustaining a pro-inflammatory state.[40-42] As was shown by our study and others smoking is more prevalent in obese patients which can contribute to the systemic inflammatory response and account for relatively higher AF recurrence rates post RF ablation.[43-45] As is well described in cardiomyopathy of obesity, gradual accumulation of adipose tissue among muscle fibers with pressure-induced atrophy , lipotoxicity and myocyte apoptosis in combination with above pro AF milieu can promote negative atrial remodeling and arrhythmogenecity.[46-47]

Several studies in the past have shown significant correlation between OSA, obesity and AF.[48-50] Intermittent hypoxemia, hypercapnia, chemoreceptor excitation, and surges in adrenergic tone resulting in elevated blood pressures, left ventricular afterload during an apneic episode can possibly contribute to AF in patients with OSA.[51] Left atrial dilatation and probable fibrosis due to prolonged exposure to elevated left ventricular filling pressures may contribute to the perpetuation of AF. Left atrial stretch has also been demonstrated to promote pulmonary vein arrhythmogenicity.[52] Use of CPAP to treat OSA significantly decreased the recurrence of AF from 82% down to 42%. [48] Unlike a prior study by Jongnarasingan et al, our study did not show any significant correlation between AF recurrence after ablation in patients with a history of OSA. We believe that active treatment with postitive pressure ventilation measures might have significantly altered the trigger mechanisms which otherwise could have made them more prone for AF.

Although, it is the largest multicenter study that looked at the impact of obesity on the success of catheter based intervention in AF, no inflammatory markers were measured and hence not taken into consideration. We used BMI as a surrogate marker of the severity of obesity in our patient population; therefore, patients with high muscle mass (men more likely than women), could have been misclassified.

Conclusions

Catheter ablation is emerging as the preferred mode of treating atrial fibrillation with higher success rates than AADs. Newer techniques and increasing experience in catheter ablation of AF are promising. However, obesity with its epidemic

Table 5 Differences in early and late recurrences amongst 4 classes

Clinical Variable	Class I N = 113	Class II N = 201	Class III N = 115	Class IV N = 82	pvalue
Early recurrence	27 (12.7%)	66 (19.1%)	44 (23.0%)	25 (17.4%)	0.05
Late recurrence	11 (5.2%)	26 (7.5%)	27 (14.1%)	12 (8.4%)	0.01

proportions is taking its toll on the incidence, persistence and recurrence of AF, which makes the need for an aggressive public policy to reduce obesity rates around the western world even more imperative.

Disclosures

There are no relevant conflicts of interests for any of the authors involving the current study topic.

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