

Predictors and rates of recurrence of atrial arrhythmias following catheter ablation in adults with congenital heart disease

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Abstract

Background: Catheter ablation is commonly performed to treat atrial arrhythmias in adult congenital heart disease (ACHD). Despite the frequency of ablations in the ACHD population, predictors of recurrence remain poorly defined.

Objective: We sought to determine predictors of arrhythmia recurrence in ACHD patients following catheter ablation for atrial arrhythmias.

Methods: We performed a retrospective study of all catheter ablations for atrial arrhythmias performed in ACHD patients between January 12, 2005 and February 11, 2015 at our institution. Prespecified exposures of interest and time from ablation to recurrence were determined via chart review.

Results: Among 124 patients (mean age: 45 years) who underwent catheter ablation, 96 (77%) were treated for macro-reentrant atrial tachycardia, 10 (7%) for focal atrial tachycardia, 9 (7%) for atrial fibrillation, 7 (6%) for atrioventricular nodal reentrant tachycardia, and 2 (2%) for atrioventricular reentrant tachycardia. 15 (12%) required transseptal/transbaffle puncture. Fifty-one percent of patients recurred with a median time to recurrence of 1639 days. By univariate and multivariable analysis, body mass index (BMI) and Fontan status were the only variables associated with recurrence. Dose-dependent effect was observed with overweight (HR = 2.37, $P = .012$), obese (HR = 2.67, $P = .009$), and morbidly obese (HR = 4.23, $P = .003$) patients demonstrating an increasing risk for arrhythmia recurrence postablation. There was no significant difference in recurrence rates by gender, age, non-Fontan diagnosis, or need for transseptal puncture.

Conclusions: In our cohort of ACHD patients, BMI was a significant risk factor for arrhythmia recurrence postablation, independent of Fontan status. These findings may help guide treatment decisions for persistent arrhythmias in the ACHD population.

KEYWORDS

adult congenital heart disease, atrial arrhythmias, catheter ablation, obesity

Abbreviations: ACHD, adult congenital heart disease; AT, atrial tachycardia; AVNRT, atrioventricular nodal reentry tachycardia; AVRT, atrioventricular reentry tachycardia; BMI, body mass index; RFA, radiofrequency ablation.

1 | INTRODUCTION

The population of adults with congenital heart disease (ACHD) continues to grow with improvements in treatment.¹ As a consequence of prior surgeries, anatomic abnormalities and aging, more than half of all ACHD patients develop atrial arrhythmias by age 65.² In the ACHD population, atrial arrhythmias are an important source of morbidity and have been associated with an almost 50% increase in mortality.² Given the frequency and impact of atrial arrhythmias, establishing treatment paradigms is crucial to improving ACHD outcomes.³ With improvements in catheter technology and mapping, there is increasing reliance on catheter ablation to treat persistent atrial arrhythmias in ACHD patients. However, there are limited data regarding patient-specific factors that impact recurrence risk postablation.

Delineation of risk factors for arrhythmia recurrence after catheter ablation in the ACHD population has the potential to impact patient selection and procedural technique. However, while there are data suggesting that recurrence risk may be higher in patients following specific repairs,⁴ there are limited data regarding the impact of modifiable patient risk factors. Obesity, in particular, is known to have pleiotropic effects on cardiovascular tissue and increase the risk of atrial fibrillation and sudden cardiac death in patients with acquired heart disease.⁵⁻⁷ While there are data to suggest that increasing body mass index (BMI) may be associated with an increased rate of postoperative arrhythmias in the ACHD population,⁸ its impact on outcomes of catheter ablation is not known. Because the prevalence of obesity is increasing in the ACHD population,⁹ understanding its impact on recurrence rates has the potential to impact treatment strategies. As such, we sought to determine the impact of patient-specific factors, including BMI, on arrhythmia recurrence rates in a cohort of ACHD patients undergoing catheter ablation for persistent atrial arrhythmias.

2 | METHODS

2.1 | Study design

We performed a retrospective study of all adult patients with congenital heart disease who underwent catheter ablation in the adult electrophysiology laboratory at Columbia University Medical Center between January 12, 2005 and February 11, 2015. The Columbia University Medical Center institutional review board approved this study prior to the onset of study procedures. This study period was selected in order to define a consistent operator experience. Patient history, BMI, prior surgical procedures, medical therapy, electrocardiographic data, and outpatient medical data were assessed and collected through chart review and confirmed by two independent electrophysiologists. BMI was stratified according standard definitions of overweight, obese, and morbidly obese. Electrophysiologic data were collected for all patients at the time of ablation and for subsequent ablations following recurrences. The primary end point of interest was time to arrhythmia recurrence following catheter ablation.

2.2 | Electrophysiology study and ablation

Electrophysiology studies were performed using standard equipment with electroanatomic mapping (CARTO, Biosense Webster, Diamond Bar, California) capabilities and with patients under conscious sedation. Vascular access was obtained and multielectrode catheters were positioned in the high right atrium, coronary sinus, tricuspid annulus, and His bundle region when ever feasible according to patient anatomy. Transseptal or transbaffle puncture was performed as needed. Intracardiac mapping was performed by a quadripolar electrode catheter with an 8-mm nonirrigated tip (Navistar; Biosense Webster, Diamond Barr, California), 4-mm closed irrigated tip (CHILLI; Boston Scientific, Natick, Massachusetts), or a 3.5-mm open-irrigated tip electrode (Navistar thermocool; Biosense Webster). Atrial and ventricular programmed stimulation were used for arrhythmia induction, with isoproterenol infusion (1-5 mcg/min) as needed. The cycle length and surface ECG morphology of induced arrhythmias were compared with those with documented clinical arrhythmias whenever possible.

Arrhythmia type was determined by the treating electrophysiologist based on electromechanical activation mapping. Arrhythmias were defined as macro-reentrant atrial tachycardia/flutter, focal atrial tachycardia, atrial fibrillation, atrioventricular nodal reentry tachycardia (AVNRT), and atrioventricular reentry tachycardia (AVRT). Radiofrequency ablation (RFA) was initiated with 50 watts power (temperature-controlled at 65°C) using 8-mm nonirrigated tip catheters, or 25-40 watts (temperature-controlled at 43-45°C) using irrigated tip catheters. In cases of reentrant atrial tachycardia/flutter, radio frequency was delivered across isthmus sites as determined by activation and entrainment mapping and differential pacing was used to confirm conduction block across ablation lines. At the time of repeat ablative procedures for recurrences, arrhythmias were categorized as "new" or "old" based on the mechanism and location compared with the initial procedure.

2.3 | Primary end point

The primary end point of interest was time from initial catheter ablation to recurrent, sustained arrhythmia. Post-RFA recurrence was defined as recurrent, symptomatic palpitations persisting for greater than 30 seconds with documented arrhythmia by device, ECG, Holter or laboratory study. In the case where a patient was lost to follow-up, time was censored from when the status of the patient was last known.

2.4 | Statistics

Data were expressed as frequency (%), median (interquartile range), or mean \pm SD as appropriate. Univariate and multivariable tests were performed for the primary end point using a Cox proportional hazard model. Multivariable models for the primary end point were prespecified to contain age, gender, and arrhythmia type. Additional variables reaching $P < .20$ in the univariate analysis were subsequently added. Assumption of proportional hazards was verified using a

formal significance test based on scaled and unscaled Schoenfeld residuals.¹⁰ A Kaplan-Meier survivor function was performed for the primary end point by diagnosis for both initial and follow-up ablative procedures. Statistical analysis was performed using STATA statistical software (Version 13.1, Stata Corp, College Station, Texas).

3 | RESULTS

One hundred fifty-five catheter ablations were performed for atrial arrhythmias in 124 ACHD patients between January 12, 2005 and February 11, 2015. Patient characteristics are delineated in Table 1. Ninety-six of the 124 (77%) initial catheter ablations were performed for the primary diagnosis of macro-reentrant atrial tachycardia. Of the remaining procedures, 10 (8%) were performed for focal atrial tachycardia, 9 (7%) were performed for atrial fibrillation,

7 (6%) were performed for AVNRT, and 2 (2%) were performed for AVRT. Median (IQR) follow-up time was 2.0 years (50-1383 days). Thirty-six (30%) patients were in sinus at the time of ablation and required arrhythmia induction, and 8 (7%) had more than one macro-reentrant circuit ablated at the time of the initial procedure. Irrigated catheters were used in 121 (98%) procedures and trans-septal or transbaffle puncture was required in 15 (12%) procedures. Mean (standard deviation) fluoroscopic time was 37 (21) minutes. One patient with dextrocardia, a double-outlet right ventricle and transposed great vessels had postprocedure heart block requiring a pacemaker. Over the course of the study period, 7 patients died a median (IQR) 17 (32.1) months postablation and 2 patients underwent heart transplantation a mean 23 (8.1) months postablation. One patient with a history of an ASD died within 30 days of catheter ablation following a pulmonary hypertensive crisis. There were no other major postprocedure complications.

TABLE 1 Patient characteristics

Male	63 (51%)
Body mass index, mean (kg/m ²)	27 (6)
Body mass index > 25	77 (62%)
Body mass index > 30	33 (27%)
Body mass index > 35	13 (10%)
Age at ablation, mean (years)	44 (14)
Diagnosis	
Atrial septal defect or ventricular septal defect	38 (31%)
Tetralogy of fallot/pulmonary stenosis/double chambered right ventricle	33 (27%)
Systemic right ventricle (D-transposed w/atrial baffle or congenitally corrected transposition of the great arteries)	11 (9%)
Single ventricle	18 (15%)
Other	24 (19%)
Prior primary procedures	
Atrial septal defect closure	26
Ventricular septal defect closure	12
Tetralogy of Fallot repair	23
Pulmonary valvotomy	9
Repair of double-chamber right ventricle	2
Mustard/Senning procedure	8
Rastelli procedure	4
"Classic" Fontan	13
Lateral tunnel or extracardiac fontan	5
Other	19
Medications	
Amiodarone	14 (11%)
Beta-blockers	58 (46%)
Sotalol	8 (6%)
Calcium channel blockers	4 (3%)
Transseptal puncture	15 (12%)

Following initial catheter ablation, there were 63 (51%) recurrent arrhythmias over the study period in 49 (46%) biventricular patients and 14/18 (78%) Fontan patients. There was no significant difference in recurrence rates for patients who had undergone an atrial switch (HR: .75, $P = .63$) or in patients with either a repaired ASD or repaired tetralogy of Fallot (HR: .85, $P = .56$). Additional univariate and multivariable predictors of initial recurrence are displayed in Table 2. BMI was associated with an increased HR for recurrence by univariate (HR: 1.09 per unit increase in BMI, $P < .001$) analysis and in a multivariable model that included Fontan status, age at procedure, gender, and arrhythmia type (HR: 1.08 per unit increase in BMI, $P < .001$). BMI was also categorized as normal weight (BMI < 25), overweight (25 < BMI < 30), obese (30 < BMI < 35), and morbidly obese (BMI > 35). With each elevation in BMI category, there was an associated increased risk for recurrence by both multivariable and univariate analyses (Table 2). While median time to arrhythmia recurrence for all patients was 1639 days, increasing BMI was associated with a decreased time to recurrence for overweight obese, and morbidly obese patients (Figure 1).

Of the 63 patients who had an arrhythmia recurrence, 34 (54%) had a repeat ablation and among them 30 (88%) were performed for macro-reentrant atrial tachycardia. Following the second ablation, 15 (44%) patients remained arrhythmia free, while median time to recurrence was 1405 days. Fourteen of the 34 (41%) patients had a new arrhythmia circuit at the time of the second ablation. Median time to recurrence was not significantly different for patients undergoing ablation for a new arrhythmia circuit (HR 2.15, $P = .14$). Twenty-seven of the 34 (79%) patients who underwent a second ablation postarrhythmia recurrence had a BMI ≥ 25 . While a trend toward significance was noted, BMI was not a predictor of recurrence following repeat catheter ablation (HR: 1.08, $P = .10$).

4 | DISCUSSION

To our knowledge, this is the first study to identify increasing BMI as a risk factor for arrhythmia recurrence following catheter ablation

Variable	Univariate		Multivariable	
	HR (95% CI)	P	HR (95% CI)	P
Male	1.22 (.74-2.02)	.42	1.35 (.79-2.31)	.27
Age	1.00 (.98-1.01)	.89	1.00 (.99-1.02)	.58
Body mass index				
Normal weight	Reference		Reference	
Overweight	2.48 (1.28-4.81)	.007	2.37 (1.20-4.65)	.012
Obese	2.93 (1.42-6.05)	.004	2.67 (1.28-5.51)	.009
Morbidly obese	3.70 (1.46-9.32)	.006	4.23 (1.61-11.10)	.003
Diagnosis				
Fontan	2.11 (1.15-3.85)	.015	2.02 (1.04-3.93)	.036
TOF/PS/DCRV	.71 (.39-1.29)	.26		
SRV	.95 (.38-2.38)	.92		
ASD/VSD	.89 (.49-1.58)	.69		
Transseptal approach				
Macro-reentrant AT	1.83 (.98-3.38)	.055	1.61 (.84-3.01)	.15
>1 Circuits ablated (at initial procedure)	1.11 (.44-2.77)	.83		
Required induction	1.03 (.58-1.81)	.91		

TABLE 2 Univariate and multivariable predictors of recurrence

Abbreviations: ASD, atrial septal defect; AT, atrial tachycardia; DCRV, double-chamber right ventricle; PS, pulmonary stenosis; SRV, systemic right ventricle; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

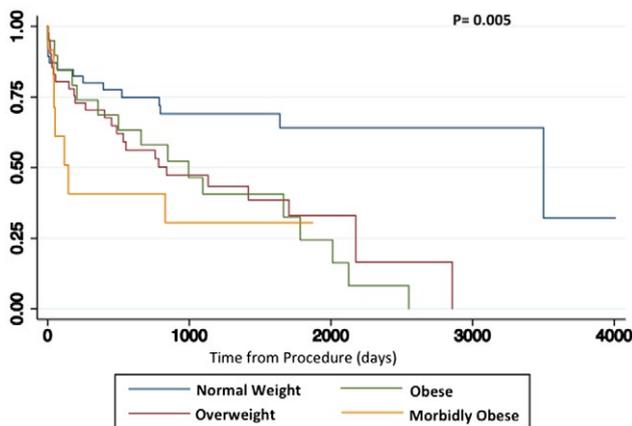


FIGURE 1 Kaplan-Meier estimates for arrhythmia recurrence by BMI category

for atrial arrhythmias in ACHD patients. With a median age of 45 years, our study represents the oldest reported cohort of ACHD patients who underwent catheter ablation for atrial arrhythmias. As such, we were uniquely positioned to determine the impact of acquired cardiovascular risk factors on procedural outcomes. In so doing, we found that every unit increase in BMI was associated with a nearly 10% increase in arrhythmia recurrence and that obese patients had a nearly threefold increased risk of recurrence when compared to individuals with a normal BMI. Given concerns for high rates of obesity in patients with congenital heart disease,⁹ this finding may have important implications as a modifiable risk factor to mitigate arrhythmia recurrence.

As the congenital heart disease population continues to age, there is a pressing need to determine the impact of acquired cardiovascular risk factors on patient outcomes. Because many ACHD patients are inappropriately counseled against activity or have exercise limitations, they may be at higher risk for weight gain. In fact, recent studies have estimated that the prevalence of obesity in the ACHD population is increasing and may be as high as 60%.¹¹ The association between weight gain and sudden cardiac death¹² in patients with acquired heart disease and the increased baseline risk for arrhythmias in the ACHD population underscore the need to establish the impact of weight gain on arrhythmia treatment. While prior studies have demonstrated an association between obesity and postoperative arrhythmias in the ACHD population,⁸ this is the first study to show an association between BMI and outcomes of catheter ablation.

Multiple mechanisms may underlie the observed association between elevated BMI and recurrence risk. Obesity has been implicated in atrial remodeling,¹³ altering underlying conduction and leading to increased interstitial fibrosis,¹⁴ inflammation,¹⁵ and lipodosis.¹⁶ In addition, paracrine effects from increased adiposity have been associated with overactivation of the inflammatory cascade and promotion of electrical dissociation and reentry.¹⁷⁻¹⁹ In patients without congenital heart disease, these mechanisms may contribute to the association between obesity and an increased risk for atrial fibrillation. In ACHD patients, where multiple atrial suture lines and atrial fibrosis from prior cardiothoracic surgery predominate, such electrostructural changes may potentiate an underlying propensity toward atrial arrhythmias.

Obesity may also complicate pharmacologic and catheter-based treatments of atrial arrhythmias.²⁰ By altering the pharmacokinetics of antiarrhythmics, pharmacologic rhythm control may be more difficult to achieve in obese ACHD patients. Catheter-based treatment may also be more complex. Obesity has been shown to be correlated with increased atrial volume and altered atrial conductivity.^{20,21} Larger atrial size may complicate generation of atrial ablation lines, particularly in the ACHD population where the anatomic substrate supporting arrhythmia generation and propagation is complex. In our study, patients with an elevated BMI had a significantly lower time to recurrence and over 75% of the patients requiring a second ablative procedure were obese. Given these findings, future studies assessing the impact of weight loss on arrhythmia management in the ACHD population are warranted.

Similar to prior studies of catheter ablation for atrial arrhythmias in the ACHD population, we found that Fontan status was a significant predictor of recurrence, independent of BMI.²² In our study, Fontan patients with a BMI > 25 and were at highest risk of recurrence. In fact, all overweight Fontan patients had at least one recurrence, while half of the Fontan patients with a normal BMI remained arrhythmia free. Because obesity has been previously associated with a higher risk of heart failure in the Fontan population,²³ these findings further suggest that purposeful weight reduction in obese patients with a palliated single ventricle should be pursued.

Despite late recurrences, catheter ablation for persistent atrial arrhythmias in ACHD patients was a safe and effective method of arrhythmia control. While patients with a Fontan and elevated BMI were at increased risk of recurrence, the majority of patients achieved multiple arrhythmia free years with half of all patients remaining arrhythmia free over a median of 4.4 years. Importantly, in patients who had a repeat ablation postrecurrence, one-third had a new arrhythmia site and/or mechanism and an additional 43% were able to achieve freedom from arrhythmia recurrence following repeat ablation. Thus, the majority of patients appeared to derive significant benefit from catheter ablation. These results reinforce that RFA should be considered early in the management of persistent atrial arrhythmias in the ACHD population.

Beyond the impact of weight gain, increasing patient age did not play a significant role in recurrence rates. Prior studies of catheter ablation for atrial arrhythmias in congenital heart disease have utilized cohorts of pediatric and young adult patients.^{4,24,25} Because aging and chronic exposure to hemodynamic abnormalities may promote fibrosis and hypertrophy, catheter ablation may be more challenging in older patients. However, despite a median patient age of 45 years, recurrence rates were similar to those previously reported in predominantly pediatric populations. In addition, although our cohort had a median age 2 decades older than those previously described, major adverse events did not appear to be more prevalent. These results suggest that similar rates of procedural success of catheter ablation for persistent atrial arrhythmias can be achieved in adults with congenital heart disease.

4.1 | Limitations

Our study has the recognized limitations of a single-center retrospective study. We may have overlooked important confounding factors and follow-up times varied among patients. We recognize that our sample size remains limited and we may have been underpowered to detect other significant clinical associations. Finally, as a single center with experience in catheter ablation in ACHD patients, our results may not be applicable to all clinical populations of adults with congenital heart disease.

5 | CONCLUSIONS

In our cohort of ACHD patients, BMI was a significant risk factor for arrhythmia recurrence postablation, independent of Fontan status. These findings may help guide treatment decisions for persistent arrhythmias in the ACHD population and suggest that future inquires into the impact of weight reduction on arrhythmia recurrence in the ACHD population are warranted.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

All authors have contributed to this study.

Conception, design, analysis, drafting of the manuscript: Lewis

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