Catheter ablation of atrial fibrillation in patients with diabetes mellitus

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BACKGROUND Diabetes mellitus (DM) is an independent risk factor for atrial fibrillation (AF). Few studies have compared clinical outcomes after catheter ablation between patients with and those without DM.

OBJECTIVE The purpose of this study was to compare AF ablation outcomes in patients with and those without DM.

METHODS We performed a retrospective analysis of 351 consecutive patients who underwent first-time AF ablation. Clinical outcomes included freedom from recurrent atrial arrhythmia, symptom burden (Mayo AF Symptom Inventory score), cardiovascular and all-cause hospitalizations, and periprocedural complications.

RESULTS Patients with DM (n = 65) were older, had a higher body mass index, more persistent AF, more hypertension, and larger left atrial diameter ($P < .05$ for all). Median (Q1, Q3) total radiofrequency duration [64.0 (43.6, 81.4) minutes vs 54.3 (39.2, 76.4) minutes; $P = .132$] and periprocedural complications ($P = .868$) did not differ between patients with and those without DM. After a median follow-up of 29.5 months, arrhythmia recurrence was significantly higher in the DM group compared to the no-DM group after adjustment for baseline differences (adjusted hazard ratio [HR] 2.24; 95% confidence [CI] 1.42–3.55; $P = .001$). There was a nonsignificant trend toward higher AF recurrence with worse glycemic levels (HR 1.29; 95% CI 0.99–1.69; $P = .064$).

CONCLUSION Although safety outcomes associated with AF ablation were similar between patients with and those without DM, arrhythmia-free survival was significantly lower among patients with DM. Poor glycemic control seems to an important risk factor for AF recurrence.

KEYWORDS Atrial fibrillation; Catheter ablation; Diabetes mellitus; Glycemic control; Outcomes

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Introduction

Diabetes mellitus (DM) is a major cardiovascular risk factor and is associated with higher morbidity and mortality.[1] Many epidemiologic studies have established DM as an independent risk factor for the development of atrial fibrillation (AF).[2,3] In a meta-analysis of several cohort and case-control studies, DM was associated with a 34% higher risk of developing AF.[3] The presence of comorbid DM and AF may confer worse prognosis than either condition alone.[4,5] Among AF patients, DM is associated with worse symptoms and quality of life, increased hospitalizations, and higher overall mortality.[5]

Catheter ablation is an established treatment of patients with symptomatic drug-refractory AF.[6] Compared with antiarrhythmic drugs, catheter ablation improved maintenance of sinus rhythm and quality of life, and reduced the risk of hospitalization in a small randomized study of patients with DM.[7] However, recurrence of AF after catheter ablation is common, and repeated procedures are often required in this population.[8]

The association between DM and catheter ablation outcomes is not clear.[6] Moreover, data on the association between glycemic control and AF recurrence after catheter ablation are limited. The objective of this study was to compare clinical outcomes after AF ablation in patients

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KEY FINDINGS

- Catheter ablation of atrial fibrillation (AF) seems to be a safe procedure in patients with diabetes mellitus (DM) and significantly reduces the symptom burden in this population. Periprocedural complications and rates of hospitalization were similar between patients with and those without DM.
- Long-term arrhythmia-free survival was significantly lower among patients with DM. Patients with DM were more likely to be on antiarrhythmic drug therapy during latest follow-up than patients without DM.
- Poor glycemic control may be an important risk factor for AF recurrence after catheter ablation among patients with DM.

with and those without DM and to determine the association between glycemic control and ablation outcomes.

Methods

Study design and population

This was an observational, retrospective cohort study performed within the Duke Center for Atrial Fibrillation. The study was approved by the Duke University Institutional Review Board and adhered to the principles articulated in the Common Rule (45 CFR 46). All AF ablation procedures performed from December 5, 2014, to January 28, 2016, in adult patients were retrospectively screened for inclusion. Only patients undergoing first-time ablation were eligible for inclusion. Patients without follow-up data or who had undergone catheter ablation other than radiofrequency ablation (eg, surgical, cryoballoon, or laser balloon) were excluded from the study. Data on baseline demographics, medical history, laboratory data, and medications before the index ablation were abstracted. Operative reports were manually reviewed to determine radiofrequency and fluoroscopy times and ablation lesion sets.

Definitions and outcomes

Patients were stratified based on the presence or absence of DM, as defined by the American Diabetes Association.[9] Preablation glycated hemoglobin A_{1c} (HbA_{1c}) level was defined as the most recent HbA_{1c} value $\leq$6 months before the index procedure. Clinical outcomes were determined at the time of last follow-up, including hospitalizations, symptom burden (Mayo AF Symptom Inventory [MAFSI] score), freedom from recurrent arrhythmia, and periprocedural complications. Arrhythmia recurrence was defined as any atrial tachyarrhythmia captured on 12-lead electrocardiogram (ECG), ambulatory monitoring (Holter monitor, implantable loop recorder, or external loop recorder), or implantable device lasting >30 seconds, or requiring cardioversion after a 3-month blanking period.[6] All patients had routine clinic follow-up visits and 12-lead ECGs scheduled at 3, 6, 9, and 12 months postprocedure and on a yearly basis thereafter, with more frequent follow-up in the presence of recurrent arrhythmia or symptoms. In addition, symptom burden and adverse events were determined by phone calls at 1 week, and 3, 6, and 12 months after the procedure. Symptoms were assessed by MAFSI score using standardized interviews conducted by the same nurse clinician.[10] Ambulatory monitoring was obtained at provider discretion in the presence of suspicious symptoms to determine arrhythmia recurrence. The incidence of hospitalization and results of ambulatory monitoring after ablation were determined by manual chart review. The methods for follow-up at Duke Center for Atrial Fibrillation have been previously reported.[11]

Radiofrequency ablation procedure

Informed consent was obtained before all ablation procedures. General anesthesia was used for all ablation procedures. Intravenous heparin was administered to maintain an activated clotting time of 300–400 seconds, and transseptal puncture was performed under direct visualization by intracardiac echocardiography. Pulmonary vein isolation was performed using continuous or point-to-point circumferential ablation with contact force-sensing open-tipped irrigated catheters. Electroanatomic mapping systems (CARTO, Biosense Webster Inc, Diamond Bar, CA; or NavX, Abbott, Minneapolis, MN) were used in all cases. Entrance and exit block were confirmed with a circular catheter or a high-resolution mapping catheter (PentaRay, Biosense Webster), and adenosine, isoproterenol, or burst pacing was administered at the operator's discretion. Additional lesion sets were performed at the discretion of the operator.[11]

Statistical analysis

Patient characteristics are summarized using either medians (25th percentile [Q1], 75th percentile [Q3]) or counts with percentages [n (%)] by DM status. Univariate comparisons of continuous variables between groups were performed using the Wilcoxon rank sum test if data were not normally distributed or the Student *t* test if data were normally distributed. Categorical variables were compared between groups using the χ^2 test or Fisher exact test.

Arrhythmia recurrence was first compared between DM and no-DM groups using the χ^2 test. Time to arrhythmia recurrence was defined as the time from index ablation to AF recurrence or last follow-up visit with a 3-month blanking period. Survival distributions were estimated using the Kaplan-Meier method and compared between groups using the log-rank test. Furthermore, Cox proportional hazards modeling was used to analyze arrhythmia-free survival between groups with and without adjustment for differences in baseline characteristics. Modeling results are presented as hazard ratio (HR) with 95% confidence interval (CI). The total MAFSI score was calculated by summing the frequency scores of all 12 AF-related symptoms. The change in MAFSI score from baseline to last available follow-up was compared between the 2 groups using the Student *t* test. A subgroup analysis was performed to examine the unadjusted association between

Table 1 Patient characteristics by DM status

Characteristic	DM (N= 65)	No DM (N= 286)	Total (N = 351)	*P* value
Follow-up duration (mo)	29.3 (8.4, 51.3)	29.5 (10.1, 49.1)	29.5 (9.4, 49.7)	.885*
Age (y)	68.0 (62.0, 72.0)	65.0 (57.0, 71.0)	66.0 (58.0, 71.0)	.023*
Male	40 (61.5)	205 (71.7)	245 (69.8)	.108†
BMI (kg/m^2)	33.5 (30.2, 37.3) (n = 64)	28.9 (25.4, 32.9) (n = 276)	29.7 (25.9, 34.4) (n = 340)	<.001*
AF type				
Paroxysmal	21 (32.3)	159 (55.6)	180 (51.3)	
Persistent	44 (67.7)	127 (44.4)	171 (48.7)	
$CHAD_2DA_2VASc$ score	4.0 (3.0, 4.5)	2.0 (1.0, 3.0)	2.0 (1.0, 4.0)	<.001*
Hypertension	57 (87.7)	181 (63.3)	238 (67.8)	<.001‡
Previous stroke/TIA	8 (12.3)	20 (7.0)	28 (8.0)	.201[4]
Coronary artery disease	18 (27.7)	54 (18.9)	72 (20.5)	.112†
Peripheral artery disease	1 (1.5)	10 (3.5)	11 (3.1)	.697‡
Dyslipidemia	41 (63.1)	141 (49.3)	182 (51.9)	.045
COPD	8 (12.3)	16 (5.6)	24 (6.8)	.061‡
Obstructive sleep apnea				.214‡
None	35 (53.8)	187 (65.4)	222 (63.2)	
Untreated	10 (15.4)	35 (12.2)	45 (12.8)	
Treated	20 (30.8)	64 (22.4)	84 (23.9)	
Heart failure	19 (29.2)	82 (28.7)	101 (28.8)	.928†
LVEF (%)	55.0 (50.0, 55.0) (n = 62)	55.0 (55.0, 55.0) (n = 275)	55.0 (55.0, 55.0) (n = 337)	.364*
Left atrial diameter (cm)	4.5 (4.0, 4.9) (n = 55)	4.0 (3.5, 4.5) (n = 252)	4.1 (3.6, 4.6) (n = 307)	<.001*
Serum creatinine (mg/dL)	1.0 (0.8, 1.3)	1.0 (0.9, 1.1)	1.0 (0.9, 1.2)	.528*
Preablation HbA_{1c}	6.8 (6.1, 7.5) (n = 47)	—	—	
Insulin use	10 (15.6)	—	—	
Oral agent	49 (76.6)	—	—	
Metformin	37 (56.9)	—	—	
Sulfonylurea	11 (16.9)	—	—	
Thiazolidinediones	2 (3.1)	—	—	
GLP-1 agonist	2 (3.1)	—	—	
DPP-4 inhibitor	5 (7.7)	—	—	
SGLT2 inhibitor	5 (7.7)	—	—	
Meglitinides	1 (1.5)	—	—	
Cardiovascular medication				
Beta-blocker	46 (70.8)	165 (57.7)	211 (60.1)	.052†
Calcium channel blocker	25 (38.5)	92 (32.2)	117 (33.3)	.331†
ACE-I	33 (50.8)	73 (25.5)	106 (30.2)	<.001†
ARB	13 (20.0)	45 (15.7)	58 (16.5)	.403†
Aldosterone antagonist	3 (4.6)	24 (8.4)	27 (7.7)	.440‡
Digoxin	5 (7.7)	10 (3.5)	15 (4.3)	.131†
Statin	41 (63.1)	102 (35.7)	143 (40.7)	<.001†
Preablation AAD				.357‡
Amiodarone	10 (15.4)	36 (12.6)	46 (13.1)	
Class IC	4 (6.2)	39 (13.6)	43 (12.3)	
Class III	21 (32.3)	95 (33.2)	116 (33.0)	
None	30 (46.2)	116 (40.6)	146 (41.6)	
Preablation device				.021‡
PPM	6 (9.2)	28 (9.8)	34 (9.7)	
ICD	0 (0.0)	16 (5.6)	16 (4.6)	
CRT	3 (4.6)	1 (0.4)	4 (1.1)	
Implantable loop recorder	0 (0.0)	3 (1.1)	3 (0.9)	
No device	56 (86.2)	237 (83.2)	293 (83.7)	

Values are given as median (Q1, Q3) or n (%) unless otherwise indicated.

AAD = antiarrhythmic drug; ACE-I = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin receptor blocker; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; DM = diabetes mellitus; DPP-4 = dipeptidylpeptidase-4; GLP-1 = glucagon-like peptide-1; HbA_{1c} = hemoglobin A_{1c}; ICD = implantable cardioverter–defibrillator; LVEF = left ventricular ejection fraction; PPM = permanent pacemaker; SGLT2 = sodium-glucose cotransporter-2; TIA = transient ischemic attack.

*Wilcoxon rank sum test.

†χ^2 test.

‡Fisher exact test.

Table 2 Procedural characteristics by DM status

Characteristic	DM (N = 65)	No DM (N = 286)	Total (N = 351)	*P* value
Total radiofrequency duration (min)	64.0 (43.6, 81.4)	54.3 (39.2, 76.4)	55.7 (39.5, 77.6)	.132*
Total fluoroscopy duration (min)	23.0 (13.9, 30.3)	20.1 (12.3, 28.0)	20.6 (12.4, 28.3)	.280*
Additional ablation				
CFAE	4 (6.2)	22 (7.7)	26 (7.4)	.798†
FIRM	1 (1.5)	3 (1.0)	4 (1.1)	.561†
Left atrial appendage	0 (0.0)	1 (0.3)	1 (0.3)	1†
Left atrial roof line	13 (20.0)	34 (11.9)	47 (13.4)	.083‡
SVC isolation	2 (3.1)	5 (1.7)	7 (2.0)	.618†
Posterior wall isolation	1 (1.5)	12 (4.2)	13 (3.7)	.476†
Right carinal isolation	15 (23.1)	68 (23.8)	83 (23.6)	.905‡
Mitral isthmus line	4 (6.2)	6 (2.1)	10 (2.8)	.093†
CTI line	10 (15.4)	45 (15.7)	55 (15.7)	.944‡
AAD at discharge				.122†
Amiodarone	15 (23.1)	36 (12.6)	51 (14.6)	
Class IC	4 (6.2)	29 (10.2)	33 (9.4)	
Class III	21 (32.3)	83 (29.1)	104 (29.7)	
None	25 (38.5)	137 (48.1)	162 (46.3)	

Values are given as median (Q1, Q3) or n (%) unless otherwise indicated.

CFAE = complex fractionated atrial electrogram; CTI = cavotricuspid isthmus; FIRM = focal impulse and rotor modulation; SVC = superior vena cava; other abbreviations as in Table 1.

*Wilcoxon rank sum test.

†Fisher exact test.

‡χ^2 test.

arrhythmia-free survival and the following variables: preablation HbA_{1c} levels as both a continuous variable and dichotomized variable ($\leq$7% or >7% based on American Diabetes Association treatment goals),[9] insulin use, sulfonylurea use, and metformin use using Cox proportional hazards models. Restricted cubic splines with 4 knots at the 5th, 35th, 65th, and 95th percentiles were used to examine the functional form of HbA_{1c} and time to arrhythmia recurrence. Proportional hazard assumption of the Cox models was verified using an appropriate Wald test. Analyses were performed in R Version 3.5.3 and SAS 9.4 (SAS Institute, Cary, NC).

Results

Baseline characteristics

Among the 351 consecutive patients who underwent first-time catheter ablation of AF during the study period, 65 (18.6%) had DM. Baseline characteristics of the study patients are listed in Table 1. Patients with DM were significantly older (68 [62, 72] years vs 65 [57, 71] years; $P = .023$), had a higher median body mass index (33.5 [30.2, 37.3] kg/m^2 vs 28.9 [25.4, 32.9] kg/m^2; $P < .001$), had more persistent AF (67.7% vs 44.4%; $P = .001$), and had higher CHA_2DS_2VASc scores (4.0 [3.0, 4.5] vs 2.0 [1.0, 3.0]; $P < .001$). Patients with DM also had a greater prevalence of hypertension (87.7% vs 63.3%; $P < .001$) and dyslipidemia (63.1% vs 49.3%; $P = .045$), and a larger median left atrial diameter (4.5 [4.0, 4.9] cm vs 4.0 [3.5, 4.5] cm; $P < .001$). Patients with DM were more likely to be treated with angiotensin-converting enzyme inhibitors (50.8% vs 25.5%; $P < .001$) and statins (63.1% vs 35.7%; $P < .001$).

Procedural characteristics

Total radiofrequency duration [64.0 (43.6, 81.4) minutes vs 54.3 (39.2, 76.4) minutes; $P = .132$] and fluoroscopy duration [23.0 (13.9, 30.3)] minutes vs 20.1 (12.3, 28.0) minutes; $P = .280$] did not differ between DM and no-DM groups (Table 2). Patients were equally likely to undergo additional ablations during the index procedure regardless of DM status, with the most common techniques being left atrial roof line (20.0% vs 11.9%; $P = .083$) and right carinal isolation (23.1% vs 23.8%; $P = .905$). There was no difference in antiarrhythmic medications prescribed at discharge ($P = .122$).

Ablation outcomes

After catheter ablation, all patients had clinic follow-up with routine ECGs, and the majority of patients (99.7%) had telephone follow-up by a nurse clinician to detect symptomatic recurrence or adverse events. There was no significant difference in the frequency of ambulatory monitoring or implantable device interrogation performed to detect AF recurrence in patients in the DM and no-DM groups (60.0% vs 62.2%; $P = .738$) (Table 3). After median follow-up of 29.5 (9.4, 49.7) months, patients with DM had a significantly higher rate of AF recurrence than patients without DM (56.9% vs 33.9%; $P = .001$). There was no significant difference in AF symptoms between the 2 groups (32.3% vs 29.0%; $P = .600$). Antiarrhythmic drug use was significantly higher in the DM group (44.6% vs 25.9%; $P = .001$), whereas the frequency of repeat ablations did not differ between the 2 groups (24.6% vs 19.9%; $P = .401$).

The Kaplan-Meier curve illustrating freedom from AF recurrence is shown in Figure 1. Arrhythmia-free survival was significantly lower in the DM group compared to the no-DM group ($P < .001$). In addition, DM was associated with a significantly higher risk of AF recurrence, after

Table 3 Follow-up and ablation outcomes by DM status

Outcomes	DM (N = 65)	No DM (N = 286)	Total (N = 351)	*P* value
Periprocedural complications				.868‡
Access site bleeding	1 (1.5)	4 (1.4)	5 (1.4)	
Stroke/TIA	0 (0.0)	3 (1.0)	3 (0.9)	
Acute heart failure	1 (1.5)	3 (1.0)	4 (1.1)	
Proarrhythmia (AT/AFL)	1 (1.5)	4 (1.4)	5 (1.4)	
Phrenic nerve paralysis	1 (1.5)	1 (0.3)	2 (0.6)	
Urinary tract infection	1 (1.5)	7 (2.4)	8 (2.3)	
Pericardial effusion/tamponade	0 (0.0)	0 (0.0)	0 (0.0)	
Any monitoring*	39 (60.0)	178 (62.2)	217 (61.8)	.738§
Ambulatory monitoring (mo)†	35 (53.8)	157 (54.9)	192 (54.7)	.878§
3	6 (17.1)	58 (36.9)	64 (33.3)	.029‡
6	10 (28.6)	58 (36.9)	68 (35.4)	.349§
9	9 (25.7)	24 (15.3)	33 (17.2)	.144‡
12	4 (11.4)	20 (12.7)	24 (12.5)	1‡
18	10 (28.6)	26 (16.6)	36 (18.8)	.010§
≥24	23 (65.7)	63 (40.1)	86 (44.8)	.006§
Ablation outcome				
AF recurrence	37 (56.9)	97 (33.9)	134 (38.2)	.001§
AF symptoms	21 (32.3)	83 (29.0)	104 (29.6)	.600§
AAD use				.001‡
Amiodarone	15 (23.1)	19 (6.6)	34 (9.7)	
Class IC	3 (4.6)	14 (4.9)	17 (4.8)	
Class III	11 (16.9)	41 (14.3)	52 (14.8)	
None	36 (55.4)	212 (74.1)	248 (70.7)	
Repeat ablations	16 (24.6)	57 (19.9)	73 (20.8)	.401§
All-cause hospitalization	19 (29.2)	62 (21.7)	81 (23.1)	.192§
Cardiovascular hospitalization	10 (15.4)	43 (15.0)	53 (15.1)	.065‡
Arrhythmia	8 (80.0)	24 (55.8)	32 (60.4)	
Heart failure	0 (0.0)	11 (25.6)	11 (20.8)	
Myocardial infarction	0 (0.0)	3 (7.0)	3 (5.7)	
Significant bleeding	0 (0.0)	4 (9.3)	4 (7.5)	
Stroke/TIA	2 (20.0)	1 (2.3)	3 (5.7)	

Values are given as n (%) unless otherwise indicated.

AFL = atrial flutter; AT = atrial tachycardia; other abbreviations as in Table 1.

*Any monitoring includes monitoring by device interrogation or ambulatory monitoring beyond routine electrocardiographic monitoring.

†Ambulatory monitoring includes Holter monitor, event monitor, and implantable loop recorder.

‡Fisher exact test.

§χ^2 test.

adjusting for age, body mass index, AF type, hypertension, dyslipidemia, and left atrial diameter (HR 2.24; 95% CI 1.61–3.46; *P* = .001) (Table 4).

All-cause periprocedural adverse events were infrequent and did not differ between the 2 groups (DM 5, no-DM 22; *P* = .868). No stroke or transient ischemic attack events were observed in patients with DM, whereas 3 stroke or transient ischemic attack events were observed in patients without DM. There were no cases of hemodynamically significant pericardial effusions or tamponade. The rates of cardiovascular hospitalization (15.4% vs 15.0%; *P* = .065) and all-cause hospitalization (29.2% vs 21.7%; *P* = .192) did not differ between the 2 groups. Among 250 patients with baseline and follow-up MAFSI scores (DM 46, no-DM 204), no significant difference in the reduction in total MAFSI symptom score was observed (–6.5 ± 5.7 vs –7.1 ± 5.5; *P* = .575) (Figure 2).

Glycemic control and AF recurrence

Among patients with DM, 47 patients (72%) had documented preablation HbA_{1c} levels. The majority of DM patients had satisfactory glycemic control, with median HbA_{1c} level of 6.8 (6.1, 7.5). Restricted cubic splines showed a linear relationship between HbA_{1c} and time to arrhythmia recurrence; therefore, the unadjusted analysis of the outcome was fitted on HbA_{1c} as a linear term. Overall, there was a trend toward higher AF recurrence with increased HbA_{1c} levels, but this did not reach statistical significance (HR 1.29; 95% CI 0.99–1.69; *P* = .064) (Table 5). Similarly, there was a nonsignificant trend toward higher risk of AF recurrence in patients with HbA_{1c} >7% compared to HbA_{1c} ≤7% (HR 1.70; 95% CI 0.83–3.51; *P* =.149). Freedom from AF recurrence by HbA_{1c} level (>7% vs ≤7%) is shown in Figure 3. The log-rank test showed no significant difference between these survival distributions (*P* = .143). There was no association between any of the diabetes medications and risk of AF recurrence.

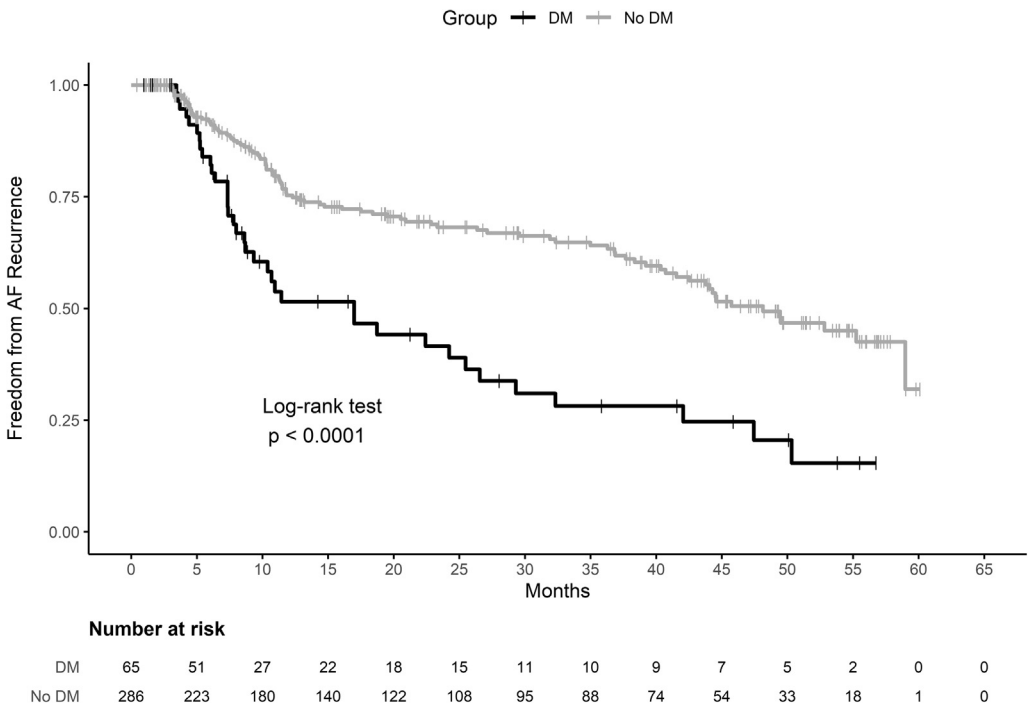

Figure 1 Kaplan-Meier plot of atrial fibrillation (AF)–free survival after a 3-month blanking period by diabetes mellitus (DM) status. Numbers at the bottom represent survivor counts.

Discussion

In this retrospective cohort study, we investigated the association between DM and outcomes after catheter ablation of AF. The 3 main findings of our analysis are as follows. First, patients with DM had lower arrhythmia-free survival after AF ablation compared to patients without DM. Second, there was no association between DM and risk of periprocedural complications or hospitalization after catheter ablation. Third, poor glycemic control before AF ablation may be associated with an increased risk of arrhythmia recurrence in patients with DM.

Several studies have evaluated whether DM is a risk factor for AF recurrence after ablation, with conflicting results.[12–15] In the present study, we found that DM is an independent risk factor for arrhythmia recurrence. Patients with DM had significantly lower arrhythmia-free survival than patients without DM after median follow-up of 29.5 months and more frequently were on antiarrhythmic drug therapy. Recently, a multicenter observational study (n = 2504) found that DM was associated with a higher rate of atrial arrhythmia recurrence after median follow-up of 17 months.[14] Patients with DM had lower arrhythmia-free survival after ablation of persistent AF but had comparable outcomes after ablation of paroxysmal AF. These findings are consistent with our study, which demonstrated a greater burden of persistent AF among patients with DM, which may have contributed to the higher rate of AF recurrence. Previous studies have shown that DM promotes proarrhythmic atrial remodeling, which may contribute to AF progression and explain the decreased long-term efficacy of catheter ablation in this population.[12,15,16] Nevertheless, our study showed that patients with DM demonstrated a significant improvement in symptom burden by MAFSI score after catheter ablation. This finding is important, as DM has been associated with worse symptoms and quality of life among patients with AF, and the primary indication for AF ablation is improvement of quality of life.[5] Therefore, our experience suggests that catheter ablation remains an effective treatment of patients with DM, despite the increased risk for AF recurrence.

Safety outcomes associated with AF ablation were similar between patients with and those without DM. This result is consistent with previous studies, which found no significant difference in procedural adverse events and hospitalization rates in patients with DM compared to the general population.[8,14] A recent meta-analysis reported an overall complication rate of 3.5% after catheter ablation in patients with DM.[8]

Table 4 Association between DM and AF recurrence with and without covariates

Variable	HR (95% CI)	*P* value
Unadjusted		
DM vs no DM	2.36 (1.61–3.46)	<.001
Adjusted		
DM vs no DM	2.24 (1.42–3.55)	.001
Age at procedure	1.01 (0.99, 1.03)	.604
BMI (kg/m^2)	0.99 (0.96–1.02)	.520
AF type: Persistent vs paroxysmal	2.04 (1.34–3.10)	.001
Hypertension	0.98 (0.65–1.49)	.930
Dyslipidemia	0.90 (0.61–1.32)	.576
Left atrial diameter	1.14 (0.90–1.46)	.285

CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

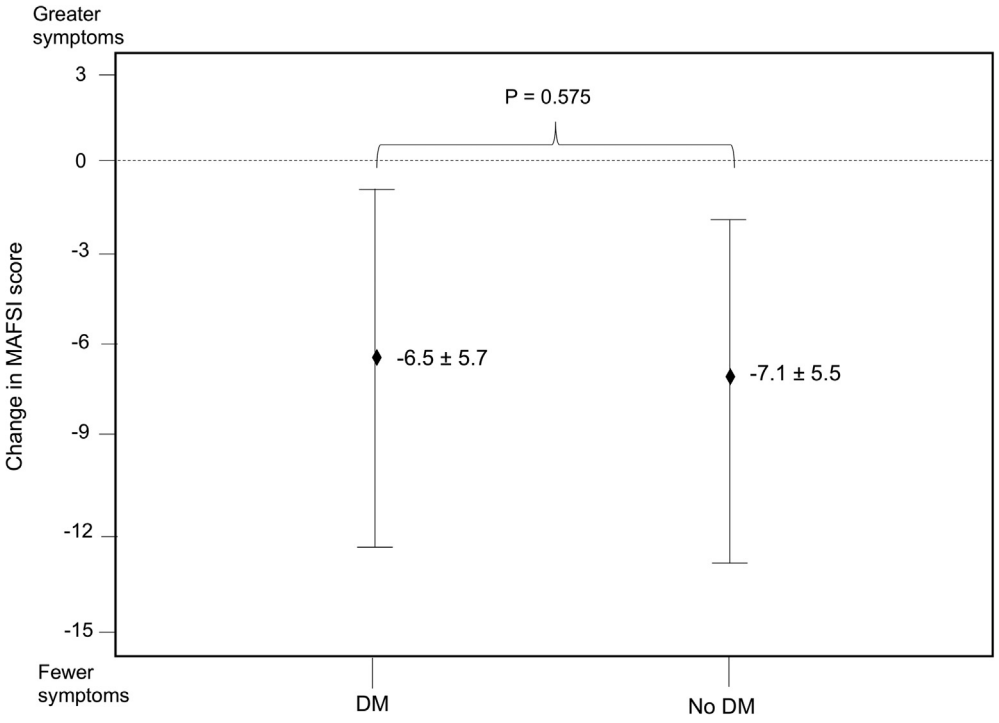

Figure 2 Change in total Mayo AF Symptom Inventory (MAFSI) symptom frequency score from baseline to latest follow-up stratified by diabetes mellitus (DM) status. *Diamonds* represent mean change in total MAFSI score from baseline to latest follow-up. *Vertical lines* represent standard deviation.

In the present analysis, we observed a slightly higher all-cause periprocedural complication rate of 7.7%. However, our study cohort included patients who were older and had a higher prevalence of hypertension and structural heart disease, which may account for the difference in observed outcome. The overall evidence suggests that AF ablation in patients with DM is not associated with increased procedural risk, despite the higher burden of comorbidities in this population.

Several studies have shown that glycemic control may affect ablation outcomes in patients with DM. In a retrospective study of 298 patients with type 2 DM, worsening trend in glycemic levels was associated with significantly higher risk of arrhythmia recurrence after catheter ablation.[17] In a meta-analysis of 15 studies on catheter ablation outcomes, higher HbA_{1c} levels were associated with higher risk of AF recurrences in patients with DM.[8] In the ARREST-AF (Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation) trial, intensive risk factor management, including improved glycemic control (HbA_{1c} <7%), was associated with a nearly 5-fold higher odds of arrhythmia-free survival after ablation.[18] In the present study, we observed a trend toward higher AF recurrence with worse glycemic control, but this did not reach statistical significance (P = .064). This result may be related to the modest sample size and resultant limited power of the study. Large prospective multicenter studies are needed to define the role of glycemic control in ablation outcomes, particularly given the increasing prevalence of DM and AF.

Recently, the type of DM medication used for glycemic control has been shown to impact AF risk. In a population-based cohort study, metformin and thiazolidinediones were associated with decreased risk of incident AF, whereas insulin use was associated with increased risk of incident AF.[19] In a prospective cohort study, pioglitazone was associated with a significantly lower risk of AF recurrence after ablation, which has been attributed to its anti-inflammatory and antioxidant properties.[20] The role of other DM medications on ablation outcomes is not known. In the present study, we found no significant association between metformin, sulfonylurea, or insulin use and AF recurrence after ablation. Additional analyses involving a larger number of patients are needed to determine the effect of these DM medications on ablation outcomes.

Study limitations

First, this was a single-center, retrospective, observational study with a relatively small sample size. Second, the

Table 5 Association between glycemic control and diabetes medications and risk of AF recurrence

Variable	HR (95% CI)	*P* value
HbA_{1c} continuous	1.29 (0.99–1.69)	.064
HbA_{1c} >7% vs ≤7%	1.70 (0.83–3.51)	.149
Insulin use	0.90 (0.39–2.05)	.795
Sulfonylurea use	1.42 (0.54–3.71)	.476
Metformin use	1.33 (0.69–2.55)	.394

Abbreviations as in Tables 1 and 4.

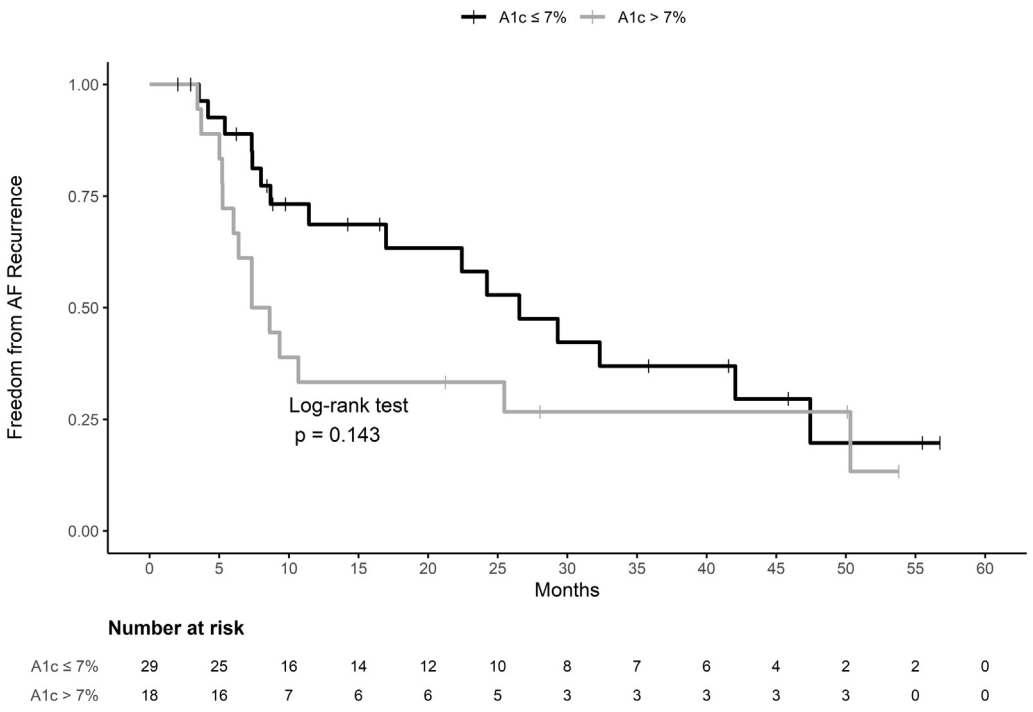

Figure 3 Kaplan-Meier plot for freedom from atrial fibrillation (AF) recurrence by hemoglobin A_{1c} (A1c) level. Numbers at the bottom represent survivor counts.

majority of patients in the DM group had satisfactory glycemic control and minimal renal impairment, which may limit the generalizability of our findings to patients with controlled DM. Finally, the lack of a standardized arrhythmia detection strategy (eg, implantable loop monitor) may limit detection of asymptomatic recurrences. However, each patient was followed by a clinical electrophysiologist after the procedure and underwent diagnostic studies as needed to detect arrhythmia recurrence, which reflects real-world clinical practice.

Conclusion

Catheter ablation of AF seems to be a safe procedure in patients with DM and significantly reduces the symptom burden of this population. However, long-term arrhythmia-free survival is significantly lower among patients with DM. Larger prospective studies are needed to determine the impact of glycemic control and DM medications on catheter ablation outcomes in this population.

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