Incidence, duration, pattern, and burden of de novo atrial arrhythmias detected by continuous ECG monitoring using an implantable loop recorder following ablation of the cavotricuspid isthmus

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BACKGROUND Following cavotricuspid isthmus (CTI) ablation, many patients with atrial flutter (AFL) are diagnosed with atrial fibrillation (AF). The incidence, duration, pattern, and burden of AF remain undefined. These may have implications for the management of these patients.

OBJECTIVE To classify the incidence, duration, pattern, and burden of AF/AFL using an implantable loop recorder (ILR) after CTI ablation.

METHODS We enrolled consecutive patients with CTI-dependent AFL, no known history of AF, and CHA2DS2-VASc ≥ 2. An ILR was implanted before or within 90 days of ablation. The time to first AF/AFL, pattern, duration, and burden of longest AF/AFL were determined. Five distinct AF/AFL cohorts were identified: no AF/AFL and those with recurrences of isolated, clustered, frequent, or persistent AF/AFL.

RESULTS Fifty-two patients (81% male; 73 ± 9 years; CHA2DS2-VASc 3.7 ± 1.2) were followed for 784 (interquartile range [IQR] 263, 1150) days. AF/AFL occurred in 44 (85%) patients at 64 (IQR 8, 189) days post-CTI ablation and was paroxysmal in 31 (70%) patients (burden 0.6% [IQR 0.1, 4.8]). AF/AFL was isolated (n = 5, 11%), clustered (n = 7, 16%), frequent (n = 19, 43%), and persistent (n = 13, 30%). The longest AF episode was <24 hours in 27 (61%) patients.

CONCLUSION Following CTI ablation in AFL patients, although AF/AFL occurs in most patients, the burden is low and episodes were <24 hours in the majority of patients. Additional studies are needed to determine whether long-term electrocardiographic monitoring can help guide management of patients undergoing CTI ablation.

KEYWORDS Atrial fibrillation; Atrial flutter; Catheter ablation; Cavotricuspid isthmus ablation; Implantable loop recorder
KEY FINDINGS

- The vast majority of patients with diagnosis of typical atrial flutter and no known atrial fibillation who undergo cavitricuspid isthmus (CTI) ablation will develop in follow-up atrial arrhythmias—atrial fibrillation (AF) or atrial flutter (AFL).
- In a majority of the patients AF/AFL are paroxysmal and of short duration, less than 24 hours.
- Overall burden of AF/AFL post CTI ablation is low (0.6%).
- The first episode of AF/AFL occurs in the first 6 months post ablation in 75% of the patients.
- Four patterns of AF/AFL occurrence were identified: isolated, clusters, frequent, and persistent.
- Diabetes and use of angiotensin-converting enzyme inhibitors / angiotensin receptor blockers was associated with higher likelihood of having episodes >24 hours.

collected. All patients had history of paroxysmal or persistent typical AFL, as demonstrated by either ECGs at least 7 days apart or extended continuous ECG outpatient monitoring and need for electrical cardioversion for restoration of sinus rhythm. There was no known history of AF, by standard evaluation in the office with an ECG and/or external monitoring, and all patients had a CHA2DS2-VASc score ≥ 2. All patients were implanted with an ILR (Medtronic LINQTM, Medtronic, Minneapolis, MN) at any point in time prior to or within 90 days of the CTI ablation. All patients provided consent for data collection and follow-up. The study protocol was approved by the Western Institutional Review Board and complied with Good Clinical Practice guidelines.

Ablation procedure

All patients with persistent AFL were anticoagulated with warfarin or a direct oral anticoagulant for at least 3 weeks prior to ablation. Preprocedure anticoagulation was not required in patients with paroxysmal AFL presenting for ablation in sinus rhythm. In patients taking warfarin, an international normalized ratio (INR) was obtained weekly prior to ablation to ensure the INR was ≥2.0. A transesophageal echocardiogram, to assess the left atrial appendage for thrombus, was obtained only in patients presenting for ablation in AFL, in whom the INR was <2.0 or if they reported any missed doses of their direct oral anticoagulant in the 3 weeks prior to ablation. All patients underwent CTI ablation guided by 3-dimensional electroanatomic mapping system (either CARTO 3; Biosense Webster, Diamond Bar, CA or RHYTHMIA; Boston Scientific, Marlborough, MA) in conjunction with an open-irrigated ablation catheter (ThermoCool SmartTouch® open irrigated ablation catheter; Biosense Webster or INTELLANAV MIFI™ open irrigated ablation catheter; Boston Scientific). The endpoint of ablation was the demonstration of bidirectional block across the CTI. No other arrhythmia was ablated, and no patient was treated with an antiarrhythmic drug (AAD) after ablation. The duration of anticoagulation after ablation was left to the discretion of the physician; however, all patients presenting in AFL were anticoagulated for a minimum of a month post ablation.

ILR implant and follow-up

The ILR was implanted either prior to, at the time of, or within 90 days of ablation using local anesthesia in the left fourth intercostal space. The programmed indication for the ILR was “suspected AF” or “AF monitoring,” which defaulted the device to standardized settings for AF detection. Once the ILR was implanted, it was immediately paired to a MyCareLink™ (Medtronic) patient monitor. ECG data transfer occurred wirelessly on a daily basis. All device-detected AF episodes were adjudicated by a technician and electrophysiologist, who determined the duration and pattern of all true AF episodes.

The time to first occurrence of AF, duration of longest AF (along with overall burden), and pattern of AF were determined. Patients were divided into 5 distinct groups based on their recurrence pattern (Figure 1): (1) no AF during follow-up; (2) isolated AF episodes—single AF episode followed by >6 months until another AF episode; (3) clusters of AF episodes—more than 1 episode of AF within a month followed by >6 months until another AF episode; (4) frequent AF episodes—multiple AF episodes without any 6-month AF-free period; (5) persistent AF—AF lasting continuously for more than 7 days.

Statistical analyses

Continuous data are presented as means with standard deviations and were compared using Student t test or analysis of variance. All categorical data are presented as proportions and were analyzed using χ² or Fisher exact tests. Unadjusted survival curves for selected variables were estimated with the use of the Kaplan-Meier method and groups were compared using the log-rank test. A value of P < .05 was considered to be statistically significant. All statistical tests were performed using the IBM/SPSS statistical package (version 19.0; IBM Corp, Armonk, NY).

Results

The cohort included 52 patients (81% male; 73 ± 9 years; CHA2DS2-VASc 3.7 ± 1.2; left atrial diameter 4.4 ± 0.7 cm); paroxysmal AFL was present in 19 (37%) patients and 25 (48%) patients presented in AFL at the time of ablation. The vast majority of patients (n = 45, 87%) were on oral anticoagulation at the time of ablation. Only 1 patient was on an AAD at the time of ablation, and none were on an AAD after ablation.

Bidirectional block across the CTI was achieved in all patients. During the procedure, AF developed in 4 patients; each patient required cardioversion to restore sinus rhythm. An ILR
was implanted immediately post ablation in 44 (85%) patients, 4 patients had an ILR implanted 165 (interquartile range [IQR] 136, 206) days prior to procedure and in 4 patients ILR was implanted 56 (IQR 36, 64) days after ablation. There were no acute procedure-related complications; however, 1 patient developed a pulmonary embolism 6 days after ablation. This patient had presented for ablation in sinus rhythm and was not placed on anticoagulation after the ablation.

![Figure 1](image)

**Figure 1** Patterns of atrial fibrillation (AF) and atrial flutter detected by loop recorder. 
- **A**: Isolated: single AF episode followed by >6 months until another AF episode. 
- **B**: Cluster: more than 1 episode of AF within a month followed by >6 months until another AF episode. 
- **C**: Frequent: multiple AF episodes without any 6-month AF-free period. 
- **D**: Persistent AF: AF lasting continuously for more than 7 days. AT = atrial tachycardia.

Table 1

Demographics of the study population and comparison of patients who did and did not develop an atrial tachyarrhythmia during follow-up

| Demographics                          | Total cohort | Atrial arrhythmia n = 44 | No atrial arrhythmia n = 8 | P value |
|---------------------------------------|--------------|--------------------------|-----------------------------|---------|
| Age (y) ± SD                          | 73 ± 9       | 72 ± 9                   | 75 ± 3                      | .16     |
| Male, n (%)                           | 42 (81%)     | 37 (84%)                 | 5 (63%)                     | .17     |
| Paroxysmal atrial flutter, n (%)      | 19 (37%)     | 14 (32%)                 | 5 (63%)                     | .12     |
| CHA2DS2-VASc score                    | 3.7 ± 1.0    | 3.6 ± 1.2                | 4.1 ± 1.0                   | .18     |
| Comorbidities, n (%)                  |              |                          |                            |         |
| Congestive heart failure              | 12 (23%)     | 12 (27%)                 | 0 (0%)                      | .17     |
| Hypertension                          | 50 (96%)     | 43 (98%)                 | 7 (88%)                     | .29     |
| Diabetes                              | 18 (35%)     | 15 (34%)                 | 3 (38%)                     | 1.00    |
| Prior stroke                          | 7 (13%)      | 5 (11%)                  | 2 (25%)                     | .29     |
| Coronary and vascular disease         | 21 (40%)     | 18 (41%)                 | 3 (38%)                     | 1.00    |
| Body mass index                       | 28 ± 5       | 28 ± 5                   | 31 ± 7                      | .35     |
| Creatinine clearance, mL/min          | 78 ± 33      | 78 ± 35                  | 78 ± 22                     | .95     |
| Obstructive sleep apnea, n (%)        | 8 (15%)      | 6 (14%)                  | 2 (25%)                     | .41     |
| Echocardiogram                        |              |                          |                            |         |
| Left atrial diameter, cm              | 4.4 ± 0.7    | 4.4 ± 0.7                | 4.0 ± 0.3                   | .02     |
| Left ventricular ejection fraction, % | 53 ± 10      | 52 ± 11                  | 59 ± 3                      | .002    |
| Cardiovascular medication, n (%)      |              |                          |                            |         |
| Beta-blockers                         | 42 (81%)     | 37 (84%)                 | 5 (63%)                     | .15     |
| Calcium channel blockers              | 9 (17%)      | 7 (16%)                  | 2 (25%)                     | .53     |
| ACEI/ARBs                             | 31 (60%)     | 27 (61%)                 | 4 (50%)                     | .55     |
| Antiplatelets                         | 19 (37%)     | 15 (34%)                 | 4 (50%)                     | .39     |

Bold values indicate statistical significance.
ACEI = angiotensin-converting enzyme inhibitors; ARBs = angiotensin receptor blockers.
During a median follow-up of 784 (IQR 263, 1150) days, 44 (85%) patients were diagnosed with an atrial tachyarrhythmia for the first time (Table 1, Figure 2). No patient was lost to follow-up. The median time to first episode of an atrial arrhythmia was 64 (IQR: 4, 189) days. Arrhythmia occurred in the first month post ablation in 21 (48%) patients and within the first 6 months in 33 (75%) patients. Atrial arrhythmias observed post CTI ablation were entirely asymptomatic in 27 (61%) patients.

Figure 2  The incidence of atrial fibrillation / atrial flutter after ablation of the cavotricuspid isthmus.

Figure 3  Duration of longest episode of atrial fibrillation (AF) / atrial flutter observed following ablation of the cavotricuspid isthmus.
AF alone was demonstrated in 39 (89%) patients, AF and recurrent typical AFL in 3 (7%) patients, and atypical AFL only in 2 (4%) patients, as confirmed by ECG and repeat ablation in 4 out of 5 patients. No patient presented with an isolated recurrence of typical AFL. As compared to patients without an atrial arrhythmia, patients who developed an atrial arrhythmia had a larger left atrial diameter (4.4 ± 0.7 cm vs 4.0 ± 0.3 cm, \( P = .02 \)) and lower left ventricular ejection fraction (52% ± 11% vs 59% ± 3%, \( P = .002 \); Table 1).

These episodes were paroxysmal in 31 (70%) patients, with the longest episode ranging from 8 minutes to 54.1 hours, and persistent in 13 (30%) patients. Of the 31 patients with a paroxysmal atrial arrhythmia, in 27 (87%) patients, all recurrences were <24 hours in duration (Figure 3). As compared to patients in whom all recurrences of an atrial arrhythmia were <24 hours, those with episodes >24 hours were more likely to suffer from diabetes mellitus and be treated with angiotensin-converting enzyme inhibitors / angiotensin receptor blockers (Table 2).

Four distinct pattern of arrhythmia recurrence were observed (Figure 4). Recurrences occurred as an isolated episode (n = 5, 11%), clustered episodes (n = 7, 16%), frequent episodes (n = 19, 43%), and persistent form (n = 13, 30%). All patients who experienced either an isolated episode or clustered episodes were asymptomatic. The pattern changed during the follow-up period in only 9 (20%) patients; specifically, 1 patient progressed from an isolated to clustered pattern, 4 patients from an isolated to frequent pattern, 1 patient from a clustered to frequent pattern, and 3 patients from a frequent to persistent pattern. The time to first atrial arrhythmia occurrence, duration of longest atrial arrhythmia, lifetime burden of these recurrences, and clinical interventions in each of these 4 categories is summarized in Table 3 (and Supplemental Figure).

The median overall burden of atrial arrhythmias at the last follow-up was only 0.6% (IQR: 0.1, 4.8). Of note, in this ILR, both true- and false-positive events contribute to the overall burden; it is not possible to generate a burden assessment that is limited only to true AF episodes. We further characterized our patients into 4 distinct groups based on whether they had true and/or false AF episodes detected by the ILR. These groups included (1) patients without any true or false detection of an atrial arrhythmia (n = 3, 6%); (2) patients with only true detection of an atrial arrhythmia (n = 24, 46%); (3) patients with only false detection of an atrial arrhythmia (n = 5, 10%); and (4) those with both true and false detection of an atrial arrhythmia (n = 20, 38%). Thus, 25 (48%) patients had at least 1 false detection of AF. The duration of longest “AF” episode and lifetime burden in those with a false detection were significantly shorter than observed in patients with a true detection (P = .001 and P = .02, respectively, Figure 5).

None of the 5 patients with an isolated recurrence and 2 (29%) of the 7 patients with a cluster of an atrial arrhythmia post ablation required any intervention (Table 3). In contrast, 8 of the 19 patients (42%) with frequent recurrences and 9 of the 13 patients (69%) with persistent AF required an intervention. These included a pacemaker implant in 3 patients, cardioversion in 9 patients, initiation of an AAD in 8 patients, and repeat ablation in 11 patients. Ablations included pulmonar y vein isolation (PVI) alone (n = 6), PVI + redo CTI ablation (n = 1), redo CTI ablation alone (n = 2), and ablation of an atrial tachycardia (n = 2).

There were 7 patients on no anticoagulation at the time of ablation. Following the ablation, 2 of these patients remained off anticoagulation during follow-up. In 5 patients, anticoagulation was stopped at a median of 45 (IQR 24, 46) days. Of the 13 patients (69%) with persistent AF required an intervention. These included a pacemaker implant in 3 patients, cardioversion in 9 patients, initiation of an AAD in 8 patients, and repeat ablation in 11 patients. Ablations included pulmonary vein isolation (PVI) alone (n = 6), PVI + redo CTI ablation (n = 1), redo CTI ablation alone (n = 2), and ablation of an atrial tachycardia (n = 2).

Discussion

In this study, we evaluated patients with a history of paroxysmal or persistent typical AFL referred for catheter ablation,
which is a cohort commonly seen in clinical practice. None of the patients had a known history of AF by standard evaluation in the office with an ECG and/or external monitoring and all had an elevated risk of thromboembolism, as defined by a CHA2DS2-VASc score of ≥2. Using an ILR for long-term continuous ECG monitoring, we found that during more than 2 years of postablation follow-up, 85% of patients had at least 1 episode of AF/AFL. This is the largest such cohort reported to date followed long-term with continuous ECG monitoring using an ILR.

Patients who developed AF/AFL had a larger left atrial diameter and lower ejection fraction than patients who remained AF-free. Half the patients developed AF/AFL within the first month of ablation; 75% developed AF/AFL within 6 months of ablation. The overall AF/AFL burden was low (0.6%) and 70% of the episodes were paroxysmal (most commonly lasting <24 hours). Diabetes and use of angiotensin-converting enzyme inhibitors / angiotensin receptor blockers was associated with a higher likelihood of having episodes lasting >24 hours. Finally, we identified 4 distinct patterns of AF/AFL recurrences in these patients. The high rate of AF after CTI ablation has raised discussion about the value of PVI at the time of CTI ablation, even in patients without any documented episodes of AF. The Prevent-AF Study I randomized 50 patients with AFL to undergo either CTI ablation alone or CTI ablation along with PVI using a cryoballoon. All patients had long-term ECG monitoring using a Reveal XT ILR. Of note, the patients were young (mean age 57 years) and had a low CHA2DS2-VASc score (mean 1.78), but had a very large left atrial diameter (mean 5.2 cm). AF was seen in 12% of patients who underwent CTI and PVI and in 52% of patients who underwent CTI ablation alone (P = .003). Similarly, the AF burden was significantly lower in patients who underwent CTI ablation and PVI (4.0% vs 8.3%, P = .034). From a clinical standpoint, however, it is unclear whether one would manage a patient differently whether the patient had 4.0% or 8.3% burden of AF, which makes the role of prophylactic PVI unclear given the increased procedure time and associated risk of complications inherent to the combined procedure. The REDUCE AF study studied a larger cohort of 216 patients. Patients were randomized to either CTI ablation alone or CTI ablation and PVI using radiofrequency energy. Patients were followed for a mean of 18 months; most patients did not have an ILR. Patients who underwent the combined procedure had significantly higher freedom from a recurrent atrial arrhythmia (71.3% vs 60.2%, P = .044). However, no information was provided about the burden or pattern of AF observed in these patients.

A recent meta-analysis analyzed data from the 4 prior studies that have compared CTI ablation to CTI ablation and PVI in patients with history of AFL alone. These studies have shown a higher freedom from atrial arrhythmias in patients who underwent the combined procedures (odds

Figure 4 Pattern and longest episode duration of atrial fibrillation (AF) / atrial flutter after ablation of the cavotricuspid isthmus, stratified by pattern of arrhythmia recurrence.
Although the procedure and fluoroscopy times were longer in patients undergoing the combined procedures, there was no statistically significant difference in complication rates. However, these studies have not reliably addressed either the burden or pattern of AF recurrences.

Understanding the incidence, burden, and pattern of AF occurring after CTI ablation may be important to inform decisions regarding the need for anticoagulation in these patients. Current guidelines recommend the following: “for patients with atrial flutter, anticoagulant therapy is recommended according to the same risk profile used for AF.”

Thus, patients evaluated in our study would merit lifelong anticoagulation and there would be no need for long-term ECG monitoring. The need to address subsequent AF could be driven exclusively by patient symptoms. However, in our opinion, there are limitations to this approach.

First, it has been previously demonstrated that although most patients with AFL also have AF, there are indeed patients who only have AFL. These patients have similar stroke rate to patients without AF or AFL; the risk of stroke appears to be elevated in those patients with both AF and AFL. In
our study, 15% of patients had no AF after AFL ablation, as confirmed by long-term ECG monitoring with an ILR. Second, another proposed definition of ILR-determined success is monthly AF burden <0.5%, which corresponds to a cumulative AF time of <3.6 hours in a month. In our study, 22 (42%) patients met this definition of success. Further data are needed to determine if these patients could be safely spared the risks inherent to long-term anticoagulation. In 27 (52%) patients all AF episodes lasted <24 hours. A prior study has shown very low risk of thromboembolism in these types of patients; in fact, a randomized clinical trial is currently underway that compares the efficacy of aspirin to apixaban in this patient population. Finally, 13 (25%) patients had an isolated or clustered pattern of AF recurrence. It has been suggested that these patterns may be amenable to a “pill-in-the-pocket” approach to anticoagulation, which could significantly reduce the cumulative exposure to oral anticoagulation in these patients.

An interesting finding in this study was the association between diabetes and occurrence of an atrial arrhythmia lasting ≥24 hours after CTI ablation. Diabetes has recently been shown to be associated with lower arrhythmia-free survival after catheter ablation of AF. We chose to investigate a cut-off of < or ≥24 hours for 2 reasons. First, as previously mentioned, the role of anticoagulation for episodes <24 hours remains undefined. Second, a recent analysis shows a significantly lower likelihood of arrhythmia-free survival following catheter ablation of AF in patients whose episodes were ≥24 hours prior to ablation. Identification of diabetes as a risk factor affords us a possible venue to pursue an opportunity for intervention. The DECLARE-TIMI 58 has shown that dapagliflozin, a sodium-glucose cotransporter 2 inhibitor, significantly decreased the incidence of reported episodes of AF/AFL in high-risk patients with type 2 diabetes mellitus. Future studies need to investigate the role of sodium-glucose cotransporter 2 inhibitors post CTI ablation as a means to reduce the likelihood of AF/AFL post CTI ablation.

**Limitations**

All ILRs used in this study were from a single manufacturer with a proprietary algorithm for AF detection. Episodes of
AF <2 minutes in duration cannot be detected by the device. The generalizability to other long-term ECG monitoring devices is unknown. The vast majority of patients did not have the ILR prior to CTI ablation. Thus, it is possible that some patients had AF prior to ablation but were clinically undiagnosed.

Conclusion
In summary, continuous ECG monitoring using an ILR shows that the vast majority of patients who underwent CTI ablation for management of AFL develop an atrial tachyarrhythmia post ablation. However, episodes are commonly asymptomatic, paroxysmal, and associated with low burden and duration. The advent of technology that facilitates long-term and continuous ECG monitoring allows us to refine our understanding of AF/AFL in patients undergoing CTI ablation for management of AFL. This is a pilot and hypothesis-generating study. Additional studies are now needed to determine whether long-term ECG monitoring can help guide and inform management of these patients.

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Appendix
Supplementary data
Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.cvdhj.2020.10.003.

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