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Circulation: Arrhythmia and Electrophysiology

ORIGINAL ARTICLE

Colchicine to Prevent Atrial Fibrillation Recurrence After Catheter Ablation: A Randomized, Placebo-Controlled Trial

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BACKGROUND: Inflammation may promote atrial fibrillation (AF) recurrence after catheter ablation. This study aimed to evaluate a short-term anti-inflammatory treatment with colchicine following ablation of AF.

METHODS: Patients scheduled for ablation were randomized to receive colchicine 0.6 mg twice daily or placebo for 10 days. The first dose of the study drug was administered within 4 hours before ablation. Atrial arrhythmia recurrence was defined as AF, atrial flutter, or atrial tachycardia >30 s on two 14-day Holters performed immediately and at 3 months following ablation.

RESULTS: The modified intention-to-treat population included 199 patients (median age, 61 years; 22% female; 70% first procedure) who underwent radiofrequency (79%) or cryoballoon ablation (21%) of AF. Antiarrhythmic drugs were prescribed at discharge in 149 (75%) patients. Colchicine did not prevent atrial arrhythmia recurrence at 2 weeks (31% versus 32%; hazard ratio [HR], 0.98 [95% CI, 0.59–1.61]; *P*=0.92) or at 3 months following ablation (14% versus 15%; HR, 0.95 [95% CI, 0.45–2.02]; *P*=0.89). Postablation chest pain consistent with pericarditis was reduced with colchicine (4% versus 15%; HR, 0.26 [95% CI, 0.09–0.77]; *P*=0.02) and colchicine increased diarrhea (26% versus 7%; HR, 4.74 [95% CI, 1.95–11.53]; *P*<0.001). During a median follow-up of 1.3 years, colchicine did not reduce a composite of emergency department visit, cardiovascular hospitalization, cardioversion, or repeat ablation (29 versus 25 per 100 patient-years; HR, 1.18 [95% CI, 0.69–1.99]; *P*=0.55).

CONCLUSIONS: Colchicine administered for 10 days following catheter ablation did not reduce atrial arrhythmia recurrence or AF-associated clinical events, but did reduce postablation chest pain and increase diarrhea.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: atrial fibrillation ■ catheter ablation ■ colchicine ■ inflammation ■ pericarditis

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Catheter ablation by means of pulmonary vein isolation can prevent the recurrence of atrial fibrillation (AF). It is more effective in restoring sinus rhythm and may be associated with greater quality of life improvement than medical therapy.[1,2] However, catheter ablation is still limited by high rates of atrial arrhythmia (atrial tachycardia/AF) recurrence.[1,3]

Radiofrequency or cryoballoon ablation causes necrosis of cardiac tissue, accompanied by an inflammatory response. Previous studies have shown that postablation elevation in biomarkers of inflammation such as C-reactive protein or interleukin-6, peaking 1 to 2 days following catheter ablation is associated with early atrial arrhythmia recurrence.[4–6] Early recurrence

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Abstract presented at Heart Rhythm Society Meeting in May 2023.
Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCEP.123.012387.
For Sources of Funding and Disclosures, see page 9.
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WHAT IS KNOWN?

- Inflammation may promote atrial arrhythmia recurrence after catheter ablation of atrial fibrillation.
- Colchicine is a widely available anti-inflammatory agent.

WHAT THE STUDY ADDS

- In this randomized, placebo-controlled trial, colchicine administered for 10 days after catheter ablation did not prevent atrial arrhythmia recurrence at 2 weeks or at 3 months following ablation.
- Postablation chest pain consistent with pericarditis was reduced with colchicine and colchicine increased diarrhea.
- During a median follow-up of 1.3 years, colchicine did not reduce a composite of emergency department visit, cardiovascular hospitalization, cardioversion or repeat ablation.

Nonstandard Abbreviations and Acronyms

AF	atrial fibrillation
CIRCA-DOSE	Cryoballoon Versus Irrigated Radiofrequency Catheter Ablation: Double Short Versus Standard Exposure Duration
IMPROVE-PVI	Impact of Short-Course Colchicine Versus Placebo After Pulmonary Vein Isolation
IQR	interquartile range

has been associated with recurrence beyond 3 months of ablation.[7,8] In addition, any recurrent atrial arrhythmia may be associated with health care utilization, such as a visit to the emergency department, hospitalization, or cardioversion.

Reducing postablation inflammation may result in less early atrial arrhythmia recurrence and improve clinical outcomes following catheter ablation. Colchicine is a widely available anti-inflammatory agent that reduces cardiovascular events in patients with atherothrombotic disease.[9,10] We evaluated a 10-day treatment with colchicine in patients undergoing catheter ablation for AF in a randomized, double-blind, placebo-controlled clinical trial.

METHODS

The IMPROVE-PVI (Impact of Short-Course Colchicine Versus Placebo After Pulmonary Vein Isolation) was planned as a pilot and proof-of-concept study, conducted at a single academic center (Hamilton General Hospital, McMaster University, Hamilton, ON, Canada). The study protocol and the statistical analysis plan are available in the Supplemental Methods. This trial conforms to the principles outlined in the Declaration of Helsinki. Approvals by Health Canada and the local research ethics board (Hamilton Integrated Research Ethics Board) were obtained before study initiation. All study participants provided written informed consent. The trial was planned and coordinated at the Population Health Research Institute, McMaster University and was sponsored by Hamilton Health Sciences, Hamilton, ON, Canada. Study data were collected and managed using Research Electronic Data Capture (REDCap) tools.[11,12] This study followed the CONSORT (Consolidated Standards of Reporting Trials) reporting guideline for randomized clinical trials and is registered with ClinicalTrials.gov (URL: https://www.clinicaltrials.gov; unique identifier: NCT04160117). Deidentified data that support the findings of this study are available from the corresponding author upon reasonable request.

Participants

Adult patients scheduled for catheter ablation for AF (radiofrequency or cryoballoon ablation; first or repeat procedure) were eligible for inclusion. Planned pulmonary vein isolation was mandatory, but additional ablation of the cavotricuspid isthmus and other lesions was allowed. Key exclusion criteria were contraindications to colchicine (eg, coadministration of certain medications, serious gastrointestinal disease, overt hepatic disease, or severe renal disease). Full eligibility criteria are listed in Table S1.

Study Intervention

On the day of their scheduled catheter ablation, patients were randomly assigned 1:1 to receive either colchicine 0.6 mg twice daily or matching placebo for 10 days after catheter ablation. The first dose of the study drug was administered within 4 hours before the procedure. Colchicine dosage and timing of administration were determined based on its proven efficacy for the prevention of perioperative AF and postpericardiotomy syndrome in patients undergoing cardiac surgery and pharmacokinetics of colchicine following oral administration.[13–16] The randomization schedule with permuted blocks of varying size was computer generated by a statistician not otherwise involved in study conduct. Overencapsulation was used to blind the study drug and sequentially numbered containers were provided by the local research pharmacy. If the study drug needed to be halted due to the occurrence of side effects (eg, gastrointestinal upset), patients were advised to resume treatment at a reduced dose upon resolution (ie, 1 capsule per day), but to stop the treatment after a total of 10 days after catheter ablation. Patients, physicians, and study personnel involved in outcome assessment were blinded to treatment allocation.

Catheter Ablation

All procedures were performed under general anesthesia. Using ultrasound guidance, catheters were inserted via femoral and jugular veins. For radiofrequency ablation, the Carto 3 system (Biosense Webster, Inc, Irvine, CA) was used for electroanatomic mapping, and the procedure was performed without fluoroscopy, with navigation based on 3-dimensional mapping and intracardiac echocardiography. Pulmonary vein isolation was achieved by point-by-point wide antral circumferential ablation using an irrigated (surround flow), contact force-guided catheter. Settings were 50 W power, applied for 8 s (posterior wall)

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and 10 to 12 s (ridge/septum), respectively. For cryoballoon ablation, the Arctic Front system (Medtronic, Inc, Minneapolis, MN) was used. Duration and number of applications per vein were based on the CIRCA-DOSE study (Cryoballoon Versus Irrigated Radiofrequency Catheter Ablation: Double Short Versus Standard Exposure Duration) protocol.[17,18] Repeat procedures were performed using radiofrequency ablation only. Ablation beyond pulmonary vein isolation was left at the discretion of the treating physician. Total procedure time was defined as the time from lines insertion until lines removal. Patients remained under careful observation and telemetry for at least 4 hours following catheter ablation, and were usually discharged from the hospital on the same day.

Feasibility Outcomes

The primary goal of this study was to establish the feasibility of a large-scale trial powered for clinical outcomes. We prespecified that we would infer feasibility of enrollment and study implementation whether (1) patients could be enrolled at a rate of 11 patients per month at 1 center, (2) at least 90% of participants would take at least 80% of assigned study drug (ie, ≥16 of 20 capsules, as reported by the patient at the 14-day follow-up visit), and (3) a 6-month follow-up visit could be completed for >90% of patients.

Clinical Outcomes

We hypothesized that colchicine would reduce atrial arrhythmia recurrence following catheter ablation. Atrial arrhythmia recurrence was defined as >30 s of AF, atrial flutter, or atrial tachycardia detected on two 14-day portable heart rhythm monitors (pocketECG; Medicalgorithmics, Warsaw, Poland) and confirmed by 2 cardiac electrophysiologists unaware of treatment assignment. The first Holter was applied immediately after the procedure and the second Holter was applied at ≈3 months following catheter ablation.

We also hypothesized that a composite clinical outcome (consisting of emergency department visit, cardiovascular hospitalization, cardioversion, or repeat ablation for atrial arrhythmia) would be reduced with colchicine; as would each of its components. Other clinical outcomes included postablation chest pain consistent with pericarditis (defined as patient-reported chest pain after catheter ablation, which may have been supported by evidence of new or worsening pericardial effusion on ECG or friction rub on auscultation), noninfectious diarrhea (defined as ≥3 loose stools in the absence of an overt infectious cause), and all-cause mortality. Full-outcome definitions are provided in Table S2.

Follow-up was conducted via telephone at 14 days, 6 months, and 12 months after catheter ablation, and every 12 months thereafter. In addition, there was a final visit for all patients once the last patient enrolled had completed the 6-month follow-up visit.

Statistical Analysis

A sample size of 200 patients was primarily chosen to demonstrate enrollment feasibility for a large-scale trial powered for clinical outcomes. The 95% CI associated with the targeted monthly enrollment rate was 10 to 12 patients per month and center, indicating that the main trial would be feasible as it would require 6 sites enrolling 10 patients per month over ≈1.5 years to achieve a total enrollment of 1000 patients. Assuming an estimated incidence of 50% in the placebo group, a sample size of 200 patients provided 80% power to detect a 40% relative risk reduction in the clinical secondary outcome of atrial arrhythmia recurrence.

Baseline characteristics were summarized as median (interquartile range [IQR]) for continuous variables and as counts (percentages) for categorical variables. The feasibility outcomes were descriptively analyzed in the intention-to-treat population (ie, randomized patients who did not meet any exclusion criteria). All clinical outcome analyses were conducted in the modified intention-to-treat population (ie, randomized patients who did not meet any exclusion criteria and who underwent catheter ablation). Outcomes were analyzed using time-to-event analysis. Cox proportional-hazards models were built to estimate treatment effects, shown as hazard ratio with 95% CI. Adjusted analyses including prespecified covariates were performed as sensitivity analyses. Subgroup analyses focused on ablation energy (ie, radiofrequency or cryoballoon ablation) were performed for selected outcomes. Between-group differences in the burden of AF on the first and on the second Holter were assessed using the Wilcoxon rank-sum test. A 2-sided $P<0.05$ was considered statistically significant for all analyses. All analyses were performed in SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

A total of 202 patients scheduled for catheter ablation for AF were enrolled between January 14, 2020, and September 14, 2021 (Figure S1). Of these, 101 patients were assigned to receive colchicine and 101 to receive placebo. Two patients meeting exclusion criteria (serious gastrointestinal disease and previous enrollment in the trial) were erroneously enrolled in the study and discontinued following the first dose of the study drug. Of 199 of 200 patients in the intention-to-treat population with available data (99.5%), 176 (88.4%) were fully compliant with the study drug. The rate of full compliance with the study drug was lower in patients randomized to receive colchicine than in the placebo group (81.0% versus 96.0%). Both permanent discontinuation of the study drug (13.0% versus 3.0%) and dose reduction to 1 capsule per day (14.0% versus 1.0%) were more common in the colchicine group (Table S3). The 6-month follow-up visit was completed for all patients who were alive at the time of the scheduled visit (100.0%). Final follow-up visits were conducted in May 2022.

Patient Characteristics

A total of 199 patients were included in the modified intention-to-treat population (1 patient's procedure was aborted before ablation due to a pericardial effusion). The median (IQR) age of the patients was 61 (55–68) years and 44 (22.1%) were female (Table 1). The majority (69.8%) of catheter ablations represented a first procedure (Table 2). Catheter ablation was acutely successful

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Table 1. Baseline Characteristics

	Colchicine (n=99)	Placebo (n=100)
Age, y; median (IQR)	62 (56–69)	61 (54–66)
Female, n	22	22
BMI, kg/m^2; median (IQR)	29.7 (25.9–32.5)	29.8 (25.7–33.1)
Congestive heart failure, n	7	12
Hypertension, n	50	39
Coronary artery disease, n	6	9
Prior stroke, n	5	9
Chronic kidney disease, n	8	4
Diabetes, n	9	10
Chronic obstructive pulmonary disorder, n	2	7
Any alcohol use, n	61	61
No. of drinks per week, median (IQR)	5 (2–7)	5 (2–8)
Tobacco use		
Active smoker, n	3	10
Past smoker, n	33	32
Never smoker, n	63	58
Medication		
ACE inhibitor/ARB/ARNI, n	36	35
Calcium-channel blocker (verapamil-type), n	14	16
Digoxin, n	3	5
β-Blocker, n	55	56
Mineralocorticoid antagonist, n	2	4
Statin, n	30	32
Oral anticoagulation, n*	95	92
Antiarrhythmic therapy†		
None, n	24	26
Propafenone, n	7	2
Flecainide, n	10	29
Sotalol, n	26	21
Amiodarone, n	32	21
Dronedarone, n	0	1

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BMI body mass index; and IQR, interquartile range.

*Reported before catheter ablation.

†Captured at hospital discharge following catheter ablation.

in all patients receiving ablation. Most patients (74.9%) were discharged on an antiarrhythmic drug.

Atrial Arrhythmia Recurrence

A total of 194 patients (97.5%) were compliant with the first Holter. Thirty patients (31%) randomized to colchicine and 31 patients (32%) randomized to placebo experienced atrial arrhythmia recurrence in the first 2 weeks following catheter ablation (hazard ratio with colchicine, 0.98 [95% CI, 0.59–1.61]; *P*=0.92; Figure 1; Table 3). There was no difference in the incidence of arrhythmia subtypes. In patients with AF detected on the first Holter, median (IQR) burden of AF was 3.5% (0.9%–25.5%) in the colchicine group versus 6.8% (3.4%–45.9%) in the placebo group (*P*=0.10).

Compliance with the second Holter was 93.0%. The median time from catheter ablation to the start of the second monitoring period was 82 days. There was no difference between colchicine and placebo in the incidence of atrial arrhythmia recurrence (13 [14%] versus 14 [15%] patients; hazard ratio with colchicine, 0.95 [95% CI, 0.45–2.02]; *P*=0.89; Figure 2), and no difference in the incidence of arrhythmia subtypes detected on this Holter. In patients with AF detected on the second monitor, median (IQR) burden of AF was 7.3% (0.5%–9.6%) and 5.6% (0.4%–15.2%) in patients randomized to colchicine and placebo, respectively (*P*=0.90).

Clinical Outcomes

At the 14-day visit, 4 patients randomized to colchicine and 15 patients randomized to placebo reported postablation chest pain consistent with pericarditis (hazard ratio with colchicine, 0.26 [95% CI, 0.09–0.77]; *P*=0.02). Diarrhea occurred in 26 patients and 7 patients receiving colchicine and placebo, respectively (hazard ratio with colchicine, 4.74 [95% CI, 1.95–11.53]; *P*<0.001; Table 3).

The median (IQR) follow-up duration after catheter ablation was 1.3 (1.0–1.7) years. At the 6-month visit, 61 (62.2%) patients randomized to colchicine and 57 (57.0%) patients randomized to placebo were off antiarrhythmic therapy (Table S4). There was no reduction

Table 2. Procedural Details

	Colchicine (n=99)	Placebo (n=100)
Type of procedure		
First, n	71	68
Repeat ablation, n	28	32
Radiofrequency ablation, n	84	73
Total radiofrequency time, min; median (IQR)	12.2 (9.6–16.5)	11.6 (9.5–14.4)
Cryoballoon ablation, n	15	27
Total cryoablation time, min; median (IQR)	16.3 (11.5–21.0)	16.7 (14.0–21.3)
Concomitant ablation		
None, n	51	57
Cavotricuspid isthmus, n	37	37
Complex fractionated atrial electrograms, n	3	1
Other, n	16	18
Total procedure duration, min; median (IQR)	167 (128–195)	155 (112–184)

IQR indicates interquartile range.

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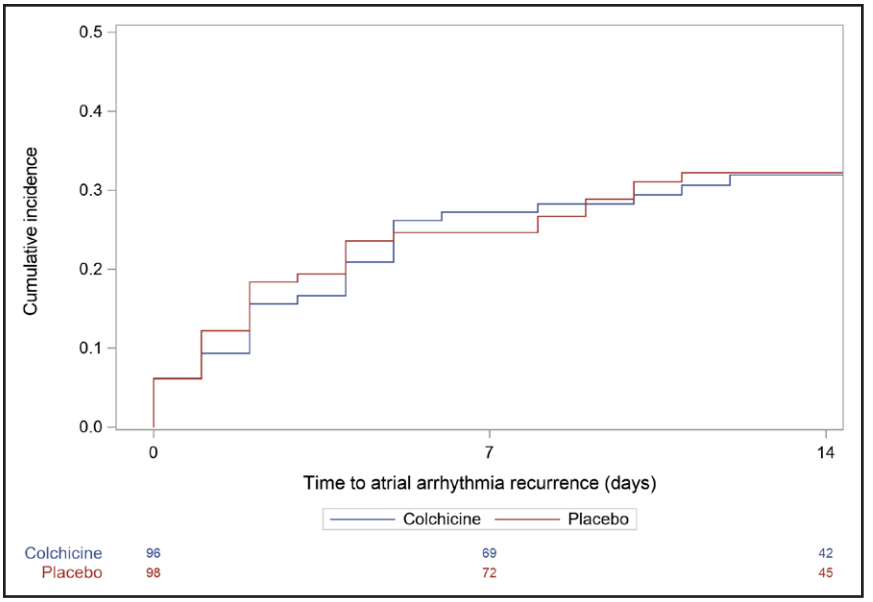


Figure 1. Atrial arrhythmia recurrence detected on a 14-day Holter during the first 2 weeks following catheter ablation.
AF indicates atrial fibrillation; and AT; atrial tachycardia.

in the composite clinical outcome of emergency department visit, hospitalization for cardiovascular cause, cardioversion, or repeat ablation with colchicine (29.0 versus 24.6 per 100 patient-years; hazard ratio with colchicine, 1.18 [95% CI, 0.69–1.99]; *P*=0.55; Figure 3). There was no between-group difference in any of the individual components of this composite outcome. One patient in the colchicine group died 24 days after cryoballoon ablation. This patient had taken the full course of the study medication and was doing well at the 14-day follow-up visit, with no adverse events reported. The cause of death was reported to be sepsis. There were no deaths in the placebo group.

Sensitivity Analyses

Sensitivity analyses adjusted for prespecified covariates yielded consistent results for the effects of colchicine on atrial arrhythmia recurrence and on the clinical outcomes (Table S5).

Subgroup Analyses

Subgroup analyses focused on ablation energy did not suggest a differential treatment effect of colchicine for the prevention of atrial arrhythmia recurrence during the first 2 weeks or atrial arrhythmia recurrence at 3 months in patients undergoing radiofrequency versus cryoballoon ablation (Table 4). However, there was suggestion of a greater reduction in postablation chest pain consistent with pericarditis in patients undergoing radiofrequency ablation (hazard ratio with colchicine, 0.14 [95% CI, 0.03–0.63]) than in those receiving cryoballoon ablation (hazard ratio, 1.17 [95% CI, 0.20–7.00]; *P* value for interaction=0.07).

DISCUSSION

This randomized pilot trial enrolled >10 patients per month and demonstrated high rates of compliance with the study drug (>88%) and the visit schedule (100% complete follow-up at 6 months). Beginning the morning of AF ablation, colchicine, administered for 10 days, did not reduce atrial arrhythmia recurrence or a composite of clinically important outcomes associated with arrhythmia recurrence. Colchicine reduced postablation chest pain consistent with pericarditis but increased diarrhea.

Early atrial arrhythmia recurrence following catheter ablation is common.[7] Using continuous loop monitoring, investigators found an incidence of 61% recurrence during the first 3 months in a cohort of patients with paroxysmal AF undergoing contact force-guided radiofrequency or cryoballoon ablation.[8] Their study showed a 3.5-fold increase in symptomatic atrial arrhythmia recurrence after a 3-month blanking period in patients with early recurrence.[8] Other studies demonstrated that brief and transient increases in biomarkers of inflammation, such as C-reactive protein or interleukin-6, peak within days following catheter ablation.[4–6]

Colchicine has been shown to reduce inflammation after cardiac intervention and reduces perioperative AF and postpericardiotomy syndrome in patients undergoing cardiac surgery.[13–15] A single study evaluated colchicine administered at a dose of 0.5 mg twice daily for 3 months in 161 patients undergoing catheter ablation of AF.[19] In the absence of antiarrhythmic drugs, colchicine, started on the day of catheter ablation, reduced C-reactive protein, and interleukin-6 through day 4 of treatment. There was a significant reduction in early atrial arrhythmia recurrence ≥30 s detected on six 48-hour Holters

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Table 3. Outcomes Following Catheter Ablation

	Colchicine, n	Placebo, n	Hazard ratio (95% CI)	*P* value
14-d outcomes*				
Postablation chest pain consistent with pericarditis	4/99	15/99	0.26 (0.09–0.77)	0.02
Diarrhea	26/99	7/99	4.74 (1.95–11.53)	<0.001
Atrial arrhythmia recurrence†				
Recurrence during the first 2 wk	30/96	31/98	0.98 (0.59–1.61)	0.92
AF	28/96	26/98	1.09 (0.64–1.85)	0.77
Atrial flutter	10/96	8/98	1.30 (0.51–3.30)	0.58
Atrial tachycardia	0/96	3/98	Not estimable	
Recurrence at 3 mo	13/91	14/94	0.95 (0.45–2.02)	0.89
AF	8/91	11/94	0.74 (0.30–1.84)	0.52
Atrial flutter	5/91	4/94	1.31 (0.35–4.88)	0.69
Atrial tachycardia	2/91	3/94	0.71 (0.12–4.22)	0.70
Composite clinical outcome‡	30/99	26/100	1.18 (0.69–1.99)	0.55
Emergency department visit or cardiovascular hospitalization	25/99	23/100	1.06 (0.60–1.88)	0.83
Cardioversion	13/99	11/100	1.23 (0.55–2.74)	0.62
Repeat ablation	7/99	7/100	1.02 (0.36–2.91)	0.97
Death	1/99	0/100	Not estimable	

AF indicates atrial fibrillation.
*One patient in the placebo group was not available for assessment of the 14-d outcomes.
†Only patients who were compliant with the Holter were included in the analysis.
‡Defined as any of emergency department visit, hospitalization for cardiovascular cause, cardioversion, or repeat ablation for AF, atrial flutter/left atrial tachycardia.

applied every 2 weeks over 3 months, with a particularly large treatment effect observed in the first 10 days following catheter ablation.[19] An extension of this study suggested an ongoing reduction in atrial arrhythmia recurrence beyond 3 months after catheter ablation but did not assess clinical outcomes.[20]

Our study protocol permitted the use of antiarrhythmic drugs following ablation. With 75% of patients being discharged on an antiarrhythmic agent, the incidence of atrial arrhythmia recurrence during the continuous monitoring period in the first 2 weeks following ablation was significantly lower at 31%. There was no reduction in atrial arrhythmia recurrence, arrhythmia by subtype, or burden of AF with colchicine.

Cardioversion or repeat ablation due to recurrent atrial arrhythmia are clinically relevant outcomes that materially affect patient well-being. Consistent with the lack of effect on ECG-documented atrial arrhythmia recurrence

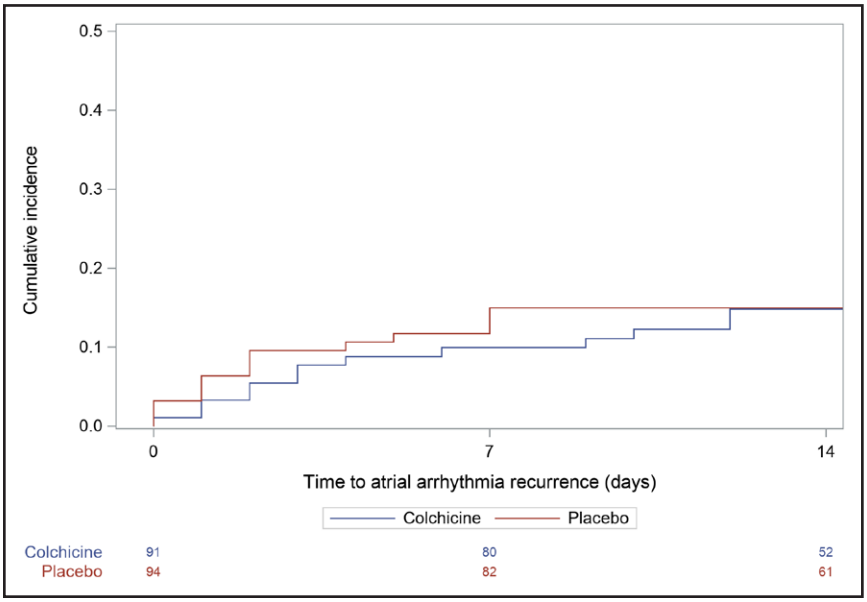


Figure 2. Atrial arrhythmia recurrence detected on a 14-day Holter at 3 months following catheter ablation.
AF indicates atrial fibrillation; and AT; atrial tachycardia.

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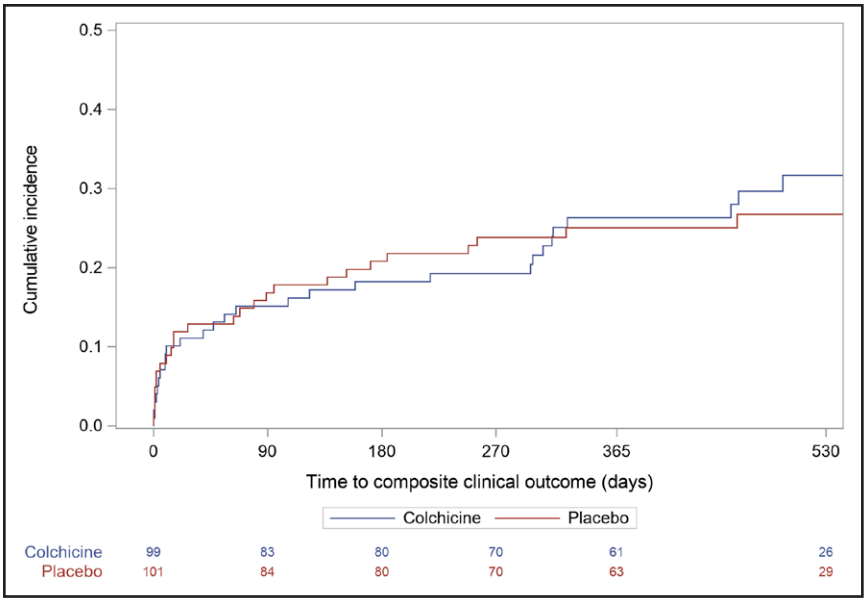


Figure 3. Composite clinical outcome (emergency department visit, hospitalization for cardiovascular cause, cardioversion, or repeat ablation) during follow-up.

and burden of AF, colchicine did not reduce the incidence of cardioversion or repeat ablation during follow-up. Finally, there were also no differences in the incidences of emergency department visit or cardiovascular hospitalization, and in the composite clinical outcome of all these AF-associated clinical events between patients randomized to colchicine and placebo. Widely referred to as a blanking period, our study shows that about 1 in 6 patients experiences a clinical event during the first 3 months following ablation, highlighting the unmet medical need of this patient population.

Despite its neutral effect on atrial arrhythmia recurrence, there was a reduction in patient-reported chest pain with colchicine. This reduction was observed within days following catheter ablation, suggesting anti-inflammatory effects of short-term treatment with colchicine. This finding is in line with evidence on the efficacy of colchicine in the prevention and treatment of pericarditis and postpericardiotomy syndrome following cardiac surgery.[13,15,21,22] The observed rate in the placebo group (15%) is consistent with previous reports on pericarditis following catheter ablation.[23] Although our definition of pericarditis differed from more stringent definitions,[24] the observed beneficial effect of colchicine on postablation chest pain in this placebo-controlled, double-blind trial was clinically meaningful. Subgroup analyses suggested a greater treatment effect in patients receiving radiofrequency ablation compared with patients undergoing cryoballoon ablation. Another recent, open-label trial did not find a reduction in pericarditis with colchicine 0.6 mg twice daily administered for 7 days following catheter ablation.[25] However, periablation use of colchicine was associated with a reduction in pericarditis in a recent observational study.[26]

Although gastrointestinal side effects are relatively common with colchicine, the increase in diarrhea with the 10-day treatment was substantial and clinically significant. The observed 26% incidence in the intervention arm is much higher than in previous trials testing colchicine at doses of ≥1.0 mg per day.[27] Possible reasons for the discrepancy in diarrhea incidence between our and

Table 4. Subgroup Analyses According to Ablation Energy

	Colchicine, n (%)	Placebo, n (%)	Hazard ratio (95% CI)	*P* value for interaction
14-d outcomes				
Postablation chest pain consistent with pericarditis				
Radiofrequency ablation	2/84 (2.4)	12/72 (16.7)	0.14 (0.03–0.61)	0.07
Cryoballoon ablation	2/15 (13.3)	3/27 (11.1)	1.17 (0.20–7.00)	
Atrial arrhythmia recurrence during the first 2 wk				
Radiofrequency ablation	24/81 (29.6)	20/72 (27.8)	1.06 (0.58–1.92)	0.83
Cryoballoon ablation	6/15 (40.0)	11/26 (42.3)	0.94 (0.35–2.54)	
Atrial arrhythmia recurrence at 3 mo				
Radiofrequency ablation	11/77 (14.3)	10/68 (14.7)	0.96 (0.41–2.26)	0.94
Cryoballoon ablation	2/14 (14.3)	4/26 (15.4)	0.86 (0.16–4.72)	

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other studies include differences in outcome definitions and patient characteristics, as well as potential interaction of colchicine with concomitant medications. Our findings are consistent with a reported 3-fold increase in gastrointestinal upset in a recently published open-label trial testing colchicine 0.6 mg twice daily for 7 days following catheter ablation.[25]

Limitations

First, this was a small, single-center trial with relatively few outcome events. Second, we did not use implantable loop recorders, likely resulting in underestimation of atrial arrhythmia recurrence in both treatment groups. Finally, the evaluation of atrial arrhythmia recurrence and the clinical composite outcome were not sufficiently powered to definitively exclude a clinically significant benefit with colchicine.

Conclusions

Colchicine administered for 10 days following catheter ablation for AF did not reduce atrial arrhythmia recurrence or a composite outcome of clinical events associated with AF. Colchicine did reduce postablation chest pain consistent with pericarditis, and it increased diarrhea.

ARTICLE INFORMATION

Received August 9, 2023; accepted November 22, 2023.

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Acknowledgments

The authors would like to thank Diane Lourenco and Gita Sobhi at Hamilton Health Sciences Pharmacy Research Support Services for preparation of study medication, Purnima Rao-Melacini, Juliet Nakamya, and Edward Chongsi for statistical support, Heather Beresh, Toni Newman, Laura Heenan, and Jessica Tyrwhitt at the Population Health Research Institute for help with the study coordination and conduct, and Ganesan Karthikeyan at the All India Institute of Medical Sciences, New Delhi, for serving as the Safety Monitor of this trial.

Sources of Funding

This trial was supported by the Hamilton Health Sciences' New Investigator Fund and the Innovation Fund of the Alternative Funding Plan for the Academic Health Sciences Centres of Ontario. Dr Benz reports a personal research grant from the German Heart Foundation (Deutsche Herzstiftung e.V.).

Disclosures

Dr Benz reports lecture fees from Bristol Myers Squibb. Dr Amit reports serving on an advisory board for Johnson & Johnson. Dr Connolly reports institutional research grants and honoraria from Boehringer Ingelheim, Portola/Alexion Pharmaceuticals, Bristol Myers Squibb/Pfizer, Bayer, and Daiichi Sankyo. Dr Conen reports consultation fees from Roche Diagnostics and Trimedics and speaker fees from Servier and Bristol Myers Squibb/Pfizer. Dr McIntyre reports research support paid to his institution from AOP Pharma and honoraria from Trimed Therapeutics and Servier. Dr Roberts reports consulting fees from Bristol Myers Squibb and Ionis Pharmaceuticals. Dr Wong holds a McMaster University Department of Medicine Early Career Research Award and reports speaking fees from Biosense Webster. Dr Healey reports research grants and speaking fees from Medtronic and Boston Scientific and consulting fees from Boston Scientific. Other authors report no conflicts.

Supplemental Material

Supplemental Methods
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Figure S1

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