Single-dose Intraoperative Steroid Administration Does Not Impact Early Atrial Fibrillation Recurrence

Kolade Agboola[1], Michael Dietrich[1], Roshan Karki[2], Fahad Lodhi[1], Trevon McGill[1], Samuel Asirvatham[2], Abhishek Deshmukh[2], and Christopher DeSimone[2]

[1]Mayo Clinic Rochester
[2]Mayo Clinic

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Abstract

Background: Inflammation is integral in the pathogenesis and propagation of atrial fibrillation (AF). Peri-ablation administration of steroids has been shown to significantly reduce AF recurrence at 3 months. We sought to determine the effect of intraoperative dexamethasone on early recurrence at both 3 months and 12 months post-ablation. Methods: A cohort of 94 adult patients (>18 years) underwent catheter ablation at Mayo Clinic Rochester from January to March 2019. Only first-time ablation patients were included, with all re-do ablations excluded to minimize heterogeneity. Administration of intraoperative dexamethasone 4 mg or 8 mg was determined by chart review from the procedure. At our institution, intraoperative intravenous steroids are administered for postoperative nausea and vomiting (PONV) prophylaxis at the discretion of the anesthesiologist. AF recurrence was determined by ECG or cardiac monitoring at less than 3 months or between 3 months and 1 year with an in-person follow-up visit. Results: A total of 36.2% of patients received intravenous dexamethasone compared to 63.8% who did not (providing a 2:1 comparison group). The incidence of documented AF or flutter lasting greater than 30 seconds was 20.6% in the dexamethasone group versus 21.7% in the non-dexamethasone group, p value 1.00. AF or atrial flutter recurrence from 3 months to 1 year was 20.6% in the dexamethasone group compared to 21.7% in the non-dexamethasone group, p value 1.00. Conclusion: These data suggest that intraoperative intravenous dexamethasone administered during AF ablation for postoperative nausea and vomiting prophylaxis does not have a significant effect on AF recurrence rates.

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Authors: Kolade M. Agboola, MD; Michael Dietrich, MD; Roshan Karki, MD; Fahad Lodhi, MD; Trevon McGill, MD; Samuel J. Asirvatham, MD; Abhishek J. Deshmukh, MBBS; Christopher V. DeSimone, MD, PhD

Author affiliations:

[1] Department of Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

[2] Division of Cardiovascular Disease, Department of Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

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Corresponding author:

Christopher V. DeSimone, M.D., Ph.D.

Associate Professor of Medicine

Division of Cardiovascular Diseases

Mayo Clinic, Rochester, MN 55905

Desimone.christopher@mayo.edu

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Abstract:

Background: Inflammation is integral in the pathogenesis and propagation of atrial fibrillation (AF). Peri-ablation administration of steroids has been shown to significantly reduce AF recurrence at 3 months. We sought to determine the effect of intraoperative dexamethasone on early recurrence at both 3 months and 12 months post-ablation.

Objective : To evaluate the effect of single-dose intravenous dexamethasone on AF recurrence following radiofrequency catheter ablation.

Methods: A cohort of 94 adult patients (>18 years) underwent catheter ablation at Mayo Clinic Rochester from January to March 2019. Only first-time ablation patients were included, with all re-do ablations excluded to minimize heterogeneity. Administration of intraoperative dexamethasone 4 mg or 8 mg was determined by chart review from the procedure. At our institution, intraoperative intravenous steroids are administered for postoperative nausea and vomiting (PONV) prophylaxis at the discretion of the anesthesiologist. AF recurrence was determined by ECG or cardiac monitoring at less than 3 months or between 3 months and 1 year with an in-person follow-up visit.

Results: A total of 36.2% of patients received intravenous dexamethasone compared to 63.8% who did not (providing a 2:1 comparison group). The incidence of documented AF or flutter lasting greater than 30 seconds was 20.6% in the dexamethasone group versus 21.7% in the non-dexamethasone group, p value 1.00. AF or atrial flutter recurrence from 3 months to 1 year was 20.6% in the dexamethasone group compared to 21.7% in the non-dexamethasone group, p value 1.00.

Conclusion: These data suggest that intraoperative intravenous dexamethasone administered during AF ablation for postoperative nausea and vomiting prophylaxis does not have a significant effect on AF recurrence rates.

Key words: atrial fibrillation, ablation, steroids, outcomes, recurrence

Introduction

Radiofrequency (RF) ablation is a widely utilized and highly effective treatment modality for symptomatic paroxysmal and persistent atrial fibrillation (AF). RF ablation for AF is known to increase serum biomarkers of inflammation, which may be due to acute myocardial injury and healing of ablation-related atrial lesions[1]. Individuals with early recurrence of AF within the first three months after AF ablation was shown to have significantly greater odds of having an increase in serum C-Reactive Protein (CRP) levels at post-ablation follow-up, suggesting an association between increased inflammation and early recurrence of AF[2].

The effect of peri-procedural administration of nonsteroidal anti-inflammatory drugs and corticosteroids has been evaluated[3-5]. Peri-ablation administration of intravenous steroids followed by a short course of moderate-intensity oral steroids has been shown to significantly reduce AF recurrence at 3 months[5]. There

is no evidence regarding the efficacy of intravenous dexamethasone, and it is unclear if single-dose administration at the time of ablation for the prevention of postoperative nausea (PONV) yields a similar reduction in AF recurrence or inhibits adequate lesions formation and maturation.

Methods

A cohort of 94 total adult patients was retrospectively selected in consecutive order from a chronological database of AF ablation patients. We included patients >18 years of age, undergoing catheter ablation with pulmonary vein isolation for paroxysmal and persistent AF between January and March of 2019. Only first-time ablation candidates were included and all re-do ablation candidates were excluded to minimize heterogeneity. Administration of intraoperative dexamethasone was determined by chart review of the procedural anesthesia records.

Intraoperative steroids have been shown to have efficacy in reducing PONV[8-10]. It is the practice within our institutions' anesthesiology group to administer prophylactic intravenous corticosteroids at the discretion of the anesthesiologist for PONV prophylaxis, independent of the electrophysiologist performing the ablation. Thus, at the time of the procedure, the operator was essentially "blinded" to the administration of dexamethasone. AF recurrence was determined by electrocardiogram or cardiac monitoring device at less than 3 months and 3 months to 1 year, which was obtained at the time of in-person follow-up visit. The protocol was approved by our institutional review board and all patients provided informed consent.

Demographic information for each patient was obtained via a review of the electronic medical record. Administration of dexamethasone and dosing was determined by review of procedural medication administration records. Dexamethasone dosing was determined at the discretion of the anesthesiologist. Patients in the dexamethasone group either received 4 mg or 8 mg of intravenous dexamethasone during the catheter ablation procedure. Patients in the control group did not receive any intravenous steroids including dexamethasone at the time of the catheter ablation procedure. Administration of other steroidal and non-steroidal anti-inflammatory agents at the time of ablation and in the postoperative period was also reviewed. Additionally, the concomitant use of antiarrhythmic agents was determined by chart review

(*Figure 1*).

Results

A total of 94 patients were included in our study, from a population of 99 patients that were initially screened. The 5 patients that were excluded did not provide research study consent and thus were not included. Demographic data for the study population including age, gender, race, body mass index, and pertinent comorbidities are shown in Table 1 . The mean age in our study population was 62.1 ± 9.8 years. The patients were predominantly male (78.7%) and Caucasian (60.6%). Our "treatment group" was comprised of 34 patients that received dexamethasone, and 60 patients in the control group (no dexamethasone).

The rates of AF and atrial flutter recurrence, defined as episodes lasting greater than 30 seconds, were not statistically different between the two groups. A total of 13 patients (21.6%) in the control group and 7 patients (20.6%) in the experimental group developed recurrence within the first 3 months, a p-value of 1.00. At 3 months to 1 year, 13 patients in the control group (21.6%) and 7 patients (20.6%) in the experimental group had developed recurrence. The rates of direct current cardioversion (DCCV) in these groups within the first 3 months were also not significantly different (Table 2). Within the control group, 8 out of 60 (13.3%) patients required DCCV within the first 3 months compared to 4 out of 34 (11.8%) patients in the experimental group, a p-value of 1.00. Similarly, at 3 months to 1 year, there was not a significant difference in the rates of DCCV between the two groups with 7 patients (11.7%) in the control group and 3 patients (8.8%) in the experimental group (*Table 3*).

Within the control and experimental groups 38 out of 60 patients (63.3%) and 20 out of 34 patients (58.8%), respectively, were prescribed an antiarrhythmic agent within 3 months of their catheter ablation procedure. There was not a statistically significant difference in the administration of antiarrhythmic agents between these groups with a p-value of 0.67. At 3 months to 1 year, there was no statistically significant difference

in the administration of antiarrhythmic agents between the control and experimental groups (*Table 3*). Rates of antiarrhythmic drug administration in the control and experimental groups were 35.6% (21 out of 60 patients) and 44.1% (15 out of 34 patients), respectively (p-value 0.51).

Discussion

In this study, we sought to evaluate the effect of single-dose intravenous dexamethasone on AF recurrence following RF catheter ablation. Patients in our study received 4 mg or 8 mg of dexamethasone at the time of AF ablation by anesthesia and were compared to controls which did not receive any intravenous steroids in a "blinded fashion" to the operator. Our main findings were that: 1) there was no significant difference in rates of documented AF recurrence, DCCV, or prescription of antiarrhythmic agents at 3 months or 1 year follow-up. These results were suggestive of the use of single-dose intravenous dexamethasone not being associated with early and late AF recurrence and thus of utility for PONV without affecting outcomes.

In a study of Paroxysmal AF patients, those randomized to colchicine experienced a significant reduction in early and late AF recurrence compared to those who received placebo[3,4]. The serum concentration of CRP and interleukin 6 were also significantly reduced after 4 days of treatment in the colchicine group, suggesting decreased systemic inflammation leading to reduced AF recurrence[3]. Single dose intravenous corticosteroids administered at the time of ablation did not reduce post-ablation recurrence after AF[6,7]. Notably in both studies methylprednisolone and hydrocortisone were administered at the time of ablation[6,7].

The findings of our study are consistent with the findings of previous studies involving single-dose intravenous steroids at the time of catheter ablation. A prior study has shown that in 89 patients who received a single bolus injection of 100 mg hydrocortisone within 30 minutes of completing the pulmonary vein isolation procedure, there was no significant difference in immediate, early, and late AF recurrence rates[6]. A similar result was found when comparing the effects of low-dose intravenous steroids with 100 mg hydrocortisone and moderate-dose steroids with 125 mg methylprednisolone in a prior study[7]. It was felt that moderate-dose steroids were thought to decrease post-ablation inflammation, evidenced by a significant reduction in maximum body temperature and serum C-reactive protein levels compared to the low-dose steroid and control groups. However, there was no significant difference in immediate, early, or midterm atrial fibrillation recurrence[7].

Catheter ablation using radiofrequency energy involves the delivery of high frequency alternating electrical current, which heats the incident tissue underlying the catheter tip in a resistive or ohmic manner[11]. Following catheter ablation, there are both localized and systemic inflammatory responses, as well as a continued myocardial injury which results in the maturation of the newly formed lesions[1]. From a histological perspective, *in vivo* ablation studies in animal models have demonstrated infiltration of necrotic myocardium by lymphocytes and macrophages, ultimately resulting in the replacement of coagulative necrotic myocardium with fibrosis[12]. This post-ablation inflammatory response typically occurs within the first 3 days after ablation and is evidenced systemically by elevation in serum C-reactive protein (CRP) levels[1].

AF recurrence following catheter ablation is thought to be in part mediated by systemic inflammation. Interestingly, patients without early recurrence of AF within the first month have higher CRP levels compared to individuals that experienced early recurrence[13]. This suggests that increased systemic inflammation may somehow be protective against early AF recurrence. One possible explanation for this is that the degree of systemic inflammation is indicative of or proportional to the degree of local inflammation at the site of myocardial lesions. As such, a heightened local inflammatory response may lead to a more robust lymphocytic and macrophagic infiltration, yielding more fibrosis and durable lesion formation. Interestingly, there was no difference in CRP levels between individuals with and without late recurrence, suggesting that systemic inflammation affects recurrence more acutely and less so chronically[12].

The underlying mechanism of myocardial lesion formation following catheter ablation may provide insight into the potential effects of steroids and other anti-inflammatory agents. If steroids reduce the acute post-ablation inflammatory response that is responsible for lesion maturation, then steroids may impair lesion maturation and promote the late recurrence of AF. In our study, we did not observe such a phenomenon

as there was not a significant difference in AF recurrence between individuals that received intraoperative dexamethasone and those that did not. As we have discussed, there is some evidence in support of the alternative hypothesis which suggests a benefit to suppression acute post-ablation inflammation with steroids and anti-inflammatory agents, such as colchicine[3-5]. However, these studies were performed with relatively small study populations and there has yet to be a large multicenter randomized trial to investigate this question. A more extensive and in-depth investigation is needed to determine the true effects of steroids on AF recurrence, as well as to determine the potential role of systemic and local inflammation in AF recurrence.

Figure 1. Study Design Schematic

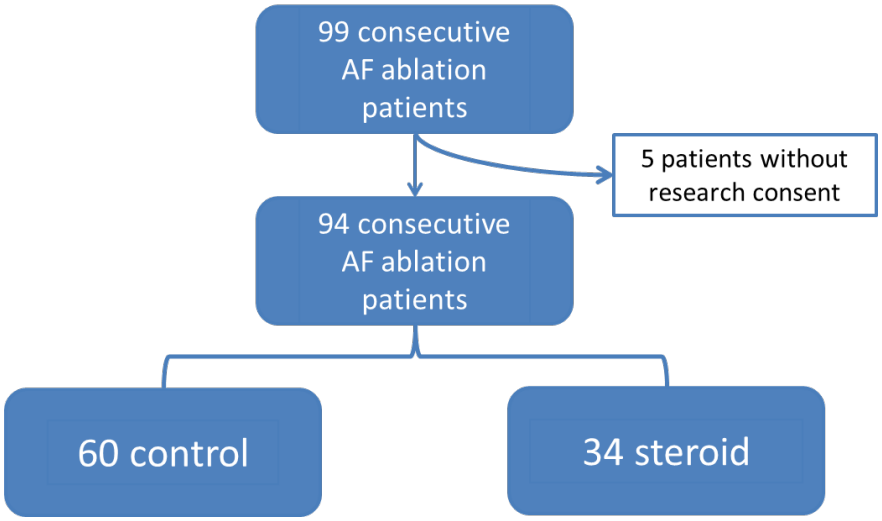

Table 1. Population Demographics

	Total Study Population (N = 94)
Age at procedure (years)	
Mean (standard deviation)	62.1 (9.8)
Median (Min, Max)	64.5 (29.0, 79.0)
Gender	
Female	20 (21.3%
Male	74 (78.7%)
Race	
African American	8 (13.3%)
American Indian/Alaskan Native	1 (1.1%)
Asian Indian	1 (1.1%)
Non-Hispanic or Latino	31 (33.0%)
White	57 (60.6%)
Did not identify	2 (2.1%)
BMI (kg/m^2)	
Mean (standard deviation)	30.8 (6.1)
Median (Min, Max)	29.9 (20.3, 49.7)
CHA_2DS_2 VASc Score	
Mean (standard deviation)	2.0 (1.3)
Median (Min, Max)	2.0 (0.0, 7.0)
Diabetes Mellitus	
No	83 (88.3%)

Yes	11 (11.7%)
Hypertension	
No	34 (36.2%)
Yes	60 (63.8%)
Heart Failure	
No	69 (73.4%)
Yes	25 (26.6%)
Left Ventricular Ejection Fraction (%)	
Mean (standard deviation)	55.7% (10.6)
Median (Min, Max)	59.0% (15.0, 69.0)
Diastolic Dysfunction	
No	47 (50.0%)
Yes	47 (50.0%)
Left Atrial Volume Index	
Mean (standard deviation)	41.5 (13.0)
Median (Min, Max)	40.5 (16.0, 78.0)
Valvular Heart Disease	
No	85 (91.4%)
Yes	8 (8.6%)
Stroke or TIA	
No	85 (90.4%)
Yes	9 (9.6%)
Coronary Artery Disease	
No	76 (80.9%)
Yes	18 (19.1%)
Obstructive Sleep Apnea	
No	48 (51.1%)
Yes	46 (43.6%)
CPAP Therapy	
No	53 (56.4%)
Yes	41 (43.6%)
Autoimmune Disease	
No	90 (95.7%)
Yes	4 (4.3%)
Malignancy	
No	90 (95.7%)
Yes	4 (4.3%)
Renal Function – Creatinine	
Mean (standard deviation)	1.1 (0.2)
Median (Min, Max)	1.1 (0.6, 1.8)
Hepatic Function – AST, ALT	
Mean (SD)	34.2 (24.0), 33.9 (35.0)
Median (Min, Max)	27.0 (12.0, 140.0), 29.5 (8.0, 319.0)
Anti-inflammatory Medication	
No	42 (44.7%)
Yes	52 (55.3%)
Intraoperative Dexamethasone	
No	60 (63.8%)
Yes	34 (36.2%)
Antiarrhythmic Agent within 3 months	
No	36 (38.3%)

Yes	58 (61.7%)
Antiarrhythmic Agent	
Sotalol	15 (25.9%)
Dofetilide	8 (13.8%)
Amiodarone	21 (36.2%)
Flecainide	11 (19.0%)
Propafenone	2 (3.4%)
Dronedarone	1 (1.7%)
Antiarrhythmic Agent within 3 months to 1 year	
No	57 (61.3%)
Yes	36 (38.7%)
Antiarrhythmic Agent	
Sotalol	11 (32.4%)
Dofetilide	3 (8.8%)
Amiodarone	10 (29.4%)
Flecainide	9 (26.5%)
Propafenone	1 (2.9%)

Table 2:

	Control (N = 60)	**Dexamethasone (N = 34)**	**P-value**
Antiarrhythmic use			
No	22 (36.7%)	14 (41.2%)	0.67
Yes	38 (63.3%)	20 (58.8%)	
DCCV			
No	52 (86.7%)	30 (88.2%)	1.00
Yes	8 (13.3%)	4 (11.8%)	
AF Recurrence			
No	47 (78.3%)	27 (79.4%)	1.00
Yes	13 (21.7%)	7 (20.7%)	

Table 3:

	Control (N = 60)	**Dexamethasone (N = 34)**	**P-value**
Antiarrhythmic use			
No	38 (64.4%)	19 (55.9%)	0.51
Yes	21 (35.6%)	15 (44.1%)	
DCCV			
No	53 (88.3%)	31 (91.2%)	0.74
Yes	7 (11.7%)	3 (8.8%)	
AF Recurrence			
No	47 (78.3%)	27 (79.4%)	1.00
Yes	13 (21.7%)	7 (20.7%)	

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