



Original Research

Prophylactic Intravenous Aminophylline for Preventing Bradyarrhythmias During Coronary Atherectomy: A 10-Year Single-Center Experience



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ABSTRACT

Background: Aminophylline, an adenosine antagonist, can be used to prevent adenosine-mediated bradyarrhythmias.

Methods: Retrospective, observational, descriptive analysis of patients undergoing rotational atherectomy with intravenous (IV) aminophylline pretreatment during a 10-year period (2010-2020). The primary composite outcome was the occurrence of a documented bradyarrhythmia requiring pharmacologic intervention and/or temporary pacemaker (TPM) implantation.

Results: A total of 296 patients received IV aminophylline pretreatment. The primary composite outcome occurred in 1.7% (n = 5) of patients. None of the patients required rescue TPM. Bradyarrhythmias were documented in 2.4% (n = 7) of patients. Pharmacologic interventions, typically with IV atropine, were used in 15% (n = 43) of patients. Per-vessel analyses demonstrated that patients undergoing atherectomy to the circumflex and right coronary arteries were more likely than those undergoing atherectomy to other vessels to have bradyarrhythmias requiring pharmacologic intervention (3.4% vs 0%, $P = .01$).

Conclusions: In this 10-year single-center experience using IV aminophylline pretreatment to prevent major bradyarrhythmias in patients undergoing coronary atherectomy, none of the patients required rescue TPM implantation. These data demonstrate that coronary atherectomy can be performed safely without prophylactic TPM, with aminophylline pretreatment and selective use of atropine representing an effective noninvasive approach.

Coronary artery calcification can hinder successful stent delivery and optimal expansion and contribute to higher rates of angiographic and ischemic complications.¹⁻⁴ Coronary atherectomy can be used for plaque modification in such lesions to facilitate percutaneous coronary intervention (PCI).⁵⁻⁸ However, it can be associated with intraprocedural bradyarrhythmias and transient atrioventricular (AV) block, particularly when performed in the right coronary artery (RCA) or in a dominant left circumflex (LCx) artery.^{2,9}

To avoid significant bradyarrhythmias and the potential for hemodynamic decompensation, one prophylactic strategy is the implantation of a transvenous temporary pacemaker (TPM) prior to coronary atherectomy. This invasive approach, however, has intrinsic

procedural risk and economic costs. Aminophylline, a nonselective adenosine receptor antagonist, can prevent adenosine-related bradyarrhythmias during atherectomy by enhancing sinoatrial node automaticity and AV node conduction.^{10,11} Although aminophylline has been used to prevent and treat adenosine-mediated bradyarrhythmia in a variety of clinical scenarios,¹¹⁻¹⁶ limited published data exist on its use to prevent bradyarrhythmias in patients undergoing rotational atherectomy.

The present study describes a 10-year single-center experience using intravenous (IV) aminophylline pretreatment without prophylactic TPM to prevent bradyarrhythmias in patients undergoing rotational atherectomy.

Abbreviations: AV, atrioventricular; CABG, coronary artery bypass graft; IV, intravenous; LCx, left circumflex; PCI, percutaneous coronary intervention; RCA, right coronary artery; SA, sinoatrial; STEMI, ST-elevation myocardial infarction; TPM, temporary pacemaker.

Keywords: aminophylline; bradyarrhythmia; rotational atherectomy; temporary pacemaker.

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Methods

Study design and patient population

This is a retrospective, observational, single-center, institutional review board-approved study that examined consecutive adult patients undergoing coronary angiography with rotational atherectomy at Mayo Clinic in Rochester, Minnesota from August 21, 2010, to October 26, 2020. Patients included in the analysis received IV aminophylline pretreatment prior to rotational atherectomy. Baseline and procedural characteristics were collected using the Mayo PCI Registry, which is a robust database with periodic data quality monitoring, auditing, and validation. Additional procedural characteristics and atherectomy data were abstracted from cardiac catheterization reported and entered in Research Electronic Data Capture.¹⁷ Patients with a permanent pacemaker at baseline, <18 years of age, and/or who did not receive aminophylline pretreatment were excluded (Supplemental Figure S1).

Rotational atherectomy

Arterial access was obtained via the femoral or radial artery approach using a 6F to 8F sheath. Atherectomy was performed with burr sizes ranging from 1.25 to 2.15 mm. After rotational atherectomy, PCI with stenting was performed at the discretion of the operator.

Prophylactic aminophylline administration

An institutional protocol for IV aminophylline administration in the cardiac catheterization laboratory is used (Supplemental Methods), in which 250 mg aminophylline is diluted in 250 mL of normal saline and infused intravenously over 20 minutes by nursing staff at an infusion rate of 750 mL/hour prior to coronary atherectomy. For rotational atherectomy, a standard flush solution was used during the study period containing a combination of 2000 units of heparin, 5 mg of nitroglycerin, and ROTAGLIDE (Boston Scientific) in 1000 mL normal saline. The timing of aminophylline's initiation, as well as initiation of rotational atherectomy in relationship to aminophylline's initiation, were at the discretion of the primary operator. The timing and dosage of aminophylline were abstracted from the electronic health records as documented in the cardiac catheterization laboratory or pharmacy reports. Likewise, the primary operator determined whether the 20-minute infusion should be completed per-protocol or stopped earlier. Rapid administration can result in hypotension and bradycardia. The institutional wholesale acquisitional cost of a 250 mg/10 mL vial of aminophylline is \$13.25.

Study endpoints

The primary composite outcome was the occurrence of any documented bradyarrhythmia and the use of any pharmacologic intervention and/or rescue TPM implantation. Rescue pharmacologic medications included atropine, epinephrine, norepinephrine, dopamine, and/or dobutamine. Secondary analyses addressed the individual components of the primary outcome: documented bradyarrhythmias, pharmacologic intervention, and rescue TPM.

Statistical analysis

Baseline characteristics and procedural characteristics for patients receiving prophylactic aminophylline administration are presented using means and SD or median [IQR]. Outcomes are reported as numbers (percentages) and odds ratios with associated 95% CIs. Logistic regression variables are compared using the Wald test. A 2-

sided *P* value < .05 was considered statistically significant for all comparisons. Analyses were performed using R version 4.1.2 (R Foundation).

Results

Baseline characteristics

A total of 296 patients receiving IV aminophylline pretreatment prior to rotational atherectomy were included. Baseline characteristics are shown in Table 1. The mean age of the population was 74 years and 78% were men. Common comorbidities included hypertension (94%), diabetes mellitus (43%), and previous myocardial infarction (40%), with 42% patients having prior PCI and 28% prior coronary artery bypass graft. Most patients (90%) were prescribed outpatient β -blockers. There were 4 patients (1.4%) who died during index hospitalization.

A total of 275 of patients had a 12-lead electrocardiogram available within 30 days prior to coronary atherectomy. Of these, 85% (*n* = 235) patients had documented normal sinus rhythm, whereas 13% (*n* = 37) had right bundle branch block, 13% (*n* = 35) had atrial fibrillation, and 18% (*n* = 49) had Mobitz type I heart block (Table 1).

Rotational atherectomy

The most common diagnosis in patients undergoing PCI requiring coronary atherectomy with aminophylline pretreatment was non-ST elevation acute coronary syndrome (47%) (Table 2). Indications are summarized in Table 2. Most procedures (75%) were performed via femoral arterial access.

Per-vessel analyses (*n* = 332 vessels) showed that most atherectomy runs were performed in the left anterior descending artery (40%, *n* = 133), followed by the RCA (30%, *n* = 99), left main (15%, *n* = 51), and

Table 1. Baseline characteristics of patients undergoing rotational atherectomy with aminophylline pretreatment.

	N = 296
Demographics	
Age, y	74 (9.2)
Female	66 (22%)
Medical history	
Hypertension	277 (94%)
Diabetes mellitus	127 (43%)
Chronic kidney disease	94 (32%)
End-stage renal disease on dialysis	16 (5.4%)
Peripheral arterial disease	99 (34%)
Prior myocardial infarction	118 (40%)
Prior percutaneous coronary intervention	123 (42%)
Prior coronary artery bypass graft	82 (28%)
Baseline outpatient medications	
β -blockers (<i>n</i> = 198)	178 (90%)
Calcium channel blockers (<i>n</i> = 198)	59 (30%)
Baseline 12-lead ECG	
Electrocardiogram available for review within 30 d of procedure	275 (93%)
Normal sinus rhythm	235 (85%)
Heart rate	65 [56-76]
PR length, ms	178 [158-196]
Left bundle branch block	8 (2.9%)
Right bundle branch block	37 (13%)
Left anterior fascicular block	15 (5.5%)
Atrial fibrillation	35 (13%)
Mobitz type 1 heart block	49 (18%)

Values are mean (SD), median [IQR], or *n* (%). ECG, electrocardiogram.

Table 2. Procedural characteristics of patients undergoing rotational atherectomy with aminophylline pretreatment.

N = 296	
Indication for PCI	
STEMI	12 (4.1%)
NSTE-ACS	139 (47%)
Stable angina	30 (10%)
Other PCI indication	115 (39%)
Intraprocedure characteristics	
Femoral access	222 (75%)
Radial access	73 (25%)
Contrast, volume	200 [150-250]
Total number of coronary vessels undergoing rotational atherectomy	
One vessel	265 (90%)
Two vessels	26 (8.8%)
Three vessels	5 (1.7%)
Multiple vessels undergoing rotational atherectomy	31 (11%)
Coronary vessel intervened upon with rotational atherectomy (N = 332)	
Left main artery	51 (15%)
Left anterior descending artery	133 (40%)
Left circumflex artery (including ramus intermedius)	48 (14%)
Right coronary artery	99 (30%)
Saphenous vein graft	1.0 (0.3)
Total number of atherectomy runs	2.0 [2.0-3.0]
Total time of atherectomy runs, s	62 [39-98]
Maximum burr size used, mm	
1.25	41 (14%)
1.50	183 (62%)
1.75	52 (18%)
2.00	17 (5.7%)
2.15	3 (1.0%)
Severity of stenosis, % occlusion	90 [80-90]
Lesion length, mm	24 [16-38]
Residual stenosis, % occlusion	4.7 ± 14
Number of stents deployed during procedure	2.0 [1.0-3.0]

Values are n (%), mean ± SD, or median [IQR].

NSTE-ACS, non-ST elevation-acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

LCx (14%, n=48). A total of 90% (n = 265) of patients underwent single vessel rotational atherectomy, whereas 10% (n = 31) had multivessel atherectomy (Table 2). The most common burr used was the 1.5-mm burr in 61% (n = 179) of patients. Median number of atherectomy runs was 2.00 [2.00-3.00] (range 1-11) and median total atherectomy time was 62 seconds [39-98]. A total of 288/296 (97%) patients underwent stent deployment after rotational atherectomy.

Prophylactic aminophylline administration

Specific aminophylline dosage was available in 74% (219/296) of patients, among which 92% (202/219) received the complete 250 mg IV dose. A total of 10 (3.4%) patients received the complete 250 mg IV dose administered ≥20 minutes prior to initiation of rotational atherectomy. Median time of aminophylline administration prior to atherectomy was 4 minutes [1.0-7.0]. Atropine was administered in 74 (25%) patients prior to rotational atherectomy.

Outcomes

The primary composite outcome of a documented bradyarrhythmia with a pharmacologic intervention or rescue TPM occurred in 5 (1.7%) of patients (Table 3, Central Illustration, Supplemental Table S1). None of the patients required rescue TPM (0.0%; 95% CI, 0.0-0.12). Atropine was used in 15% (n = 43) of patients. Among 10 patients receiving the complete per-protocol 250 mg of IV aminophylline (complete 20-minute infusion prior to atherectomy

Table 3. Outcomes of patients undergoing rotational atherectomy.

N = 296	
Primary outcome: documented bradyarrhythmia and pharmacologic intervention or rescue temporary pacemaker	5 (1.7%)
Bradyarrhythmia	7 (2.4%)
Rescue temporary pacemaker	0 (0%)
Pharmacologic intervention	43 (15%)
Atropine	43 (15%)
Epinephrine	0 (0.0%)
Norepinephrine	0 (0.0%)
Dopamine	0 (0.0%)
Dobutamine	0 (0.0%)

Values are n (%).

initiation), none had the primary composite outcome or documented bradyarrhythmias. None of the patients with underlying heart block (n = 63) (Mobitz type 1 heart block, left anterior fascicular block, and left and right bundle branch block) on their 12-lead electrocardiogram experienced the primary outcome or had documented major bradyarrhythmias, although 9/63 (15%) patients required rescue pharmacologic medication.

The primary composite outcome occurred most frequently in patients undergoing rotational atherectomy to the RCA (4.0%). Compared with non-RCA/LCx vessels, those with rotational atherectomy to the RCA and/or LCx had a higher frequency of the primary outcome (0.0% vs 3.4%, $P = .01$). They also were more likely to have pharmacologic interventions (7.6% vs 23%, odds ratio, 3.68; 95% CI, 1.89-7.15; $P < .001$) (Table 4, Supplemental Table S2).

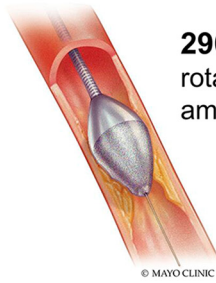
Discussion

The present study represents the largest published experience to date describing the use of IV aminophylline pretreatment for the prevention of bradyarrhythmia in patients undergoing rotational atherectomy. In this 10-year single-center experience using IV aminophylline pretreatment to prevent major bradyarrhythmias in patients undergoing coronary atherectomy, none of the patients required rescue TPM implantation. These data demonstrate that with aminophylline pretreatment and selective use of atropine, coronary atherectomy can be performed safely without prophylactic TPM. This strategy represents an effective noninvasive approach that is likely associated with lower risks and economic costs than invasive, prophylactic TPM. Although aminophylline has been used in the clinical context of bradycardia, no robust data exist regarding its use in this population. Our analysis is timely and important for physicians, given an increasing prevalence of severely calcific coronary lesions and increasing use of coronary atherectomy throughout the United States¹⁸ and Europe.⁵

Our single-center analysis documents a low rate of bradyarrhythmia requiring pharmacological intervention in patients undergoing rotational atherectomy who received prophylactic IV aminophylline pretreatment, and none of the patients in this 10-year experience required rescue TPM. Although bradyarrhythmic events requiring intervention were infrequent, they were more likely to occur in patients undergoing atherectomy to the right coronary or circumflex arteries. Despite an institutional protocol to administer 250 mg over 20 minutes, only 10 patients completed per-protocol administration prior to atherectomy initiation, and none of them had bradyarrhythmias. Whether the benefits of IV aminophylline are augmented when aminophylline is systematically administered per-protocol requires additional study.

To our knowledge, this is the largest and most comprehensive analysis that has evaluated the clinical features, procedural characteristics, and outcomes of patients receiving prophylactic IV aminophylline

INTRAVENOUS AMINOPHYLLINE PRE-TREATMENT FOR THE PREVENTION OF BRADYARRHYTHMIAS IN PATIENTS UNDERGOING ROTATIONAL ATHERECTOMY

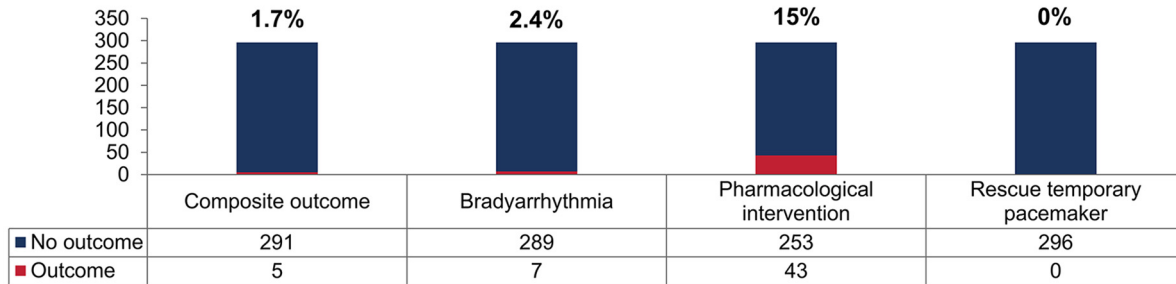


296 patients undergoing rotational atherectomy with aminophylline pretreatment



Intravenous aminophylline protocol

- Intravenous infusion
- 1 mg/mL
- Add 250 mg to 250 mL of 0.9% normal saline
- Infuse over 20 minutes, although may give less as directed by physician
- Pump rate at 750 mL per hour
- Under ideal circumstances, the full 20-minute infusion will be complete prior to atherectomy



Central Illustration.

Outcomes of patients receiving intravenous aminophylline prior to rotational atherectomy for the prevention of bradyarrhythmias.

prior to rotational atherectomy. Furthermore, data for this study were extracted from a large, high-volume tertiary center with experienced operators. Additionally, our study highlights the effectiveness and safety of an alternative approach to the prevention of bradyarrhythmias in patients undergoing coronary atherectomy, which is likely more cost-effective and safer than prophylactic TPM.

In patients undergoing orbital atherectomy without prophylactic TPM or aminophylline, Lee et al¹⁹ reported that 4% of patients experienced significant bradycardia (<50 bpm). Similar to our findings, in a small retrospective analysis of 7 RCA atherectomy cases in which aminophylline was used prophylactically, Megaly et al² found that no patients developed clinically significant bradycardia or AV block. Cha et al²⁰ showed that preprocedural IV aminophylline infusion prevented bradyarrhythmia in all 38 patients undergoing rotational atherectomy without hemodynamic side effects. Several other studies have shown similar results with aminophylline pretreatment during rheolytic thrombectomy.^{14,15}

Historically, empiric transvenous TPM placement was considered a prerequisite to rotational atherectomy of the RCA or a dominant LCx due to concern of transient microvascular ischemia of the cardiac conduction system and associated AV block.^{5,21} More recently, this practice has come into question given the associated complications, increased cost, improved procedural techniques such as smaller burrs, lower burr speeds, and shorter atherectomy runs, as well as pharmacologic management of transient bradycardia, which have led to a lower incidence of transient bradyarrhythmias and heart block.^{5,21} Studies have shown a higher frequency of complications with the use of prophylactic TPM. In a retrospective analysis of 6999 consecutive PCI interventions, von Sohsten et al²² found that 8/743 (1%) patients undergoing rotational atherectomy experienced cardiac tamponade within 36 hours of the procedure, with 7 cases caused by right ventricular perforation from TPM wire placement. Similarly, in a retrospective analysis of 134 patients undergoing rotational atherectomy of whom 50% had TPM placed, Mitar et al⁹ found that 1 patient experienced cardiac tamponade caused by TPM placement requiring pericardiocentesis.

In addition, contemporary rotational atherectomy techniques exist that may minimize the incidence of bradycardia and no reflow, which include smaller burr sizes (<1.5 mm), lower burr speeds, and restricting each pass to a short duration (<20-30 seconds).^{5,19} In our current experience, operators used smaller burr sizes, with 75% of atherectomy runs completed using a burr size ≤1.5 mm. Our data suggest that IV aminophylline pretreatment, in conjunction with proper procedural technique, provides a safe, effective, and likely cost-effective strategy in the prevention of bradyarrhythmia during rotational atherectomy.

Similar to previous studies,^{9,14,15} we found that rotational atherectomy in the RCA had the highest incidence of major bradyarrhythmia. In addition, we found a higher frequency of the primary outcome and a higher risk of rescue pharmacologic interventions during atherectomy to the RCA and/or LCx compared with non-RCA/LCx lesions. These findings might be explained by ischemic and adenosine-mediated effects in the sinoatrial nodal artery, which is predominantly supplied by the RCA, or in the dominant coronary vessel supplying the AV nodal artery. In contrast, rotational atherectomy to left anterior descending

Table 4. Outcomes according to target vessel.

	Non-RCA/LCx (N = 185)	RCA/LCx (N = 147)	P
Primary outcome: documented bradyarrhythmia and pharmacologic intervention or rescue temporary pacemaker	0 (0%)	5 (3.4%)	.01
Bradyarrhythmia	0 (0%)	7 (4.8%)	.003
Rescue temporary pacemaker	0 (0%)	0 (0%)	–
Pharmacologic intervention	14 (7.6%)	34 (23%)	<.001
Atropine	14 (7.6%)	34 (23%)	<.001
Epinephrine	0 (0%)	0 (0%)	–
Norepinephrine	0 (0%)	0 (0%)	–
Dopamine	0 (0%)	0 (0%)	–

Values are n (%).

LCx, left circumflex artery; RCA, right coronary artery.

artery or non-dominant LCx lesions is less likely to predispose to these conduction abnormalities.⁹ Accordingly, in high-risk patients (ie, low resting heart rates, high-degree AV conduction disease, and/or long, diffuse calcified lesions in the RCA or dominant LCx) undergoing atherectomy to the RCA and/or dominant LCx, per-protocol IV aminophylline pretreatment should be completed to mitigate the potential risk major bradyarrhythmias given its effectiveness, ease of administration, and safety.

Our study has limitations. First, it is a retrospective, observational, single-center descriptive analysis of our clinical experience. Second, given our study addresses a 10-year clinical experience that involved several transitioning electronic health records systems and variable approaches to medications administered in the cardiac catheterization laboratory, barriers existed to obtain specific aminophylline dosages in all patients, for which reason several patients had missing specific aminophylline dosages in their records. Third, given the low event rate and absence of a control group, larger studies are needed to establish whether there are particular subgroups that derive benefit. It is reasonable to consider that aminophylline use may be best reserved for those with high-risk features. Conversely, however, given the ease of use and low cost, broader use can occur as observed in our experience. Fourth, recognizing this is a single-center descriptive study, larger studies are needed, with comparisons needed to those using prophylactic TPM as well as other devices such as orbital atherectomy. Last, our findings are specific to our institution's protocol, and there may be alternative methods that require study. We do not routinely hold β -blockers or calcium channel blockers and whether holding these medications prior to elective PCI with atherectomy is beneficial requires study.

Conclusion

In this 10-year single-center experience using IV aminophylline pretreatment to prevent major bradyarrhythmias in patients undergoing coronary atherectomy, none of the patients required rescue TPM implantation. Given that alternative prophylactic strategies such as TPM implantation are associated with procedural risks and higher costs, aminophylline represents a safe and cost-effective strategy for patients undergoing rotational atherectomy.

Declaration of competing interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics statement and patient consent

The present is a retrospective, observational (consent waived), single-center study approved by the institutional review board. The research reported has adhered to the relevant ethical guidelines.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography & Interventions* at [10.1016/j.jscai.2023.100590](https://doi.org/10.1016/j.jscai.2023.100590).

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