Early dose of Adenosine, postRadiofrequency abLation of accessory pathwaY in determining acute procedural Success (EARLY Study)

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Abstract

Introduction Post ablation of the accessory pathway (AP), the patient is observed in the catheterization laboratory for a variable period for resumption of pathway conduction. Aim of the study was to determine whether the administration of intravenous adenosine at 10 minutes after ablation of accessory pathway (AP) would have the same diagnostic accuracy as waiting for 30 minutes in predicting the resumption of AP conduction. **Methods:** This was a prospective interventional study conducted in two centers. Post ablation of the AP, intravenous adenosine was administered at 10 minutes to look for dormant pathway conduction. The response was recorded as positive (presence of pathway conduction), negative (absence), or indeterminate (not able to demonstrate AV and VA block and inability to ascertain AP conduction). **Results:** The study included 110 procedures performed in 109 patients. Adenosine administration at 10 minutes showed positive result in 3 cases (2.7%), negative result in 99 cases (90%) and indeterminate result in 8 cases (7.3%). Reconnection of accessory pathway at 30 minutes post ablation was seen in 8 cases (7.3%). Of these 8 cases, 10minutes adenosine administration showed positive test in 3 patients and negative test in 5 patients. Adenosine test at 10 minutes has a sensitivity, specificity, positive predictive value, and negative predictive value of 37.5%, 100%, 100% and 94.9% in identifying the recurrence of accessory pathway conduction at 30 minutes, respectively. **Conclusion:** Absence of pathway conduction on administration of adenosine 10 minutes post ablation does not help predict the absence of resumption of conduction thereafter.

Title page

Manuscript title

E arly dose of **A** denosine, post**R** adiofrequency ab**L** ation of accessory pathwa**Y** in determining acute procedural Success (EARLY Study)

Short title:

Early adenosine - predicting AP recurrence

Keywords:

Supraventricular tachycardia, Adenosine, Accessory pathway, ablation, preexcitation

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request

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Abstract

Introduction

Post ablation of the accessory pathway (AP), the patient is observed in the catheterization laboratory for a variable period for resumption of pathway conduction. Aim of the study was to determine whether the administration of intravenous adenosine at 10 minutes after ablation of accessory pathway (AP) would have the same diagnostic accuracy as waiting for 30 minutes in predicting the resumption of AP conduction.

Methods:

This was a prospective interventional study conducted in two centers. Post ablation of the AP, intravenous adenosine was administered at 10 minutes to look for dormant pathway conduction. The response was recorded as positive (presence of pathway conduction), negative (absence), or indeterminate (not able to demonstrate AV and VA block and inability to ascertain AP conduction).

Results:

The study included 110 procedures performed in 109 patients. Adenosine administration at 10 minutes showed positive result in 3 cases (2.7%), negative result in 99 cases (90%) and indeterminate result in 8 cases (7.3%). Reconnection of accessory pathway at 30 minutes post ablation was seen in 8 cases (7.3%). Of these 8 cases, 10minutes adenosine administration showed positive test in 3 patients and negative test in 5 patients. Adenosine test at 10 minutes has a sensitivity, specificity, positive predictive value, and negative predictive value of 37.5%, 100%, 100% and 94.9% in identifying the recurrence of accessory pathway conduction at 30 minutes, respectively.

Conclusion:

Absence of pathway conduction on administration of adenosine 10 minutes post ablation does not help predict the absence of resumption of conduction thereafter.

Keywords:

Supraventricular tachycardia, Adenosine, Accessory pathway, ablation, preexcitation

Main Text

Introduction

Catheter ablation is a definitive therapy for supraventricular tachycardia that involves an accessory pathway (AP). The acute success rate of catheter ablation is around 90-95% with a recurrence rate of 5-10%.[1-3] The resumption of accessory pathway conduction within 24 hours is defined as early recurrence.[4-6] After ablation of the AP, the patient is observed for resumption of pathway conduction in the catheterization laboratory. This observation period is variable, and most centers have done so for a minimum of 30 minutes after successful radiofrequency application.[7]

Adenosine is a natural nucleoside with a short half-life, used for unmasking latent preexcitation.[8,9] It is given after catheter ablation to unmask dormant AP conduction by slowing atrioventricular conduction and causing membrane hyperpolarization.[10,11] Timing of adenosine administration post-ablation varies in different studies from 15 to 30 minutes.[10,12] We hypothesized that administration of intravenous adenosine at 10 minutes after ablation would have the same diagnostic accuracy as waiting for 30 minutes in predicting a resumption of AP conduction. The waiting period and the total procedure time could be abbreviated if this was true.

Methods:

Patient population:

This was a prospective interventional study conducted in two tertiary care centers. Ethics committee approval for the study was obtained from each of the centers.

Inclusion criteria: Informed consent was obtained from patients undergoing accessory pathway ablation. Those who underwent successful radiofrequency ablation of AP were included in the study.

Exclusion criteria: The following patients were excluded

Patients with multiple APs

2. Atriofascicular pathways

3. Patients with concealed septal AP where distinguishing transient retrograde conduction via AP or AV nodal system was inconclusive. However, septal accessory pathways with manifest preexcitation were included in the study.

4. Patients who had COPD (Chronic obstructive pulmonary disease) and bronchial asthma where intravenous adenosine could lead to an acute exacerbation.

Multiple APs, atriofascicular pathway and concealed septal AP were diagnosed during the electrophysiological study (EPS) and hence patients with these pathways were excluded after EPS.

Electrophysiology Study:

Electrophysiology study was performed using Workmate Claris System with EP-4 Cardiac Stimulator (St Jude, SN Paul, MN, USA). Procedures were performed under local anesthesia with conscious sedation. A minimum of four catheters were used during the study. Quadripolar catheters were placed in the right ventricular apex, His bundle region, right atrial appendage and a decapolar catheter was placed in the coronary sinus. Ventricular and atrial programmed stimulation was performed. Antegrade and retrograde conduction properties of the AP were assessed. When tachycardia was induced, it was determined to be AVRT (atrioventriucular reentrant tachycardia) based on its electrophysiological properties and diagnostic pacing maneuvers during tachycardia.[13,14]Non-irrigated catheters were used for ablation in most patients and irrigated catheters were used if the former created ineffective lesions or for pathways in the coronary sinus.

On successful ablation of the AP, a timer was started. At 10 minutes after ablation, an intravenous adenosine bolus of 18 mg was administered through a large bore peripheral line immediately followed by a bolus of 20 ml normal saline. In patients with bidirectional AP conduction prior to ablation, it was necessary to demonstrate the absence of antegrade and retrograde AP conduction during adenosine administration. In patients with pathways capable of only unidirectional conduction, it was sufficient to demonstrate it being absent on adenosine testing. The test was considered positive or negative depending on whether adenosine resulted in the resumption of pathway conduction, albeit intermittent (Figure 1,2) or not (Figure 3). If the test was negative, programmed and burst pacing to demonstrate pathway conduction followed by intravenous adenosine was repeated at 30 minutes and the study was terminated if there was no AP reconnection. If the adenosine test at 10 minutes was positive, the pathway was remapped and ablated once there was a return of consistent conduction. Post-procedure ECG was taken after 24 hours.

If AV block and VA block were not demonstrated with the 18mg iv adenosine bolus and the presence or absence of AP conduction could not be ascertained, the test was considered indeterminate.

The sensitivity, specificity, positive and negative predictive value of adenosine testing at ten minutes to identify the recurrence of accessory pathway conduction at 30 minutes were calculated.

Statistical analysis

Continuous variables are presented as mean ± SD (standard deviation). Discrete variables are presented as percentages. All statistical calculations were performed using SPSS version 16.0.

Results

The study included 110 procedures performed on 109 patients. One patient underwent two procedures due to recurrence of AP conduction four months after the initial ablation. There were 63 (57.8%) males and 46 (42.2%) females. The mean age of patients was 38.61 years.

Bidirectional conduction was present in 77 (70%) cases, retrograde only conduction was present in 29 (26.4%) cases and antegrade only conduction was present in 4 (3.6%) cases. The most common site of AP insertion was left lateral (52.7%) followed by left posterior (13.6%) and right posteroseptal (13.6%) (Figure 4).

Procedural characteristics

The mean procedural time was 172 + 83 minutes. The mean time taken from the initiation of radiofrequency energy application to block in AP conduction was 4.96 + 2.98 seconds (Table 1).

Adenosine administration at 10 minutes was positive in 3 cases (2.7%), negative in 99 cases (90%), and indeterminate in 8 cases (7.3%). (Central illustration)

Reconnection of the accessory pathway at 30 minutes post-ablation was seen in 8 patients (7.3%). Of these, adenosine at 10 minutes showed positive results (evidence of intermittent pathway conduction) in 3 patients. (Table 2) In the other 5 patients, the adenosine test at 10 minutes was negative (no pathway conduction). Thus, adenosine test at 10 minutes has a sensitivity, specificity, positive predictive value, and negative predictive value of 37.5%, 100%, 100%, and 94.9% in identifying the recurrence of accessory pathway conduction at 30 minutes, respectively (Central illustration). In 8 patients who had accessory pathway reconnection at 30 minutes, pathway location was left lateral in 5 patients, CS in 2, and midseptal in 1 patient (Table 3). Of these 8 patients, 6 had bidirectional conduction, antegrade only conduction in 1 patient, and concealed conduction in 1 patient.

Discussion:

This was a prospective interventional study exploring the idea that administration of intravenous adenosine bolus at 10 minutes post radiofrequency ablation of an AP might identify dormant pathway conduction which will otherwise require a waiting period of 30 minutes. It was hypothesized that absence of conduction with adenosine at 10 minutes would predict the same at 30 minutes. We found that adenosine testing at 10 minutes had a low sensitivity of 37.5% and a negative predictive value of 94.9%. Hence, it does not appear to be reliable enough to allow an abbreviation of the waiting period.

Alvarez et al utilized adenosine triphosphate [ATP] at the end of 5 minutes after ablation to unmask dormant accessory pathway conduction.[5] The present study utilized intravenous adenosine as it is widely available while Alvarez et al utilized ATP which is currently not widely available. We postulated that administration of adenosine at 10 minutes rather than at 5 minutes would increase the predictive ability of AP recurrence at 30 minutes. In that study 108 ATP tests were performed in 100 patients and had 9 positive tests, 82 negative tests and 17 tests were indeterminate. They reported a sensitivity of 69%, which is higher than in our study, but still far from ideal. There were 4 early recurrences among the 82 patients with negative tests (4.9%) in their study while ours had 5 early recurrences among 99 patients with negative tests (5.1%).

In the present study, there were 8 indeterminate tests out of 110 tests (7.2%) while Alvarez et al had 17 (15.7%).[5] The smaller number of indeterminate results in the present study could have been due to administration of a higher dose of adenosine 18mg through a large bore peripheral intravenous line which was immediately followed by a bolus of 20 ml normal saline.

Adenosine prolongs conduction in the AV node and causes AV block transiently. Adenosine reduces the refractoriness of AP conduction.[15] Spotniz et al proposed three models for unmasking dormant accessory pathway conduction: slow conduction, linking, and excitation recovery model.[10] Of these, 90% of the unmasking of AP conduction was due to excitation recovery model wherein the administration of adenosine caused membrane hyperpolarization and thereby reduced pathway refractoriness. The early recurrence of pathway conduction is a marker of late recurrence, and it can represent about 50% of total recurrences.[4] Hence, it is of paramount importance to detect early recurrence by monitoring the patient for 24 hours post-procedure.

When there is a reversible injury to the accessory pathway as in the perilesional zone of radiofrequency ablation, the pathway is partially depolarized, making it unexcitable, and refractory to impulse conduction. Adenosine by causing membrane hyperpolarization makes the pathway re-excitable and thereby unmasks dormant accessory pathway conduction. After any reversible injury, the pathway regains its electrophysiological properties after a variable period, which are hastened by adenosine. However, this recovery time is ill-defined, and 10 minutes is probably insufficient when compared to 30 minutes.

Strengths and Limitations:

This was a prospective interventional study. This study determined the predictive accuracy of adenosine administered 10 minutes after ablation to identify recurrence of pathway conduction at 30 minutes. The electrophysiological characteristics of the accessory pathway in the study population are like that of published data.

Adenosine was not administered prior to ablation to look for any adenosine-sensitive AP conduction. Early recurrence was diagnosed based on conduction at 30 minutes and an ECG taken 24 hours after the procedure. 24-hour continuous ECG monitoring was not done.

Conclusion:

Absence of conduction on administration of adenosine 10 minutes after the ablation of an accessory pathway does not help predict the absence of resumption of conduction thereafter. This study does not recommend performing adenosine testing at 10 minutes to abbreviate the waiting period after accessory pathway ablation.

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Table legends

Table 1: Procedural Characteristics

Footnote: SD – standard deviation

Table 2: Comparison of adenosine testing at 10 minutes with presence of pathway conduction at 30 minutes

Footnote: Nil

Table 3: Characteristics of accessory pathways which reconnected at 30minutes post ablation

Footnote: Nil

Figure legends

Figure 1: Positive adenosine test

On administration of iv Adenosine, there is unmasking of antegrade pathway conduction indicating positive adenosine test (top panel). Return of preexcitation is transient and lasts only few seconds (bottom panel). From top to bottom, I, II and V2 represent leads I, II and V2 of 12 lead surface ECG. HRA represents distal bipole of right atrial catheter in right atrial appendage. His d represents distal bipole of quadripolar catheter in His bundle position. CS p represent proximal bipole of a decapolar catheter in coronary sinus.

Figure 2: Positive adenosine test – Concealed AP

Part A – With ventricular pacing done after ablation of concealed left lateral accessory pathway, there is concentric atrial activation.

Part B - After administration of iv Adenosine, there is transient eccentric atrial activation with 3:1 VA conduction suggesting retrograde pathway conduction - positive adenosine test. From top to bottom, I, and V1 represents leads I, and V1 of 12 lead surface ECG. LA represents distal bipole of quadripolar catheter in LA. His d represents distal bipole of quadripolar catheter in His bundle position. CS p, CS m and CS d represent proximal, mid, and distal bipole of a decapolar catheter in coronary sinus, respectively. RVd represent distal bipole of the catheter in right ventricular apex

Figure 3: Negative adenosine test

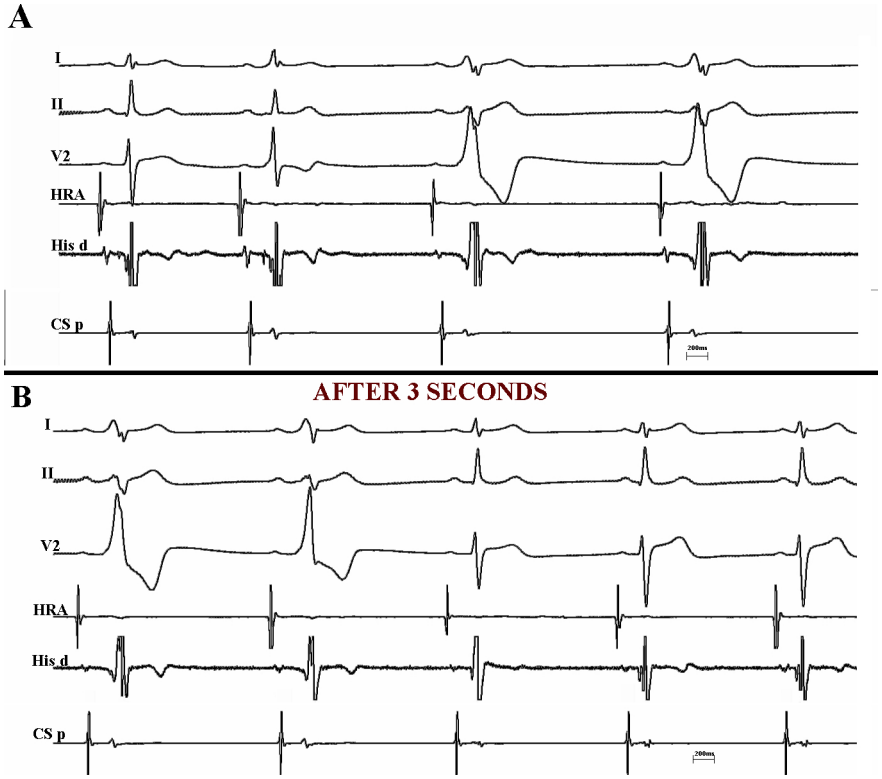
After administration of iv Adenosine, AV block is seen (Shown as blocked P wave in figure). Ventricular pacing is started after this and shows no VA conduction confirming absence of accessory pathway conduction in both directions. CS d represent distal bipole of a decapolar catheter in coronary sinus. Rest of the catheter positions and abbreviations are same as in Figure 2.

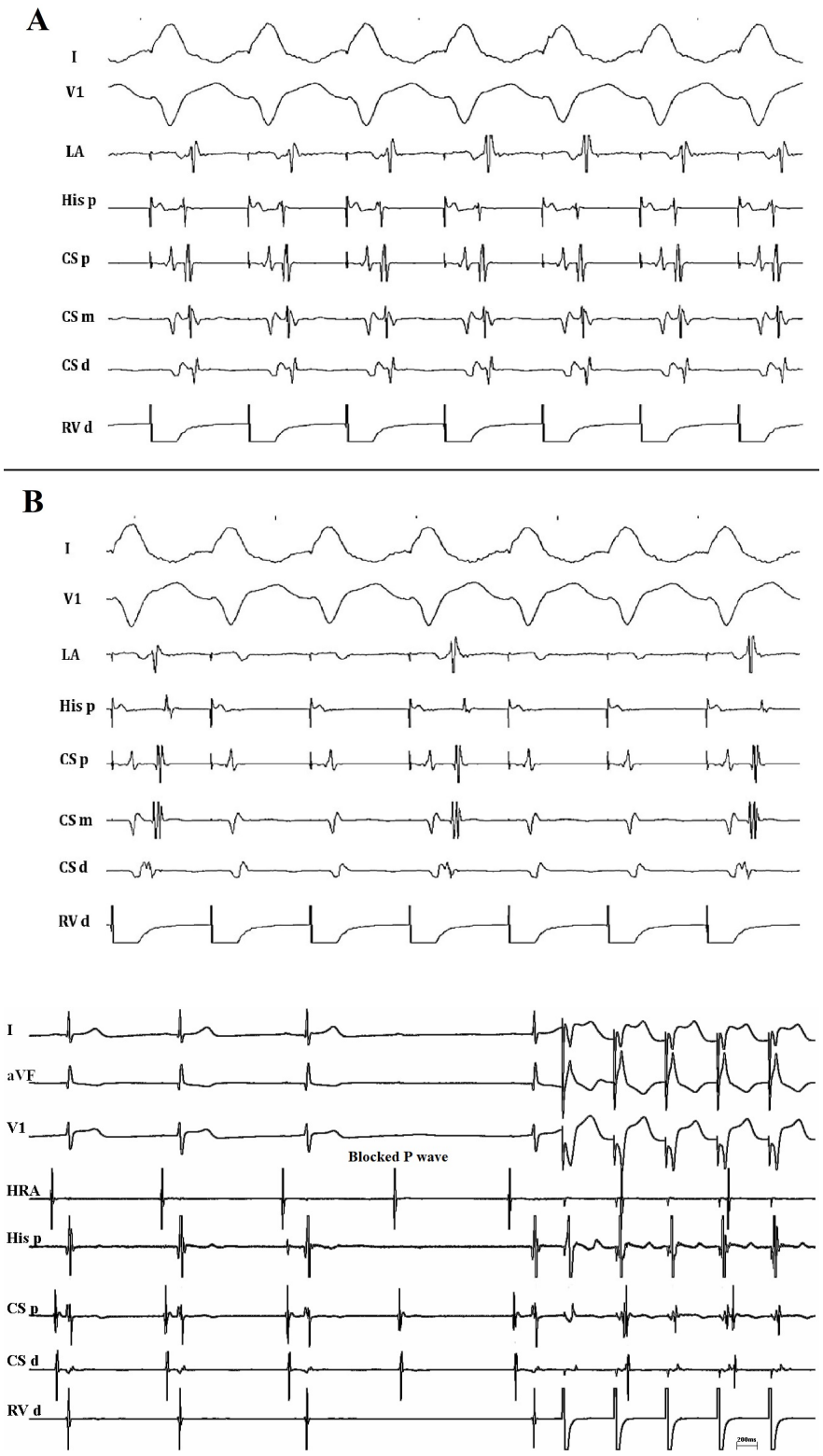
Figure 4: Location of accessory pathway

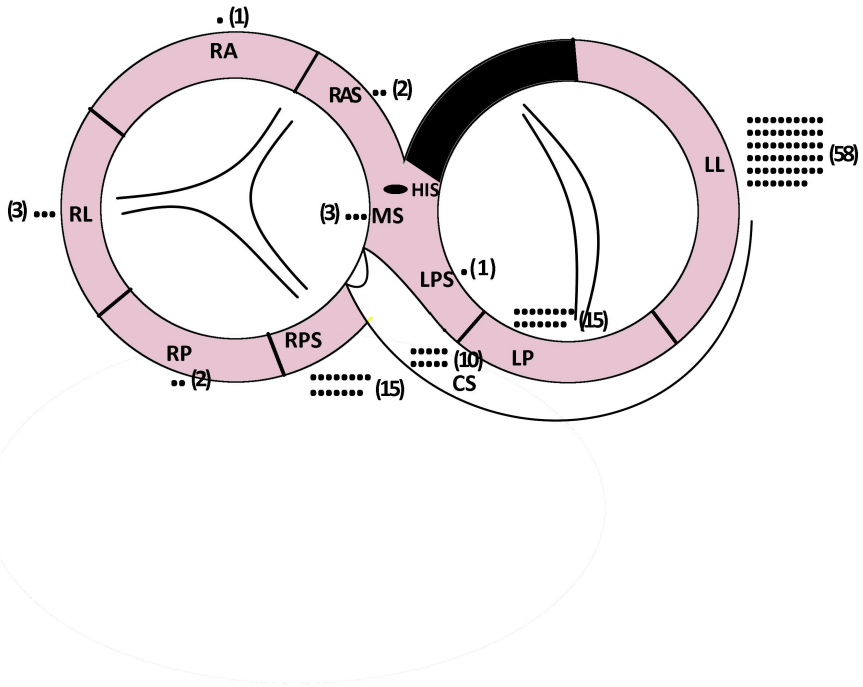
Dots represent the number of cases that satisfied inclusion criteria, at each location. CS – Coronary sinus, MS-midseptal, LL-left lateral, LP – left posterior, LPS–left posteroseptal, RA – right anterior, RAS – right anteroseptal, RL – right lateral,RP – right posterior, RPS – right posteroseptal.

Central illustration (Graphical Abstract Image):

Graphical abstract text: Flow chart showing the study data and predictive ability of adenosine testing at 10minutes for accessory pathway recurrence at 30minutes.







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