Adenosine-5′-Triphosphate Test for the Noninvasive Diagnosis of Concealed Accessory Pathway
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OBJECTIVES This study assessed the use of adenosine triphosphate (ATP) in the noninvasive diagnosis of concealed accessory pathway (AP) and dual atrioventricular (AV) node physiology in patients with inducible AV reentrant tachycardia (AVRT).

BACKGROUND Administration of ATP during sinus rhythm identifies dual AV node physiology in 76% of patients with inducible sustained slow/fast AV nodal reentry tachycardia (AVNRT).

METHODS Incremental doses of ATP were intravenously administered during sinus rhythm to 34 patients with inducible sustained AVRT involving a concealed AP and to 27 control patients without AP or dual AV node physiology. One study group patient could not complete the study and was excluded from analysis.

RESULTS The AV reentrant echo beats (AVRE), or AVRT, suggestive of the presence of concealed AP, were observed after ATP administration in 24 (73%) study patients and in none of the control group. Electrocardiographic signs suggestive of dual AV node physiology were observed after ATP administration in 7 (21%) study patients and in none of the control group. Most instances of AVRE/AVRT were preceded by a slight increase (<50 ms) in PR interval. In 8 of 9 patients tested, neither AVRE nor AVRT was no longer observed following ATP administration after successful radiofrequency ablation of the AP. In the remaining patient, a different AVRE due to the presence of an additional AP was observed. Administration of ATP during sinus rhythm may be a useful bedside test for identifying patients with concealed AP who are prone to AVRT and those with associated dual AV node pathways. (J Am Coll Cardiol 2000;36:803–10) © 2000 by the American College of Cardiology

CONCLUSIONS

Regular, paroxysmal supraventricular tachycardia (PSVT) occurring in patients without antegradely conducting accessory pathways (AP) is due to atrioventricular nodal reentry tachycardia (AVNRT) in 51% of cases, atrioventricular reentrant tachycardia (AVRT) in 34% of cases, and to various mechanisms in the remaining 15% (1). We recently showed that administration of adenosine-5′-triphosphate (ATP) during sinus rhythm identifies dual atrioventricular (AV) node physiology in 76% of patients with inducible sustained slow/fast AVNRT (2). Because the AV nodal conduction delay caused by the administration of ATP during sinus rhythm may allow the occurrence of AV reentrant orthodromic echo beats (AVRE) or AVRT in patients with concealed AP, we sought to assess the use of ATP in the noninvasive diagnosis of such APs. We also analyzed the incidence of dual AV node physiology using ATP test in these patients.

METHODS

Patient population. The study group consisted of consecutive patients from Tel-Aviv and Sheba medical centers who had suspected and subsequently proven inducible sustained AVRT at electrophysiologic study performed during the course of a radiofrequency ablation procedure. All patients had sustained AVRT induced before or after the intravenous (IV) administration of isoproterenol and were evaluated in the absence of antiarrhythmic drug therapy. At the time of electrophysiologic study no patient had evidence of antegrade conduction over an AP using appropriate atrial pacing techniques.

A control group included patients who had no electrophysiologic evidence of AP or dual AV node physiology nor inducible tachycardia on isoproterenol after they underwent ablation of their slow pathway with radiofrequency energy. These patients were also part of another study that evaluated the effects of radiofrequency ablation of the slow pathway on ATP-induced dual AV node physiology (3). None of the patients had a history of asthma, a contraindication to ATP administration, and none were treated with antiarrhythmic drugs or with drugs known to interfere with ATP metabolism (aminophylline, dipyridamole, benzodiazepines).

ATP test. The ATP test was performed after the patients gave informed consent. The effects of ATP were evaluated during sinus rhythm. The ATP (Striadyne, Wyeth Laboratories, France) was injected through a right antecubital vein as a rapid bolus followed by a 20-ml flush of normal saline. The initial dose of ATP was 10 mg. Repeated doses (with 10-mg increments) were given at 1–2 min intervals after return of sinus rate to control, until one of the following prospectively defined end points was observed: 1) occurrence of ≥1 AVRE (see following text) or 2) second-degree or third-degree AV block. The test was discontinued...
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In our previous study (2), we found an excellent basis on the analysis of simultaneous 12-lead surface ECG definitions during ATP test (see following text) was also noted but was not considered a study end point.

To avoid possible catheter-induced trauma to APs (4) or catheter-induced arrhythmias, the baseline ATP test was performed in all study patients prior to placement of any electrode catheter in the cardiac chambers. The ATP test was repeated after radiofrequency ablation of the accessory pathway in nine patients who had ECG signs suggesting the presence of a concealed AP at initial ATP test. In these nine patients, the ATP test was performed while electrode catheters were in the cardiac chambers.

ECG definitions during ATP test. The ECG signs suggestive of the presence of a concealed AP during ATP administration were considered to be present when at least one of the following events was observed: 1) an echo beat was present with a retrograde P wave that had a morphology and a RP relationship similar to that present during the AVRT induced at subsequent electrophysiologic study, and 2) an AVRT (sustained or nonsustained) was initiated. For study analysis, at least two consecutive AVREs were considered as AVRT. A sustained tachycardia was defined as a tachycardia lasting ≥30 s.

Electrocardiographic signs of dual AV node physiology during ATP administration (2) were considered to be present when at least one of the following events was observed: 1) PR interval increased or decreased by ≥50 ms between two consecutive sinus beats and 2) an AV nodal echo beat or AVNRT developed. All these criteria were based on the analysis of simultaneous 12-lead surface ECG only. In our previous study (2), we found an excellent correlation between the results of surface ECG recordings with those of intracardiac recordings.

The number of episodes of AVRE and AVRT as well as the mode of initiation of the first-occurring AVRE or AVRT were also analyzed.

Electrophysiologic study. After obtaining patient informed consent, the electrophysiologic study was performed using electrode catheters (Bard) placed in the His bundle area, right ventricular apex, right atrium, and in most instances the coronary sinus, as previously described (5). Briefly, the baseline electrophysiologic study included 1) delivery of one to three extrastimuli during atrial or ventricular pacing at a cycle length of 600 ms until the atrial or ventricular refractory period was reached; and 2) increment in atrial or ventricular pacing until antegrade or retrograde block in the AV node or AP, respectively, was achieved. If sustained AVRT was not induced using this protocol, isoproterenol was administered at incremental dosage until the basic sinus rhythm increased by at least 20% and the stimulation protocol was repeated. Diagnosis of the presence, involvement, and location of a concealed AP was made according to standard criteria including the delivery of single ventricular extrastimulation during tachycardia at the time the His bundle was refractory (1).

“Dual AV node physiology” was defined as a ≥50-ms increment in A2H2 value following a 10-ms decrement in the A1–A2 interval with single atrial extrastimulation (A1) administered during atrial pacing at a basic cycle length A1–A2 of 600 ms or a ≥50-ms increment in A–H value in consecutive beats following a ≤10-ms decrement in pacing cycle length during incremental atrial pacing (1,2).

Statistics. Data were expressed as mean ± SD. Statistical analysis was performed using the chi-square test. A value of p < 0.05 was considered statistically significant.

RESULTS

Patient characteristics. Thirty-four patients (Tel-Aviv Medical Center, n = 24; Sheba Medical Center, n = 10) with inducible AVRT underwent ATP test during sinus rhythm (Table 1). One patient (Patient 10) who did not reach a study end point with 40 mg ATP and who refused the administration of a higher dose was excluded from further analysis. The remaining 33 patients completed the ATP test and constituted the study group. There were 26 men and 7 women, aged 36.9 ± 17.1 years old. Thirty-two patients had sustained AVRT of the common type (RP < PR); in these patients, AVRT was inducible without isoproterenol. The remaining patient (Patient 6) had the long RP type of AVRT (RP > PR) that was inducible only during isoproterenol infusion. None of the study group patients had organic heart disease. The control group comprised 27 patients (13 women and 14 men, mean age 51 ± 18 years), none of whom had organic heart disease.

Results of ATP test in the study group. Occurrence of AVRE or AVRT. Of the 33 study group patients, 24 (73%) developed AVRE or AVRT following the administration of 10 to 30 (mean 18.3 ± 6.9) mg ATP (Table 1) (Figs. 1–4).

The doses of ATP required to demonstrate the presence of a concealed AP were 10, 20, and >20 mg in 10 (42%), 8 (33%), and 6 (25%) of the 24 patients. The remaining 9 (27%) patients developed transient second- or third-degree AV block, without AVRE or AVRT, following the administration of 10 mg to 40 mg (mean 17 ± 8) ATP.

A total of 52 AVREs (1 to 7 per patient, mean 2.5 ± 1.3) were observed in 21 (64%) of the 33 study patients (Figs. 1–3). Seven patients had 1 AVRE, 6 patients had 2 AVREs,
and the remaining 8 patients had 3 to 7 AVREs. The first AVRE occurred 10 to 23 s (mean 16 ± 3.5 s) following the ATP bolus. The first AVRE occurred following a slight increase (<50 ms) in PR interval between two consecutive beats in 13 patients associated with a slight increase, decrease, or no change in the preceding sinus cycle length in 4, 2, and 7 patients, respectively (Fig. 3). In six patients, the first AVRE occurred following a sudden increase (>50 ms) in PR interval in the patient with long RP tachycardia (Patient 6), the first AVRE followed no obvious change in the PR interval or the preceding sinus cycle length. Finally, in one patient (Patient 32), the first AVRE followed an atrial extrasystole occurring during stable sinus rhythm.

The AVRT (1 to 2 episodes) was observed following ATP administration in 10 (30%) of 33 study patients (Figs. 2 and 4). Seven of the 10 patients with AVRT also demonstrated ≥1 AVRE, which invariably occurred before AVRT (Fig. 2). AVRT was sustained in five patients and nonsustained in five. Also, AVRT occurred 10 to 45 s (19 ± 10 s) following the ATP bolus. Initiation of the first AVRT after ATP administration followed a slight (<50 ms) PR prolongation in five patients (during undisturbed sinus rhythm in three patients) or was triggered by atrial extrasystoles in three patients (Figs. 2 and 4). AVRT started during stable sinus rhythm without any measurable change in PR interval in the patient with long RP tachycardia (Patient 6). In the remaining patient (Patient 25), the mode of initiation of the AVRT could not be determined.

**OCCURRENCE OF DUAL AV NODE PHYSIOLOGY.** Electrocardiographic signs suggestive of dual AV node physiology following ATP test (2) were observed in seven (21%) of the
study patients (Figs. 1 and 2). Of these seven patients, six also exhibited AVRE (Patients 9, 11, 17, 19, 22, 34). In five of these patients, all instances of AVRE were preceded by dual AV node physiology; in the remaining patient (Patient 11) who exhibited three AVREs, only two of these echo beats followed the occurrence of dual AV node physiology (Fig. 1). None of the patients with dual AV node physiology exhibited AV nodal echo beats during ATP test.

ADVERSE EFFECTS. One patient (Patient 5) had an asymptomatic 4-s sinus pause with 10 mg ATP while reaching the study end point of second-degree AV block. Another patient (Patient 12) developed transient atrial fibrillation a few seconds after reaching the study end point of second-degree AV block. Besides the well-known mild and transient side effects related to ATP administration (flushing), no other significant adverse effects were observed.

ATP TEST AFTER RADIOFREQUENCY ABLATION. The radiofrequency ablation procedure was successful in 30 (91%) study patients and failed in 3 (Patients 23, 24, 31). In 8 patients (Patients 15, 17, 20, 26–28, 32, 34) who had AVRE or AVRT at baseline ATP test and underwent successful radiofrequency ablation of the AP, repeat ATP test using the same dose of ATP did not show AVRE or AVRT (Fig. 4). In one patient (Patient 33) who had AVRE at baseline ATP test, an AVRT involving a concealed left lateral AP was induced that had retrograde P waves with morphology and RP relationship (RP = 0.12 s) similar to that present during AVRE. After successful radiofrequency ablation of this pathway, repeat ATP test induced an atrial activity following a QRS complex (RP = 0.15 s) suspected to be either an atrial extrasystole or AVRE. This P wave was slightly different in morphology to that of the AVRE observed at baseline ATP test (more negative axis).

At repeat electrophysiologic study, a sustained AVRT was induced that involved another concealed AP located in the left posterior area about 2 cm from the first ablated pathway. The morphology of the AVRE and the RP relationship were identical to that of the retrograde P wave during AVRT. This AVRE was no longer observed following ATP after successful radiofrequency ablation of the posterior AP.

Results of ATP test in the control group. Of the 27 control patients, none exhibited AVRE, AVRT, or dual AV node physiology following the administration of 10 to 40 (mean 17 ± 9) mg ATP. In addition, none exhibited any atrial premature beat. All patients developed transient second- or third-degree AV block following ATP administration.

Electrophysiologic data. Electrophysiologic evidence of dual AV node physiology was observed in 9 (27%) of 33 study patients (Table 1). In three of these patients (Patients 1, 9, 34), two tachycardias with different rates could be documented during AVRT, reflecting antegrade AV conduction over either the slow or the fast pathway. Of these nine patients with electrophysiologic evidence of dual AV node physiology, seven (78%) exhibited ECG signs of dual

![Figure 1](image-url). Patient 11. Initiation of AV reentrant echo beats following the administration of 20 mg ATP during sinus rhythm in a patient with a concealed left free wall AP and electrophysiologic evidence of antegrade dual AV node physiology. Note that the first two echo beats follow a sudden jump in PR interval of 70 ms (dual AV node physiology) while the prolongation in PR interval preceding the third echo beat is of 40 ms only. Also note that the sinus cycle length preceding the first echo beat is regular at 710 ms.
AV node physiology by ATP test. None of the patients with electrophysiologic evidence of dual AV node physiology had inducible AV nodal echoes. Of the nine patients with dual AV nodal physiology at electrophysiologic study, seven (78%) had AVRE or AVRT at ATP test; of the 18 patients without dual AV nodal physiology, 13 (72%) had AVRE or AVRT at ATP test (p = NS).

The location of the APs in the study patients was as follows: left free wall in 19 patients, posteroseptal in 6 patients, right anteroseptal in 6 patients, and right free wall in 2 patients. Electrophysiologic evidence of dual AV node physiology was much more frequently observed in patients with left free wall APs (7 of 19; 39%) than in patients with non-left free wall APs (2 of 14; 14%) but the difference was not statistically significant (p > 0.1). The presence of AVRE or AVRT following ATP administration was observed in 11 (58%) of the 19 patients with left free wall pathways and in 13 of 14 (93%) patients with non-left free wall pathways (p < 0.05).

**DISCUSSION**

**Main findings.** In the present study, we found that the administration of ATP during sinus rhythm revealed signs suggestive of the presence of a concealed AP in a high percentage (73%) of patients with inducible sustained AVRT but in no patient from the control group. Thus, observation of AVRE or AVRT after ATP injection correlated with the induction of AVRT during electrophysiologic study with a sensitivity of 73%, a specificity of 100%, and a positive and negative predictive value of 100% and 100%, respectively. In addition, the administration of ATP during sinus rhythm enabled the diagnosis of associated dual AV node pathways in seven (21%) of the study patients but none of the control group subjects.

**Use of ATP in the diagnosis of concealed AP.** Administration of ATP during sinus rhythm has already been successfully used to establish the diagnosis of Wolff-Parkinson-White syndrome in patients with a minor degree of preexcitation and to assess the results of an ajmaline test (6). Our study is the first that shows that ATP can also be successfully used for the noninvasive diagnosis of a concealed AP in patients with PSVT. Similar observations were recently made by other investigators (7) using a fixed dose (12 mg) of adenosine at the completion of a diagnostic electrophysiologic study. In that study, AVRE were observed in 10 (80%) of 12 patients,
including 2 patients who subsequently developed AVRT. Interestingly, the incidence of AVRE/AVRT found in that study (80%) was similar to that found in our study (73%), despite the fact that the dose of adenosine used in the former study (12 mg) was equivalent to about 23 mg ATP (taking into account the different molecular weights of ATP and adenosine). Indeed, our study showed that doses of 10 mg ATP (equivalent to about 5.3 mg adenosine) were sufficient to reveal AVRE/AVRT in 42% of our patients. In theory, the use of high doses of adenosine or ATP could result in complete AV nodal block, preventing the initiation of AVRE.

**Mechanism of AVRE and AVRT during ATP test.** Our study gives further insight into the mechanism of occurrence of AVRE and AVRT during ATP test. A slight increase in PR interval associated with no change in preceding sinus cycle length represented the most frequent mechanism in patients without dual AV node physiology, whereas a marked jump in PR interval preceded the initiation of AVRE or AVRT in patients with dual AV node physiology. In the patient with long RP tachycardia, induction of AVRE and AVRT by ATP without significant change in PP and PR interval may be explained by either a small and unrecognized change in these parameters or a shortening of the retrograde atrial or accessory pathway refractory period. Finally, the occurrence during ATP test in four patients of AVRE or AVRT triggered by atrial extrasystoles emphasizes the importance in performing such testing prior to the placement of the catheters in the cardiac chambers so as to avoid catheter-induced extrasystoles.

**Dual AV node pathways and AVRT.** Dual AV node pathways were found in 8% to 40% of patients with APs undergoing electrophysiologic studies (8). The incidence of 9/33 (27%) patients observed in our study is consistent with the results contained in the literature. More importantly, we found that the administration of ATP at the dose that resulted in any of the study end points (AVRE or AVRT) allowed the noninvasive diagnosis of dual AV node physiology in seven (78%) of these nine patients.

Another interesting observation in our patients with dual AV node physiology is that none of them exhibited AV nodal echo beats, likely reflecting the lack of conduction in the retrograde fast pathway. It is tempting to speculate that the occurrence of AV nodal echo beats in any of these
patients would have prevented the occurrence of AVRE/AVRT and thereby the diagnosis of concealed AP.

**Study limitations.** The main goal of the present study was to assess the use of ATP in the diagnosis of concealed AP and secondarily to determine the incidence of dual AV node physiology in patients with AVRT. Therefore, one cannot exclude that the incidence of dual AV node physiology would have been even greater had higher doses of ATP been tested in those patients who developed AVRE or AVRT associated with a slight PR prolongation.

Although it is impossible to exclude that the first observed AVRE beats were in fact atrial premature beats, several findings in our study made this possibility unlikely: 1) in 19 of 21 patients, the first AVRE beats followed a slight (≤50 ms, n = 13) or marked (>50 ms, n = 6) prolongation of PR interval, suggesting that a critical AV nodal delay was required to allow the occurrence of these beats strongly supporting a AV reentrant mechanism; in only one patient was the first AVRE triggered by an atrial extrasystole; 2) by study design, the morphology of the P wave and its relationship with the preceding QRS complex were identical to that present during AVRT induced at electrophysiologic study; that would be a rather coincidental finding for a premature atrial beat; 3) no atrial premature beat occurred in the nine patients who had a repeat ATP test after radiofrequency ablation of their APs and exhibited AVRE beats at baseline ATP test; in the only patient (no. 33) in whom such event was suspected, subsequent electrophysiologic study suggested that this “atrial extrasystole” was likely an AVRE involving a second accessory pathway; and 4) no atrial ectopic beat was observed during ATP test in any of our 27 control group patients.

**Clinical implications.** Results of the present study show that the diagnosis of concealed AP can be suspected using the ATP test in 73% of patients with AVRT. In addition, the safety of the test suggests it could be used as a bedside test. Taking into account our previous results showing that the diagnosis of dual AV node physiology can be suspected by ATP test in 76% of patients with AVNRT (2), as well as the fact that AVNRT and AVRT together represent 85% of all cases of PSVT in patients without antegrade conducting AP (1), it is likely that ATP (or adenosine) testing could be helpful in the noninvasive diagnosis of the mechanism of PSVT in about two-thirds of patients with PSVT and no
ventricular preexcitation. Studies are being completed in our laboratories that evaluate the predictive accuracy of ATP test for identifying patients with palpitations or PSVT of unclear mechanism who are likely to benefit from invasive electrophysiologic evaluation. Further studies are required to assess the potential use of the ATP test in the noninvasive identification of other types of tachyarrhythmias, such as atrial fibrillation, taking into account the well-known fibrillatory effects of adenosine compounds at the atrial level (9).

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