Accuracy of Mode Switch Algorithms for Detection of Atrial Tachyarrhythmias

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Mode Switching in Atrial Tachyarrhythmias. ***Introduction:*** **In patients with permanent pacemakers, mode switching events often are interpreted as surrogate markers for atrial tachyarrhythmias. The aim of this study was to determine the accuracy of automatic mode switching algorithms in patients with permanent pacemakers for the diagnosis of atrial tachyarrhythmias.**

Methods and Results: **Forty patients with tachycardia-bradycardia syndrome and Medtronic Thera or Kappa 700 permanent pacemakers underwent Holter monitoring. Date, time of onset, and duration of each mode switch episode as recorded by the pacemaker and each atrial tachyarrhythmia episode as recorded by the Holter monitor were compared. Sixteen patients had a total of 54 atrial tachyarrhythmias documented on Holter monitoring (47 atrial fibrillation, 7 atrial flutter). Comparison of Holter data with pacemaker interrogation demonstrated that 53 (98.1%) of 54 atrial tachyarrhythmia episodes resulted in mode switching with one 13-second episode of mode switching during sinus rhythm. The sensitivity and specificity of mode switching for the duration of atrial tachyarrhythmias were 98.1% and 100%, respectively. The algorithms detected 98.9% of the total duration of atrial fibrillation and 96.4% of the total duration of atrial flutter.**

Conclusion: **In patients with tachycardia-bradycardia syndrome and permanent pacemakers having these mode switching algorithms, mode switching events are reliable surrogate markers for atrial tachyarrhythmias. Therefore, mode switching may serve as a valuable tool for clinical decision making and further research into the natural history and burden of atrial tachyarrhythmias.** *(J Cardiovasc Electrophysiol, Vol. 15, pp. 773-777, July 2004)*

atrial fibrillation, permanent pacemakers, mode switching, atrial arrhythmias

Introduction

Automatic mode switching (AMS) algorithms in permanent pacemakers (PPMs) were designed to prevent the tracking of supraventricular tachycardias or other rapidly occurring signals sensed by the atrial channel, thereby reducing the adverse hemodynamic and symptomatic consequences of a rapid ventricular response.[1] These programs also provide data on the time of onset and duration of AMS episodes. AMS events may be interpreted as a surrogate marker for paroxysms of atrial tachyarrhythmias (ATA), although few studies have evaluated the validity of the AMS algorithms via comparisons to simultaneous cardiac monitoring.

The prevalence and clinical importance of these AMS episodes have been described in recent studies. In patients with PPMs implanted for sinus and/or AV nodal disease, 55% developed AMS episodes over a mean follow-up period of approximately 2 years, and 98% of these patients had multiple episodes.[2] A substudy of a randomized controlled trial of atrial- versus ventricular-based pacing demonstrated that ATA episodes detected by these algorithms were associated with increased rates of death and nonfatal stroke.[3] Clinically, this information may theoretically be used to assess the need for, or efficacy of, antiarrhythmic interventions or the risk of thromboembolic events, and it may serve as a valuable research tool for evaluating the natural history and burden of ATAs, even in asymptomatic patients.

In view of the facts that AMS events are common, have clinical impact, and may be used in medical decision making and clinical research, it is imperative that these algorithms be highly accurate in the detection of ATA. The aim of this study was to measure the sensitivity and specificity of AMS algorithms for the detection of ATA.

Methods

A prospective study design was used to compare pacemaker AMS events with the recorded rhythm during continuous Holter monitoring. This protocol was approved by the Institutional Review Board, and informed consent was obtained in all patients. Eligible patients were those with known tachycardia-bradycardia syndrome implanted with Medtronic Kappa 700 or Thera DR dual-chambered PPM (Medtronic, Inc., Minneapolis, MN, USA) and P wave amplitudes $\geq$2.0 mV at the time of implant. All pacemakers were inserted using standard techniques and bipolar leads. Right atrial mapping was performed to achieve a pacing threshold $\leq$1.0 V at 0.5 ms and sensing thresholds $\geq$2.0 mV whenever possible. The right atrial appendage was the preferred site of

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implant when feasible. Real-time intracardiac electrograms were evaluated at each site to evaluate for far-field R wave sensing, and pacing at maximum output was performed in all patients to evaluate for phrenic nerve stimulation. The lower rate limit was set at 60 beats/min on all devices. Atrial sensitivity was programmed ≥4 times threshold value in the bipolar mode, and AMS was programmed "on" at nominal settings (175 beats/min). Blanketed flutter search was activated in all patients.

Holter monitoring for 24 to 48 hours was performed at 2-week intervals, and the fully disclosed tracings were manually examined for the date, time of onset, duration, and type of ATA. AMS counters were cleared prior to the start of each Holter monitoring period, and pacemaker interrogation was performed at the end of each monitoring period. The pacemaker and Holter monitor clocks were synchronized to within 5 minutes of one another. Date, time of onset, and duration of each AMS episode were recorded. The time of onset and duration of ATA as recorded by the PPM and Holter were compared. For the purposes of this study, ATA was defined as any supraventricular rhythm on Holter monitor with an atrial rate ≥175 beats/min for ≥4 beats. Mode switching was defined as the occurrence of an AMS event as recorded by the PPM. An AMS event was defined as appropriate if it occurred at the time of an ATA recorded on Holter monitor and inappropriate if it occurred during normal sinus rhythm. Sensitivity of AMS for ATA episodes was defined as the percent of ATA duration for which AMS occurred appropriately. Specificity of AMS for ATA episodes was defined as the duration of normal sinus rhythm for which AMS did not occur.

The Medtronic Kappa 700 AMS algorithm mode switches the pacing mode to DDIR if 4 of the last 7 atrial intervals are less than the programmable mode switch interval or if a blanked flutter search detects a short A-A interval.[4] The blanked flutter search algorithm searches for eight consecutive A-A intervals that measure less than twice the total functional atrial blanking period (AV interval + postventricular atrial blanking period) and <2 times the detect rate interval. If these criteria are met, the postventricular atrial refractory period will be extended for one beat and the device scans for an A-A interval less than the detect rate interval. If this occurs, then the device performs AMS instantly. AV resynchronization occurs when the last seven atrial intervals are below the upper tracking rate or when five consecutive atrial paced events occur.

The Medtronic Thera DR mode switches to DDIR when a mean atrial interval shortens to a programmable value. The algorithm calculates a running mean atrial interval from the atrial electrogram and, if the current atrial interval is less than or equal to the mean atrial interval, the mean atrial interval is shortened by 23 ms. If the current atrial interval is greater than mean atrial interval, then the mean atrial interval is increased by 8 ms. Mode switching occurs when the mean atrial interval is less than the ATA detection rate interval.[5] AV resynchronization to 1:1 atrial tracking resumes when the mean atrial interval becomes longer than the programmed upper rate interval or when five consecutive atrial paced events occur.

Data Analysis

All statistical analyses were performed using SPSS 11.5 (SPSS Corp., Chicago, IL, USA). The mean and standard deviations for continuous variables were calculated and expressed in appropriate units. Two-tailed Student's *t*-tests were performed on normally distributed variables dichotomized on the presence or absence of ATA and model pacemaker. If the normal distribution was not approximated, the Mann-Whitney *U*-test was used. Correlation coefficient for ATA duration was derived from the plot of the duration of ATA as measured by Holter monitor versus PPM. $P \leq 0.05$ was considered statistically significant for all comparisons. Sensitivity of the AMS algorithm was calculated by dividing the number of ATA minutes for which appropriate mode switching occurred by the total number of ATA minutes on Holter monitor. Specificity of the AMS algorithm was calculated by dividing the number of minutes in appropriate DDD mode by the total number of minutes in normal sinus rhythm as recorded by Holter monitor.

Results

Forty patients with a history of tachycardia-bradycardia syndrome and PPM received Holter monitors for a combined total duration of 2392 hours for an average of 59.8 hours (range 21–186) of monitoring per patient. The clinical characteristics of these patients are detailed in Table 1. Mean patient age was 72.2 ± 10.9 years. Kappa and Thera generators were implanted in 32 and 8 patients, respectively. Twelve of the 40 patients were taking antiarrhythmic agents, including 6 taking amiodarone and 6 taking sotalol. Mean P wave amplitude at the time of enrollment was 3.6 ± 1.9 mV, and mean programmed atrial sensitivity was 0.47 ± 0.13 mV. Mean bipole (tip to ring) spacing was 14.2 ± 3.9 mm. P wave amplitude at enrollment and programmed atrial sensitivities were similar between Thera and Kappa devices (3.5 ± 2.4 mV vs 3.6 ± 1.8 mV, $P = 0.87$; 0.40 ± 0.15 mV vs 0.49 ± 0.12 mV, $P = 0.09$, respectively). On average per 24 hours, there were 458 atrial premature beats and 33 atrial couplets.

Sixteen patients had a total of 54 ATA episodes (47 atrial fibrillation, 7 atrial flutter) as documented on Holter monitor. Of the ATA events, 18 occurred in 4 patients with Thera pacemakers and 36 occurred in 10 patients with Kappa devices. The 16 patients had from 1 to 16 episodes of ATA lasting from 5 seconds to 48 hours (average 4.89 hours). There was no significant difference in age, sensing thresholds, programmed sensitivities, or lead characteristics between patients with and those without documented ATA on Holter monitor (Table 2). Comparison of Holter data with PPM interrogation demonstrated that 53 (98.1%) of the 54 ATA episodes resulted in AMS (Fig. 1). The sensitivity and specificity of AMS for the duration of ATA episodes were 98.1% (95% confidence interval: 95.4%–100%) and 100% (95% confidence interval

TABLE 1
Characteristics of Study Patients

Variable	
Total no. of patients	40
Age (years)	72.2 ± 10.8
Gender (male)	25
Atrial sensitivity setting (mV)	0.47 ± 0.13
P wave at enrollment (mV)	3.6 ± 1.9
Postventricular atrial blanking period (ms)	180.7 ± 13.1
Postventricular atrial refractory period (ms)	Thera: 310 Kappa (auto): 250
Holter monitoring (hours/patient)	59.8
No. of atrial tachyarrhythmias episodes	54

Values are given as mean ± SD.

TABLE 2

Comparison of Patients With and Without Atrial Tachyarrhythmias During Holter Monitoring

Variable	+ATA	–ATA	P Value
Age (years)	73.6 ± 9.9	71.3 ± 11.5	0.53
P wave amplitude (mV)	3.3 ± 2.0	3.8 ± 1.8	0.42
Atrial sensitivity setting (mV)	0.46 ± 0.18	0.47 ± 0.08	0.82
Lead tip to ring spacing (mm)	14.7 ± 3.8	13.9 ± 4.0	0.51

ATA = atrial tachyarrhythmias.

99.5%–100%), respectively, for the combination of devices. The Pearson correlation coefficient for comparison of the duration of ATA by Holter versus PPM was 0.999 ($P < 0.01$; Fig. 2). The devices detected 98.9% of the total duration of atrial fibrillation episodes and 96.4% of the total duration of atrial flutter. For the Thera devices, the sensitivity was 100% and the specificity was 100% for the total duration of ATA. For the Kappa devices, the sensitivity was 96.7% and the specificity was 100% for the total duration of ATA.

Seven episodes of atrial flutter occurred in four patients, three of whom had Kappa 700 devices. One patient with a Thera DR had total failure to mode switch during a 113-second episode of atrial flutter, presumably due to failure to sense flutter waves falling within the postventricular blanking period and absence of a blanked flutter search algorithm in this model device. In the three patients with Kappa pacemakers, multiple inappropriate mode oscillations occurred as the AMS algorithm fluctuated between DDI and DDD pacing modes despite the persistence of prolonged episodes of atrial flutter. This was the result of undersensing of atrial flutter waves and was corrected by decreasing the atrial blanking period from 180 to 150 ms in all cases. The other three episodes of atrial flutter resulted in normal AMS activity. There was one 13-second episode of inappropriate AMS during AVF pacing in a patient with a Kappa generator. Intrinsic P waves were 3.5 mV, and the programmed atrial sensitivity was 0.5 mV. High-frequency electromagnetic interference is present on the Holter monitor during the time of inappropriate mode switching. Follow-up of this patient for 18 months since the time of implant has not shown any further episodes of mode switching.

Discussion

In early generations of dual-chamber pacemakers without AMS algorithms, paroxysmal ATAs were considered a contraindication to pacing modes with atrial tracking due to concerns of rapid ventricular tracking of atrial arrhythmias. The current models of dual-chamber pacemakers incorporate various AMS algorithms. When no ATA is present, dual-chamber pacing provides the patient with the benefits of DDD pacing. During an ATA, however, mode switching automatically changes the pacing mode to one without atrial tracking, thereby avoiding rapid pacing during the atrial arrhythmia. This feature has been shown to provide subjective improvement when compared to non-AMS devices.[6]

Performance of AMS is dependent on the accurate detection of ATA, which is related to the rate of the detected atrial arrhythmia compared to the programmed AMS rate, the length of the atrial blanking and refractory periods, and the programmed atrial sensitivity. Decreased sensitivity can

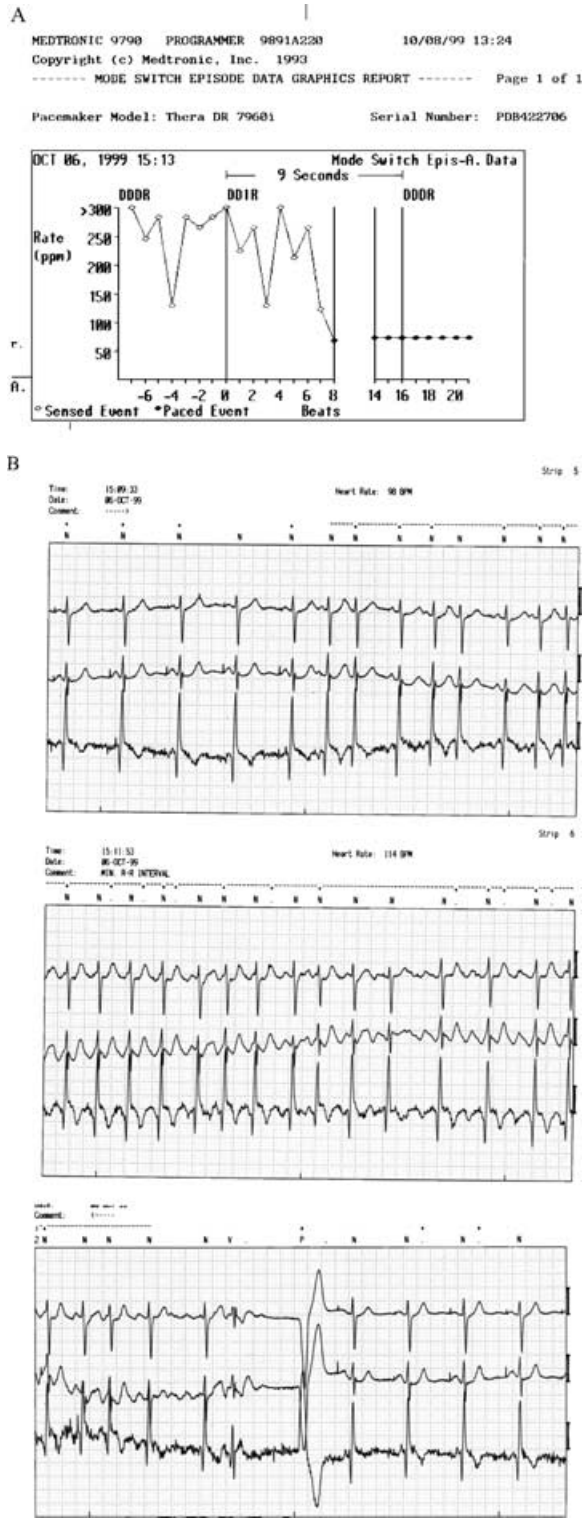

Figure 1. *Example of a mode switching event occurring on both a Thera DR pacemaker and simultaneous Holter monitor. The device was programmed in DDDR mode at a base rate of 60 beats/min and a programmed atrial sensitivity of 0.35 mV. A: Seven sensed tachycardic atrial complexes followed by a 9-second AMS episode. Mode switching to DDIR occurs, followed by a return to DDDR mode after consecutive paced events. B: Episode as recorded on Holter monitor. Top panel: Normal sinus rhythm with premature atrial depolarizations occurring at the end of the strip. Middle panel: Atrial fibrillation occurs with no evidence of atrial tracking, consistent with the mode switch to DDIR. Bottom panel: After approximately 9 seconds of atrial fibrillation, spontaneous cardioversion occurs followed by atrial pacing.*

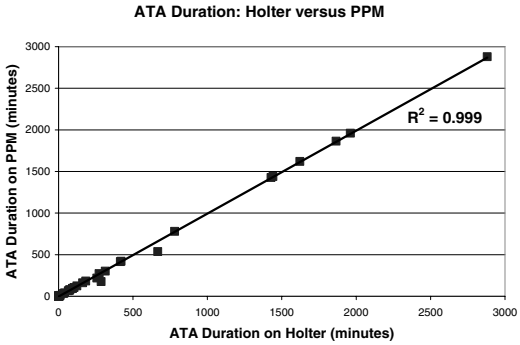

Figure 2. *Correlation of atrial tachyarrhythmia duration as recorded by Holter versus pacemaker.*

occur due to atrial fibrillation with a small or varying signal amplitudes, slower atrial tachycardias, or blanked P waves during atrial flutter. Prior reports observed a P wave amplitude during atrial fibrillation of approximately 65% of that measured during normal sinus rhythm.[7,8] Although a loss in sensitivity may be overcome by increasing the atrial sensitivity (improving the ability to detect low amplitude P waves), this can potentially result in a loss of specificity due to oversensing of noise, far-field R waves, or myopotentials. Therefore, some authors have recommended that atrial sensitivity be programmed at a 3.0- to 3.5-fold safety margin to optimize atrial sensitivity after implantation.[9,10] False-positive AMS events are most often due to far-field R wave oversensing by the atrial channel, which is more likely to occur with atrial unipolar sensing, ventricular pacing, long bipole spacing, and septal or low right atrial implants.[4] Finally, lowering the atrial detection rate will raise the sensitivity while decreasing the specificity, possibly mode switching for sinus tachycardia.

Prior reports on the sensitivity and specificity of AMS algorithms have varied widely. One prior attempt to evaluate the same devices used in the current study used digitally recorded electrograms played from a digital audio tape recorder into the atrial lead input for the device. Sensitivity of AMS for paroxysmal atrial fibrillation was 85% for the Thera and 94% for the Kappa. Failure to mode switch resulted from undersensing of atrial electrograms in each instance.[11] The manner in which atrial electrograms were digitally stored and inputted into the devices may have resulted in the lower sensitivities seen in this study compared to our own. Leung et al.[10] used a similar approach of inputting stored electrograms to the Thera DR. An exponential increase in undersensing of atrial fibrillation was noted when atrial sensitivity was set >1 mV. Oversensing of noise resulted in inappropriate mode switching or reversion to a noise response mode in 37.5% of episodes for Thera DR when the atrial sensitivity was programmed at 1.0 mV. In contrast, a false-positive rate of only 2.9% was noted using the same model when specificity was assessed using the high rate atrial graphic reports available on device interrogation.[12] These different results could be due in part to the methods used in the referenced study, which may have introduced nonclinical laboratory conditions that might not reflect the behavior of implanted devices.

Three similar reports have compared Holter monitoring to results from Thera mode switch algorithms. Two prior studies of 37 total patients found that all events were detected and that no inappropriate AMS occurred, corroborating the results of the present study.[9,13] Another study involving 45 patients found 12 false-positive events (11.6 of a total of 720 hours) all due to far-field R and T wave oversensing. Furthermore, 32 of 125 events were not detected, mostly due to the programmed parameters, which required 40 beats of tachycardia to initiate mode switching, but also from atrial undersensing and blanked flutter waves.[14]

There also have been several reports evaluating atrial high rate episodes that are used in some PPMs to decide whether or not to mode switch. Pollak et al.[15] studied atrial high rate episodes in 56 patients with Medtronic PPM with electrogram storage capability. The investigators showed that atrial high rate episodes that were >250 complexes per minute and lasted >5 minutes were confirmed to be true ATA by the stored electrograms in 15 (88%) of 17 episodes, although specificity decreased when the programmed atrial sensitivity was increased. A substudy of the Mode Selection Trial (MOST) compared ambulatory monitoring with PPM atrial high rate episode data in 47 patients.[3] Several different PPMs were used, but the atrial high rate detection criteria were all set similar as determined by Pollak et al. Five patients had ATA seen on both PPM and ambulatory monitoring; 41 had no arrhythmias with either recording; and 1 patient had a false-positive atrial high rate episode. This gave a sensitivity of 100% and specificity of 97.6%, which is similar to our study even though the investigators used stricter criteria for atrial high rate episodes.

Finally, studies using stored electrograms alone are limited by the quality of stored data, which often are not sufficient enough to correctly identify the rhythm in many cases. Sensitivity and specificity cannot be assessed using this methodology either, as there is no standard for comparison.

Atrial tachycardia and atrial flutter may present unique difficulties to the AMS algorithm, as a proportion of the atrial electrograms seen during these arrhythmias may fall within the atrial blanking period and therefore be undersensed. One of our patients with frequent mode oscillations had atrial flutter with a cycle length of 270 ms. Flutter wave undersensing was resolved by decreasing the postventricular atrial blanking period from 180 to 150 ms. A second patient with atrial flutter was completely missed by the Thera algorithm. Similar difficulties with mode switching in patients with slow atrial flutter cycle lengths from antiarrhythmic medications have been reported.[16] Another report describes a patient in whom the Kappa's blanked flutter search algorithm failed to detect atrial flutter when the formerly blanked flutter wave spontaneously conducted to the ventricles, thus causing the next flutter wave to fall in the postventricular atrial blanking period.[17]

Study Limitations

The conclusions of this study are limited by several factors. Although >2,000 hours of Holter data were evaluated, the number of ATA events was relatively small and reflects the intermittent nature of the disease. In addition, the majority of ATA events were atrial fibrillation, whereas atrial flutter may pose a greater challenge for the AMS algorithms. Although the devices detected a high proportion of the total duration of atrial flutter, 57% of the atrial flutter episodes were either partially or entirely undersensed by the PPM. It is possible that a greater proportion of atrial tachycardia/atrial flutter episodes could negatively impact on the sensitivity of the algorithm. Furthermore, the sensitivity and specificity

observed in this study may not apply to patients with higher programmed atrial sensitivities as may be required with P waves <2.0 mV. Finally, AMS algorithms vary according to manufacturer and model, and the results of this study may not apply to other devices or to all patients with tachycardia-bradycardia syndrome.

Clinical Implications

The present study demonstrated a high sensitivity and specificity of the Thera DR and Kappa 700 AMS algorithms for ATA with the use of bipolar leads and atrial sensitivity set at values at least four times sensing threshold and at nominal mode switching settings. In patients with tachycardia-bradycardia syndrome and PPM having these mode switching algorithms, AMS events are reliable surrogate markers for ATA.

Current practice guidelines for atrial fibrillation and atrial flutter include discontinuation of anticoagulation once normal sinus rhythm has been maintained for >4 weeks.[18,19] Recent studies indicate, however, that this practice may be associated with an increased risk of thromboembolic events, possibly as a result of recurrent paroxysms of ATAs despite antiarrhythmic therapy.[20,21] Complicating medical decision making are the facts that a large portion of ATAs are asymptomatic and that antiarrhythmic therapy may convert many symptomatic episodes to asymptomatic ones.[22–24] These reports support the importance of continuous and accurate monitoring in select patient populations.

The extremely high sensitivity and specificity of mode switching for ATA demonstrate that these events may be used clinically for assessing the need for anticoagulation and/or the necessity or efficacy of antiarrhythmic therapy. Furthermore, AMS events may serve as a valuable tool for further research into the natural history and burden of ATAs, even in asymptomatic patients.

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