Circadian occurrence of symptomatic paroxysmal supraventricular tachycardia in untreated patients

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ABSTRACT Fifty-two patients with paroxysmal supraventricular tachycardia were studied to determine whether there was a circadian pattern to the occurrence of this arrhythmia. Antiarrhythmic therapy was discontinued, and patients were followed until they had one recurrence of tachycardia documented by telephone transmission of the electrocardiogram. By least-squares analysis, the times of day that the 52 attacks (one from each patient) occurred were fit to a sinusoidal density function with a period of 24 hr. The highest relative incidence of tachycardia was at 4 P.M.; tachycardia was five times more likely to occur at 4 P.M. than at 4 A.M., the time of the lowest relative incidence. A second attack of tachycardia was recorded from 35 of the 52 patients. The times of the two attacks in individual patients were found to be independent; thus the times of day at which the second attacks occurred were used as a test set for the distribution estimated from the first. The empirical distribution for the times from the 35 second attacks was compared with the distribution function estimated from the 52 first attacks, and there was no significant departure; this finding confirmed the circadian pattern. Since the relative incidence of attacks of paroxysmal supraventricular tachycardia is higher in the afternoon, it may be helpful to target antiarrhythmic therapy to that time of day.


PAROXYSMAL supraventricular tachycardia occurs sporadically in affected patients. Several recent studies have shown that other cardiac events such as nonfatal myocardial infarction, silent myocardial ischemia, and sudden cardiac death demonstrate a circadian distribution in their occurrence.1–3 The purpose of the current study was to determine whether the occurrence of paroxysmal supraventricular tachycardia also demonstrates a circadian distribution.

Methods

Patients. The study population consisted of 52 consecutively referred patients (31 men and 21 women; mean age 46.2 ± 15.7 years) with a history of paroxysmal supraventricular tachycardia defined by the following electrocardiographic criteria: (1) ventricular rate greater than 120 beats/min, (2) QRS morphology that was normal, functional right bundle branch block, or functional left bundle branch block, (3) less than 0.02 sec variation in successive RR intervals, (4) no evidence of atrioventricular dissociation, and (5) episodic occurrence. The term “tachycardia” in the remainder of this manuscript describes this arrhythmia unless specified otherwise. Most tachycardias meeting this description in our hospital are caused by atrioventricular reentry (with conduction in the antegrade direction over the atrioventricular node and conduction in the retrograde direction over an accessory pathway) or by reentry within the atrioventricular node. None of the patients had any “trigger” activity by which he or she could predictably initiate tachycardia.

Protocol. We followed these patients with an aggressive protocol that included biweekly telephone contacts and regular clinic visits.4 Spontaneous, symptomatic tachycardia was documented by telephone transmission of the electrocardiogram. Electrocardiographic rhythm strips were received by a 24 hr toll-free telephone answering device located in our laboratory. The recorder was checked daily, and patients were always contacted within 24 hr of transmitting an arrhythmia to determine the times at which symptoms began and ended. This information and the electrocardiograms were stored permanently in laboratory logs books.

We collected data for our present study from 52 patients who were being followed while taking no antiarrhythmic drugs until they had a recurrence of their tachycardia. The time of the occurrence of the tachycardia was categorized into 2 hr intervals based on a 24 hr clock. By least-squares analysis, the times of day that tachycardia occurred (one attack from each patient) were fitted to a sinusoidal density function with a period of 24 hr:

\[
f(t) = \beta_o + \alpha \sin \left(2\pi t/24 + \theta\right), \quad 0 \leq t < 24, \quad \text{or equivalently,}
\]

\[
f(t) = \beta_o + \beta_1 \sin \left(2\pi t/24\right) + \beta_2 \cos \left(2\pi t/24\right), \quad 0 \leq t < 24
\]

Thirty-five of the 52 patients had another episode of tachycardia documented during a second drug-free observation period. The independence of the two times of occurrence from
each of the 35 patients was examined with the test proposed by Blum et al.5, 6 After independence of the two times was verified, the empirical distribution for the time of the second episode was compared with the estimated distribution function calculated from the 52 first episodes; goodness-of-fit was tested with the Kolmogorov statistic.7

To assess the effect of time of day on heart rate during tachycardia, we compared the distributions of heart rate among four subgroups of patients determined by the 6 hr intervals (centered at 4 A.M., 10 A.M., 4 P.M., and 10 P.M.) in which the attacks of tachycardia occurred. The four heart rate distributions were compared by the Kruskal-Wallis test.7

Results

The estimated sinusoidal density function showed that the maximum incidence of tachycardia was at 4 P.M., with a corresponding minimum incidence at 4 A.M. (figure 1). Patients were five times as likely to have tachycardia in the afternoon as in the morning. Because of the limited number of observations (one time from each of 52 patients), we restricted the mathematical model to a single sinusoid with a period of 24 hr. The estimated density function was:

\[ f(t) = 0.0417 - 0.0242 \sin \left(\frac{2\pi t}{24}\right) - 0.0159 \cos \left(\frac{2\pi t}{24}\right), \quad 0 \leq t < 24 \]

In the 35 patients who had a second episode of tachycardia recorded, the test of independence of the times of the two occurrences was insignificant (p > .50), justifying the use of the second attack times as a test set for the estimated distribution of the first. The empirical distribution for the times from the second attack were compared with the estimated distribution for the 52 first attacks, and there was no significant departure (Kolmogorov test statistic = 0.16, p > .20) (figure 2).

The patients were classified into one of four groups depending on the time at which their attack occurred: 1 A.M. to 7 A.M. (n = 6), 7 A.M. to 1 P.M. (n = 13), 1 P.M. to 7 P.M. (n = 19), and 7 P.M. to 1 A.M. (n = 11). (Heart rate during tachycardia was not available for three of the 52 patients). The median heart rates during these four intervals were 198, 189, 195, and 193 beats/min, respectively; the Kruskal-Wallis statistic was insignificant (p > .80).

Discussion

Our data regarding time of day that paroxysmal supraventricular tachycardia occurred in patients receiving no antiarrhythmic drug showed that there was a circadian pattern to this arrhythmia. The peak incidence of tachycardia was found at 4 P.M., with a corresponding minimum incidence at 4 A.M.; patients were five times more likely to have tachycardia in the afternoon than in the morning (figure 1). Because of the relatively small number of observations, we limited ourselves to examining the first harmonic of the curve; we did not attempt to identify secondary peaks and troughs in the relative incidence. However, the same basic circadian pattern was observed for a second episode of tachycardia recorded from 35 of the patients.

The time of the second episode of tachycardia was independent of the time of the first episode. Establishing this independence was methodologically important because we were therefore able to use the times from the second episode as a "test set" for the estimated distribution function calculated from the times of the first. When we did this comparison, we found that there was no significant departure between

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**FIGURE 1.** Relative frequency histogram for the occurrence of paroxysmal supraventricular tachycardia during the day. The estimated density function is shown by the smooth curve.

**FIGURE 2.** Estimated distribution function for the first attack of tachycardia (smooth curve) and empirical distribution for the second episode (step function). The empirical distribution did not depart significantly (p > .20) from the hypothesized distribution.
the observed times of the second episode and the estimated distribution function for the first (figure 2). This independence also is clinically important for understanding the behavior of these arrhythmias. It has been suggested that many patients usually have their attacks at the same time of day or night and that antiarrhythmic therapy could be tailored to this individual pattern.<sup>9</sup> We could not confirm this suggestion; our patients did not indicate any tendency to have their attacks of tachycardia at the same time of day on both occasions, excepting the tendency for attacks to occur in the afternoon in all patients.

A likely explanation for the observed circadian rhythm is fluctuations in autonomic tone. Waxman et al.<sup>9, 10</sup> showed that initiating and maintaining a reentrant supraventricular tachycardia was critically dependent on atrioventricular nodal conduction time, which was modulated by the autonomic nervous system. Increased autonomic tone, which slows atrioventricular nodal conduction velocity and sinus rate, appears to be highest at night. Cinca et al.<sup>11</sup> reported that the effective refractory period of the atrioventricular node was significantly longer at night (between midnight and 7:00 A.M.) than during the day (between 7:00 A.M. and midnight). Atrioventricular nodal conduction time (measured as the AH interval) and the functional refractory period of the atrioventricular node also were longer at night, but the increases were not significantly different.

Sinus rate is also modulated by autonomic tone. In a recent study done with ambulatory electrocardiography, sinus rate showed a circadian rhythm identical to the one that we found for paroxysmal supraventricular tachycardia.<sup>12</sup> In that study of 80 elderly subjects, the slowest heart rates were found at 4 A.M. and the fastest rates were found at 4 P.M. These peaks and troughs were identical to the peaks and troughs in relative incidence of tachycardia found in our patients (figure 1).

Studies examining the circadian occurrence of angina, silent ischemia, and myocardial infarction found a different circadian distribution; the peak incidence for occurrence of these clinical syndromes was 9 A.M.<sup>1–3</sup> Although the reasons for this distribution probably are multiple, sympathetic tone may be important in the genesis of these ischemic events. For example, a study by Muller et al.<sup>1</sup> showed that treatment with β-adrenergic receptor–blocking drugs abolished the circadian pattern in patients with myocardial infarction.

The increased likelihood of paroxysmal supraventricular tachycardia occurring during the day raises the question of whether antiarrhythmic drug therapy for this arrhythmia should be concentrated in the daytime hours. If tachycardia is less likely to occur at night, relatively lower plasma concentrations of antiarrhythmic drugs may be effective at night. In fact, Pritchett et al.<sup>4, 13</sup> have previously examined the occurrence of this tachycardia in patients who were taking a calcium-channel blocker four times daily for long-term antiarrhythmic therapy; in these patients, recurrences of tachycardia were recorded during the daytime but not at night. However, plasma drug concentrations were not measured, and the reports involved only a few patients. Although results of the current study show a clear circadian rhythm to the occurrence of this tachycardia in untreated patients, the problem of timing antiarrhythmic therapy needs further exploration.

References

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