Rate Smoothing with Cardiac Pacing for Preventing Torsade de Pointes

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Cardiac pacing remains one of the most effective means for preventing torsade de pointes in patients with long QT syndrome (LQTS). However, fatal arrhythmias may occur despite combined therapy with β blockers and pacing, and it is possible that failure of cardiac pacing for preventing arrhythmias in the long run is related (at least in part) to suboptimal pacemaker programming. Preventing sudden pauses may be especially important for preventing arrhythmias in the LQTS because such pauses are highly proarrhythmic in this patient population. Unfortunately, properly functioning pacemakers cannot be expected to prevent postextrasystolic pauses. The use of a pause-prevention pacing algorithm—rate smoothing—for preventing pause-dependent torsade de pointes is described in 12 patients with cardiac arrest or syncope due to congenital LQTS who were followed for 21 ± 11 months. ©2000 by Excerpta Medica, Inc.

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THE IMPORTANCE OF PAUSES AS TRIGGERS OF TORSADE DE POINTES

Based on the mode of arrhythmia precipitation, 2 types of torsade de pointes are identified: pause-dependent and adrenergic-dependent arrhythmias. In pause-dependent torsade de pointes, a relatively long cycle (that is, a pause) invariably precedes the ventricular arrhythmia (Figure 1). The pauses that precipitate torsade de pointes may be due to sinus arrhythmia or sinus arrest. More commonly, however, these pauses are “postextrasystolic pauses” (Figure 1).9 Two observations further emphasize the proarrhythmic role of pauses in the LQTS: (1) Bizarre QT changes (including QT prolongation and U-wave augmentation) generally become evident in the sinus complex that follows a pause (Figure 1); these changes in the contour of the QT interval of the postextrasystolic beat are the electrocardiographic representation of enhanced early afterdepolarizations, the actual triggers of torsade de pointes; (2) longer pauses are generally followed by longer runs of torsade de pointes (apparently because the sudden increment in cycle length increases the dispersion of repolarization—facilitating reentry).15 In contrast to pause-dependent arrhythmias, adrenergic-dependent torsade de pointes often follows sinus tachycardia, generally during stressful circumstances. T-wave alternans usually precedes these ventricular arrhythmias. Heart rate acceleration and sympathetic stimulation apparently play a proarrhythmic role by shortening repolarization to a lesser degree in some cardiac zones than in others, increasing the dispersion of repolarization.16

It has long been recognized that torsade de pointes in the acquired LQTS is almost invariably pause dependent.5,8,17 However, some controversy exists about the importance of pauses in the genesis of arrhythmias in the congenital LQTS. Because of the long-recognized association between “stress” and symptomatic arrhythmias in the congenital LQTS, arrhythmias in the congenital LQTS have generally been referred to as “adrenergic dependent.”10,19 However, we have presented data suggesting that the majority of arrhythmias in the congenital LQTS—including those related to stress—are also pause dependent. First, we reported that in 14 of 15 consecutive patients with congenital LQTS and documented arrhythmia, the onset of torsade de pointes was always pause dependent.9 More recently, we analyzed the mode of onset of torsade de pointes in illustrations published by others.20 From 62 episodes of torsade de pointes, 75% were preceded by pauses. Using multivariate analysis, age was the only independent predictor of the mode of
onset of torsade de pointes. Arrhythmias in infants (≤3 years old) were almost never pause dependent, whereas arrhythmias in adults, especially female, were generally pause dependent.20

**IMPORTANCE OF PAUSE-PREVENTION PACING ALGORITHMS**

In 3 of 4 episodes of pause-dependent torsade de pointes, the pause triggering the arrhythmia is a postextrasystolic pause.9,20,22 Typically, an extrasystole (short cycle) generates a compensatory pause (long cycle), which, in turn, is followed by a postextrasystolic complex with bizarre QT changes, from which more arrhythmias originate (short–long proarrhythmic sequence). A critical role of pacing may be to prevent, or at least shorten, the postextrasystolic pauses that facilitate the onset of torsade de pointes. Unfortunately, a normally functioning pacemaker cannot be expected to prevent the postextrasystolic pauses that follow spontaneous extrasystoles (Figure 2). Therefore, unique device programming—or algorithms available in certain pacemakers, as discussed below—are required to effectively prevent the proarrhythmic pauses. One way of achieving this goal is to increase the lower rate limit. Pacing faster will shorten postextrasystolic pauses, potentially reducing the risk of pause-induced torsade de pointes. However, rapid pacing for long periods may eventually be detrimental to the left ventricle.23 Unfortunately, the maximal pacing rate that can be used safely in the long run (without risking iatrogenic tachycardia-induced cardiomyopathy) is not known.23

An alternative method for preventing torsade de pointes is the use of pause-prevention algorithms. Rate smoothing is a pacing algorithm available in the Vigor and other Guidant-CPI pacemakers and defibrillators (St. Paul, MN). It was originally recommended for preventing palpitations in patients in need of pacing, but we use this algorithm for preventing pause-dependent arrhythmias.21,24

When rate smoothing is programmed “on,” each R-R interval (whether sensed or paced) is used as reference value, and the next R-R interval cannot vary by more than the programmed percentage from the reference. “Rate smoothing down” and “rate smoothing up,” which are programmed independently, dictate the maximal increment, and the maximal decrement possible in successive R-R intervals, respectively (Figure 2). For patients with LQTS, we program rate smoothing up “off” and rate smoothing down “on.” The value most commonly used for rate smoothing down is 15%. This dictates that successive R-R intervals cannot increase by more than 15%. Thus, whenever an extrasystole creates a short cycle, pacing at a relatively fast rate for a few beats follows, with the pacing rate gradually decreasing (by 15%) until the lower rate limit is reached or a spontaneous rhythm ensues (Figures 2 and 3).

So far, we have treated 12 patients with LQTS (aged 38 ± 22 years) with a pacemaker (Guidant, Vigor, 6 patients) or implantable cardioverter defibrillator (ICD) (Guidant, dual-chamber Ventak AV series, 6 patients) with rate-smoothing capabilities. Implantation followed cardiac arrest (in 7 patients) or syncope with documented torsade de pointes (in 5 patients). Implantation followed failure of β-blocker therapy in all patients and failure of β blockers and ventricular pacing in 1 patient. The last patient experienced 8 appropriate ICD shocks for documented pause-dependent torsade de pointes that deteriorated to ventricular fibrillation, before the use of rate smoothing.

Rate-smoothing-down values of 9–20% were used and β-blocker therapy was continued in all patients. After 21 ± 11 months of follow-up, all patients (except 1, who died from cancer) are alive. Two patients had recurrent arrhythmias: 1 patient with an implanted pacemaker had 1 episode of syncope (without documented arrhythmia) when she stopped taking her β blockers against medical advice. Another patient with an ICD had pause-dependent torsade de pointes when rate smoothing was temporarily turned off. The patient who had previously experienced multiple appropriate ICD shocks despite ventricular pacing, remained free of arrhythmias after she underwent implantation of dual-chamber pacing with rate smoothing. In all, 3 patients complained of palpitations. The latter were ascribed to the relatively fast pacing triggered by extrasystoles or to nonreentry persistent ventriculoatrial synchrony. However, re-

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**TABLE 1** Recommended Device Programming for the Prevention of Torsade de Pointes with Cardiac Pacing in the Long QT Syndromes *

<table>
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<th>Recommended parameters</th>
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<tr>
<td>• Program a relatively fast lower rate limit</td>
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<tr>
<td>• Program off all features that allow heart rate slowing below the lower rate limit (eg, sleep function, hysteresis)</td>
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<tr>
<td>• Avoid pauses by preventing oversensing. Also, program off all features that may lead to sudden increments in pacing cycle length (eg, hysteresis search, automatic PVARP extension)</td>
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<tr>
<td>• Prevent pauses (like postextrasystolic pauses or pauses related to sinus arrhythmia above the lower rate limit) with rate smoothing down (9%–18%)§</td>
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</table>

*Detailed discussion of the rationale for these recommendations appears elsewhere.1

1Pacing rates of ≥70 beats per minute, and ≥80 beats per minute have been recommended for adults.

2Faster rates should probably be used in small children and during periods of increased arrhythmic risk (like after labor).27

§These values are based on very limited experience.21,24

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peated Holter recordings did not reveal serious proarhythmic events.

Our limited experience precludes defining the optimal rate-smoothing parameters. Documentation of repeated events of torsade de pointes helps to select the appropriate settings: the shorter the pauses that
 trigger torsade de points, the more aggressive rate smoothing should be. On the other hand, the aggressiveness of pacing should be limited to avoid pacing within the QT interval of the extrasystoles (which, on occasion, can be considerably long). This is done by programming a relatively long upper-rate interval such as 500 msec. Accordingly, pacing should never occur before 500 msec from the last ventricular event. Long upper-rate intervals such as 500 msec, which is the equivalent of an upper-rate limit of 120 beats per minute, are well tolerated because the overwhelming majority of patients with LQTS have intact atrioventricular conduction.

It is important to note some differences that exist between the rate-smoothing algorithm in the Vigor (described above) and that of different models by the same manufacturer. When the coupling interval of an extrasystole is shorter that the upper-rate interval, the escape interval in the Vigor is the upper-rate interval + the rate-smoothing-down value. In contrast, in the Ventak series of dual-chamber defibrillators, the escape interval is the interval before the extrasystole plus the rate-smoothing-down value. Consequently, if this scenario occurs when the sinus rate is above the lower-rate interval, the rate smooth down in the Ventak will actually prolong the postextrasystolic pause. This subtle difference may be consequential for patients with LQTS. In the newer defibrillators (PRIZM series), the rate-smoothing algorithm works like in the Vigor (Jan Pieter Heemels, Guidant–CRM, Europe, personal communication).

Finally, it cannot be overemphasized, that cardiac pacing should always be used in combination with β-blocker therapy, as even rapid pacing does not mitigate the proarrhythmic effects of sympathetic stimulation. The role of cardiac pacing, when used in combination with genotype-specific antiarrhythmic drugs, remains to be defined.