Short-Coupled Variant of Torsade de Pointes
A New Electrocardiographic Entity in the Spectrum of Idiopathic Ventricular Tachyarrhythmias

Antoine Leenhardt, MD; Emmanuel Glaser, MD; Miguel Burguera, MD; Michael Nürnberg, MD; Pierre Maison-Blanche, MD; Philippe Counel, MD

**Background**
Torsade de pointes is characterized not only by its particular ECG pattern but by its context of congenital or acquired long QT syndrome and the long coupling interval of the initial premature beat.

**Methods and Results**
We observed 14 patients aged 34.6±10 years (mean±SD) with no structural heart disease who presented with syncope related to a typical ECG aspect of torsade de pointes. However, there was no evidence of long QT syndrome, and the torsade had the unusual particularity of an extremely short coupling interval of the first beat or of the isolated premature beats (245±28 milliseconds). In 10 cases they deteriorated into ventricular fibrillation. Four patients had a familial history of sudden death. Only 2 patients had a tachyarrhythmia inducible by programmed stimulation. At Holter recordings the heart rate variability was globally and significantly depressed, the vagal limb of the autonomic nervous system being predominantly affected. During a mean follow-up of 7 years there were 5 deaths (4 sudden). Nine patients are alive, 3 with implanted defibrillators and 6 treated with verapamil alone. Unlike the other types of antiarrhythmic agents including β-blockers and amiodarone, verapamil is in our experience the only drug apparently active on the arrhythmias; however, it does not prevent sudden death.

**Conclusions**
The short-coupled variant of torsade de pointes should be identified because of their ECG pattern and the risk of sudden death in young adults with no structural heart disease. (*Circulation, 1994;89:206-215.)*

**Key Words**
- intervals
- death, sudden
- fibrillation

Torsade de pointes typically is characterized by its ECG pattern of nonuniform but still organized electrical activity, with progressive changes in morphology, amplitude, and polarity of the QRS complexes, whose peaks twist around the isoelectric baseline before ending spontaneously. The main interest of clearly defining a new ECG entity, at a time when numerous ECG documents were gathered in the developing intensive care units, was to differentiate torsade de pointes from true, non-self-terminating ventricular fibrillations (VF) and polymorphic ventricular tachycardias (VT). A large part of the diagnostic problems that may remain after an attentive examination of these various types of ECG tracings is in fact resolved by the environment of torsade de pointes: the congenital long QT syndrome and its familial history, the etiologic factors of the acquired long QT syndrome, and in the precipitating causes of torsade de pointes. From the pure ECG point of view, the unusually long coupling interval (600 to 800 milliseconds) of the initial beat of the torsade de pointes is a major diagnostic criterion.

A large consensus now exists not to uniformly consider ventricular tachyarrhythmias observed in diseased hearts and to use as adequately as possible the various terms of torsade de pointes, VF, and monomorphic or polymorphic VT. In contrast, ventricular tachyarrhythmias observed in the absence of structural heart disease are much less documented, and gathering experience about "idiopathic VF" is highly suitable. This term most probably covers different clinical/ECG entities.

The purpose of this study is to report on the clinical course, ECG features, and electrophysiologic findings of 14 patients who presented with remarkably consistent patterns that may form a new ECG entity that we propose to call the short-coupled variant of torsade de pointes.

**Methods**

**Study Patients**
The 14 cases were selected among patients with no structural heart disease, referred to our institution over a period of 20 years (1972 to 1991) after severe syncopal attacks due to documented ventricular tachyarrhythmias initially qualified as VF. All patients had a physical examination, chest radiography, 12-lead ECG, and M-mode or two-dimensional echocardiography, but only 9 of them had a cardiac catheterization including right and left ventricular angiography. No cardiac biopsy was performed. All patients did have electrophysiologic investigations (with slightly different stimulation protocols), but for historic reasons only 12 of them underwent Holter monitoring and 5 underwent high-amplitude ECG.

**Twenty-four-Hour Holter Monitoring**
Holter monitoring was performed with 2- or 3-channel recorders, and the data were processed through the ATREC II system for studying arrhythmia behavior and heart rate variability (HRV). The nonspectral, time domain HRV analysis that we developed is based on selectively studying the oscillations of the heart rate according to wavelength. Briefly, a heart rate oscillation is defined as a shorter or longer sequence of RR intervals forming an acceleration or a deceleration, preceded and followed by opposite trends involving half the number of cycles of the central sequence. Shorter or longer oscillations are defined in terms of number of beats of this
central sequence independent of the heart rate value. They are quantified in terms of number (per minute) and amplitude (in milliseconds), i.e., the difference between the longest and shortest cycle within an oscillation. The product “number times amplitude” (ms · min⁻¹) provides in the time domain an equivalent of the power spectrum in the frequency domain. The “short” (central sequence of 2 to 4 cycles) respiration-related heart rate oscillations are tightly correlated with the 0.2 to 0.4 Hz peak in the frequency domain⁴ and reflect the vagally mediated modulation of the heart rate. The “mean” (8 to 12 cycles) and “long” (15 to 30 cycles) oscillations coincide with the mid- and low-frequency peaks, and they predominantly depend on neurogenic and humoral sympathetic influences. When defining the mechanism of the different types of heart rate variations, it is obvious that most phenomena depend on a balance rather than on the effect of a single action of a part of the autonomic nervous system. The heart rate oscillations covering 10 to 20 seconds, the so-called Mayer waves, are certainly involved with sympathetic innervation; however, this fact that does not imply that they only reflect the sympathetic activity and that the vagal drive is not involved.

Electrophysiological Study

Programmed electrical stimulation was performed in all patients in the absence of treatment. Single, double, and triple ventricular extrastimuli were given in sinus rhythm and on paced cycle lengths of 600, 500, and 400 milliseconds. Depending on the results and the time of the study over the 20-year period, various drugs were administered intravenously either to favor or to prevent the arrhythmia inducibility: isoproterenol infusion (at a rate sufficient to accelerate the cardiac frequency at 150 to 160 min⁻¹), atropine (2 mg), calcium gluconate (2 g), or verapamil (5 mg).

Statistical Analysis

Data are presented as mean ± SD. Data are compared using ANOVA or the paired t test when appropriate.

Results

ECG Features of Short-Coupled Variant of Torsade de Pointes

The 14 patients referred for evaluation and treatment of syncope had at least one documented episode of ventricular tachyarrhythmia of which the electrical characteristics were those observed in the torsade de pointes. This term is based on the morphology of the QRS-T complexes recorded in several leads. The example in Fig 1 is illustrative: For reasons related to the circumstances, not all the tracings were recorded in simultaneous leads as classically recommended.

To describe the ECG trace we can use Dessertenne’s original terms⁷: “A particular form of intermittent ventricular electrical activity, always of high frequency and occurring as bursts” was so described. “The regular succession of complexes appears to be ventricular in origin because there are rapid, narrow phases in which the trace is ‘thin,’ separating two slow, short, wide phases of opposing orientation in which the trace is ‘thick.’ The name torsade de pointes describes exactly the phenomenon: a sequence of consecutive complexes,
the orientation of which reverses direction every four or five cycles. The amplitude varies continuously and progressively around the isoelectric line that separates the slow phase (T wave) from the fast phase (QRS complex). The maximum amplitude of the complex always occurs concurrently in each of the three leads; the amplitude also is always larger than that of the normal QRS complex and can reach several millivolts. There are shorter (a few seconds) or longer (10 seconds or more) episodes, and their mean proper rate in our patients was 238 min⁻¹ (range, 180 to 300). The terminal complex has a morphology “similar to that of an extrasystole, with the reappearance of a T wave that has an orientation opposite to that of QRS,” but “it resembles neither the initiating complex nor the normal QRS complex” and its amplitude is “always large, not only when compared with the normal QRS complex, but also when compared with torsade de pointes.” Some torsade de pointes may, however, degenerate into VF. This may happen soon after the onset of a rapid torsade de pointes (Fig 2) or after an acceleration of its rate. A clear-cut change occurs in the electrical activity that suddenly becomes disorganized: Such a deterioration was documented in 10 of our 14 patients. Only 4 patients (patients 2, 6, 8, and 14) (Table 1) did not require resuscitation.

The main difference between the entity we describe and the classic torsade de pointes is the fact that in our cases the coupling interval of the first beat of the torsade de pointes is very short (245±28 milliseconds; range, 200 to 300) in contrast to the long coupling interval of the first beat in the classic torsade de pointes. The morphologies of this first beat and of isolated ventricular premature beats (VPBs) when present were strikingly similar in 9 patients, with a left-axis deviation (−45°) and a left bundle branch block pattern (Fig 3).

This morphology was different in the 5 other patients in terms of axis (right axis) and/or bundle branch block pattern (right), but the coupling interval was always short.

**Clinical and Laboratory Features**

The 14 patients in whom we observed the short-coupled variant of torsade de pointes had common clinical characteristics in addition to the ECG syndrome (7 men and 7 women; mean age, 34.6±10 years) (Table 1). Four patients had a familial history of sudden death (no genetic study has been performed). Three had a history of palpitations. No patient had chest pain (including before syncope), shortness of breath, alcohol or drug abuse, known toxic exposure, or was receiving antiarrhythmic drugs. A significant potassium depletion (2.9 mmol/L) was the occasion of the first episode in 1 patient (patient 8). Syncope was provoked by emotion in 2 patients (patients 3 and 14) and by exercise in 1 patient (patient 10). The initial symptom was syncope with no need of cardiac resuscitation in 13 patients. Torsade de pointes and VF were documented in these patients only shortly after their admission in the hospital, with a mean of 6.5

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**Fig 2.** Electrocardiogram. Salvo of short-coupled variant of torsade de pointes (patient 9). One episode degenerates into ventricular fibrillation (3) after a few beats of torsade de pointes, with a clear-cut change in electrical activity that suddenly becomes disorganized.
TABLE 1. Clinical and Electrocardiographic Characteristics of Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y*</th>
<th>Sex</th>
<th>Familial Sudden Death</th>
<th>Prior Symptoms</th>
<th>Documented Arrhythmia</th>
<th>CI VPB</th>
<th>VPB Morphology</th>
<th>Activity at 1st Syncope Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31/F</td>
<td>Yes</td>
<td>Syncope</td>
<td>TdP, VF</td>
<td>240</td>
<td>L axis, LBBB</td>
<td>Washing</td>
<td>3 VF</td>
</tr>
<tr>
<td>2</td>
<td>30/F</td>
<td>No</td>
<td>Syncope</td>
<td>TdP</td>
<td>280</td>
<td>L axis, LBBB</td>
<td>Resting</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>30/M</td>
<td>No</td>
<td>Syncope</td>
<td>TdP, VF</td>
<td>240</td>
<td>R axis, LBBB</td>
<td>Emotion</td>
<td>7 VF</td>
</tr>
<tr>
<td>4</td>
<td>49/M</td>
<td>No</td>
<td>Syncope</td>
<td>TdP, VF</td>
<td>240</td>
<td>L axis, LBBB</td>
<td></td>
<td>6 VF</td>
</tr>
<tr>
<td>5</td>
<td>30/F</td>
<td>No</td>
<td>Syncope</td>
<td>TdP, VF</td>
<td>270</td>
<td>L axis, LBBB</td>
<td>Resting</td>
<td>13 VF</td>
</tr>
<tr>
<td>6</td>
<td>44/M</td>
<td>Yes, 2</td>
<td>Syncope</td>
<td>TdP</td>
<td>240</td>
<td>L axis, LBBB</td>
<td>Resting</td>
<td>0</td>
</tr>
<tr>
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<td>41/F</td>
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<td>Syncope</td>
<td>TdP, VF</td>
<td>300</td>
<td>N1 axis, LBBB</td>
<td>Resting</td>
<td>2 VF</td>
</tr>
<tr>
<td>8</td>
<td>38/F</td>
<td>Yes</td>
<td>Syncope</td>
<td>TdP</td>
<td>200</td>
<td>L axis, LBBB</td>
<td>Resting</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>15/M</td>
<td>No</td>
<td>Syncope</td>
<td>TdP, VF</td>
<td>240</td>
<td>L axis, RBBB</td>
<td>Resting</td>
<td>11 VF</td>
</tr>
<tr>
<td>10</td>
<td>45/F</td>
<td>No</td>
<td>Syncope+CPR</td>
<td>TdP, VF</td>
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<td>L axis</td>
<td>Cycling</td>
<td>1 VF</td>
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<tr>
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<td>Yes</td>
<td>Syncope</td>
<td>TdP, VF</td>
<td>220</td>
<td>L axis, LBBB</td>
<td></td>
<td>1 VF</td>
</tr>
<tr>
<td>12</td>
<td>40/M</td>
<td>No</td>
<td>Syncope</td>
<td>TdP, VF</td>
<td>230</td>
<td>L axis, LBBB</td>
<td>Resting</td>
<td>6 VF</td>
</tr>
<tr>
<td>13</td>
<td>24/M</td>
<td>No</td>
<td>Syncope</td>
<td>TdP, VF</td>
<td>220</td>
<td>L axis, LBBB</td>
<td>Resting</td>
<td>23 VF</td>
</tr>
<tr>
<td>14</td>
<td>20/F</td>
<td>No</td>
<td>Syncope</td>
<td>TdP</td>
<td>280</td>
<td>? axis, RBBB</td>
<td>Emotion</td>
<td>0</td>
</tr>
</tbody>
</table>

Reference

| 8       | 25/F    | No  | Syncope               | TdP, VF        | 300                   | ?        | ?            | 1 VF                              |
| 9       | 38/M    | No  | Syncope               | TdP            | Short                 | ?        | Resting     | 0                                |
| 10      | 37/M    | No  | Syncope               | TdP            | Short                 | L axis   | LBBB        | Resting 0                        |
| 11      | 28/M    | No  | Syncope               | TdP, VF        | 290                   | L axis   | LBBB        | Lying 8 VF                       |
| 12      | 21/F    | Yes | Syncope               | TdP            | 280                   | L axis   | ?           | Resting 4 VF                     |
| 13      | 52/F    | No  | Syncope               | TdP            | 300                   | ?        | LBBB        | Resting 0                        |
| 14      | 28/M    | No  | Syncope               | TdP            | 280                   | ?        | ?           | 0                                |
| 15      | 34/M    | No  | Syncope               | TdP, VF        | 300                   | ?        | ?           | 2 VF                              |

*Age at the time of the first documented episode of torsade de pointes (TdP). CI indicates coupling interval; VPB, ventricular premature beat; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; L, left; BBB, bundle branch block; R, right; and monitoring, number of VF recurrences after the first documented episode of TdP.

ECG and Electrophysiological Findings

Surface ECG. Resting ECGs were normal in all except 1 patient (patient 10), which showed a rate-dependent left bundle branch block. When analyzed in basic tracings as well as in dynamic ECG, the repolarization phase was in all respects normal. As previously mentioned, the VPB morphology suggested an apical right ventricular origin in 9 of 14 patients.

Dynamic ECG. Holter recordings were not available in the 2 patients observed before 1974. Four patients had no VPBs during the first few days after admission. Eight patients had an average of 849±1473 VPBs/24 h, all displaying the characteristic very short coupling interval. Six patients had doublets (123±117/24 h) and salvos of more than 3 beats (30±34/24 h). All types of arrhythmias predominated at daytime. There were no statistically significant correlations between arrhythmias and sinus frequency. The relations that were evidenced were not consistent: As the mean heart rate increased, the VPB rate increased in 5 patients (patients 4, 5, 6, 8, 9) and decreased in 2 (patients 11 and 13). Only in these
were analyzed for their stable characteristic or absence of structural heart disease, was significantly lower in patients (1.11±0.11 versus 1.41±0.11, \( P<.001 \)). A more refined evaluation of the autonomic balance through HRV showed that both types of sympathetic and vagal activities were significantly depressed in patients: The vagal activity was apparently more depressed (150±97 versus 521±128 ms \( \cdot \) min\(^{-1} \), \( P<.001 \)) than the sympathetic activity (180±54 versus 305±35 ms \( \cdot \) min\(^{-1} \), \( P<.05 \)). Finally, the sympathetic/vagal ratio of the HRV was higher in patients than in normal subjects (1.56±0.93 versus 0.67±0.16, \( P<.001 \)) because of their less-decreased sympathetic activity.

Verapamil (mean dosage, 405±127 mg/d) did not change the 24-hour mean heart rate (72.7±10.3 versus 70.4±7.6 beats \( \cdot \) min\(^{-1} \)) (Fig 5), but the day-to-night ratio of the heart rate, a particularly stable characteristic of the autonomic nervous system in the absence of structural heart disease, was significantly lower in patients (1.61±0.11 versus 1.37±0.11, \( P<.001 \)).
of the heart rate increased (1.11±0.11 versus 1.27±0.14, P=.01, paired t test). HRV tended to increase, although not significantly, and the vagal activity was more influenced (150±97 versus 194±89 ms·min⁻¹) than the sympathetics (180±54 versus 199±54 ms·min⁻¹). The abnormally elevated sympathetic/vagal ratio decreased (1.31±0.84 on verapamil versus 1.56±0.93, P=NS) but, again, not significantly.

High-amplitude ECG. The high-amplitude ECG was normal in the 5 patients who underwent this investigation.

Programmed electrical stimulation, exercise stress testing, and pharmacological studies. All patients underwent an electrophysiological study without monophasic action potential recordings. There was no abnormality of the basic electrophysiological parameters, including ventricular refractoriness. Long torsades de pointes (20 to 30 beats) were reproducibly initiated in a single patient (patient 10) with 2 ventricular extrastimuli delivered during sinus rhythm: The effect of verapamil (5 mg IV) was favorable, and only short, repetitive responses (5 or 6 beats) remained inducible. A VF was provoked in 1 patient (patient 4) using 3 ventricular extrastimuli in sinus rhythm in basic conditions as well as on verapamil (720 mg/d). In 12 patients, no ventricular arrhythmia was obtained using the complete stimulation protocol. In 2 patients (patients 6 and 13), atrial pacing over 75 min⁻¹ prevented the VPBs. We occasionally observed postpause limited T-wave changes in 2 patients (patients 6 and 8). Exercise stress testing was performed in 9 patients. Isolated asymptomatic short-coupled VPBs were seen in only 2 patients (patients 4 and 14). We did not observe any lengthening of the QT interval during exercise stress testing. There were no significant changes of T-wave morphology.

Isoproterenol was administered in 11 patients. No effects were observed in 6 of them, and short-coupled VPBs disappeared in 3 patients (patients 5, 6, and 7) and increased in 2 patients (patients 1 and 8). As with exercise stress testing, we did not observe any lengthening of the QT interval or significant changes in T-wave morphology. Atropine was given in 6 patients: No effects were observed in 3 patients (patients 1, 2, and 9), but in one of them (patient 6), the repetitive forms of arrhythmia were reproducibly and dramatically increased. In contrast, a slight decrease in the VPB rate was observed in 2 patients (patients 5 and 7). The effects of calcium were studied in 8 patients: No effects were observed in 4 of them. In 3 patients (patients 1, 6, and 10) the VPB rate significantly increased, and in 1 patient (patient 7) the coupling interval was shortened.

Treatment and Follow-up

Long-term follow-up after the first documented episode of torsade de pointes ranged from 12 to 188 months (mean, 63). There were 5 deaths, and 9 patients are alive, with a mean follow-up of 7 years (range, 1 to 16). See Table 2.

Deaths. Among the 5 deaths, 1 resulted from stroke in a hypertensive patient (patient 11), and 4 occurred suddenly (patients 2, 3, 13, and 14) in undefined circumstances for patients 3 and 13 and during sleep for the 2 others. Patients 3 and 14 were on β-blockers (nadolol and propranolol, respectively) and died suddenly 46 and 24 months after the initial symptoms. Patient 13 (whose arrhythmia was apparently bradycardia dependent) had been implanted with an atrial pacemaker in another institution, without associated medical treatment, and died suddenly 12 months after the initial syncope. Patient 2 was on verapamil (360 mg/d); she had been hospitalized a few days before for palpitations in another institution, and the ECG revealed short-coupled VPBs. The treatment was not modified, and she died suddenly the night after, at home, 4 years after the initial symptoms. An autopsy was performed in only 1 patient (patient 14), and it did not reveal any cardiac abnormality.

Implantable cardioverter-defibrillator. An implantable cardioverter-defibrillator (ICD) was implanted in 3 patients. During follow-up, ICD shocks were thought to be appropriate on a clinical basis (shocks preceded by a presyncope or a syncope) and on ECG criteria (presence of isolated or repetitive short-coupled VPBs on the postshock tracings). Patient 4 was implanted because a VF was still inducible during electrophysiological testing under treatment with 720 mg/d verapamil. He experienced 4 defibrillator shocks while on verapamil during a 4-year follow-up. Patient 5 was implanted after recurrence of a presyncope on verapamil. She experienced 9 shocks while on β-blockers, verapamil alone, or verapamil combined with amiodarone during a 7-year follow-up. Interestingly, this patient had significantly less ICD interventions on verapamil than on β-blockers, and amiodarone was combined because of the poor tolerance of 720 mg/d verapamil. Patient 7 was implanted because no ventricular arrhythmia was inducible after a resuscitated sudden death: She experienced.
TABLE 2. Treatment and Clinical Course of Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Drug Therapy, mg/d</th>
<th>ICD</th>
<th>Documented Arrhythmia Recurrences</th>
<th>Clinical Course (Follow-up, mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Verapamil, 480</td>
<td>No</td>
<td>0</td>
<td>Asymptomatic VPB, 79</td>
</tr>
<tr>
<td>2</td>
<td>Verapamil, 360</td>
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<td>0</td>
<td>Sudden death, 46</td>
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<tr>
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<td>Nadolol, 80</td>
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<td>0</td>
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</tr>
<tr>
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<td>Yes</td>
<td>4</td>
<td>Shocks/ICD, 52</td>
</tr>
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<td>Yes</td>
<td>9</td>
<td>VT salvo, shocks/ICD, 107</td>
</tr>
<tr>
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<td>No</td>
<td>0</td>
<td>Asymptomatic, 189</td>
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<td>Yes</td>
<td>2</td>
<td>Shocks/ICD, 68</td>
</tr>
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<td>Asymptomatic, 19</td>
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<td>0</td>
<td>Asymptomatic VPB, 156</td>
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<tr>
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<td>Verapamil, 360</td>
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<td>0</td>
<td>Vascular stroke, 15</td>
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<tr>
<td>15</td>
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<td>No</td>
<td>0</td>
<td>Sudden death, 21</td>
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</table>

ICD indicates implantable cardioverter-defibrillator; VPB, ventricular premature beats; and VT, ventricular tachycardia.

2 appropriate defibrillation shocks without any drug treatment during a 4-year follow-up.

Drug treatment. Among the 14 patients, 2 have been treated with β-blockers and died suddenly. The other 12 patients have been initially treated with high doses of verapamil (360 to 720 mg/d). The criteria of verapamil efficiency were lengthening of the coupling interval of the VPB and significant decrease or even disappearance of the repetitive VPB. The efficiency of verapamil was documented, at least on a short-term basis, in 11 of 12 patients. Among these 11 patients, 1 (patient 2) experienced sudden death and 1 (patient 11) a fatal vascular stroke. Nine patients are alive: 3 patients with an ICD and 6 treated with verapamil alone (patients 1, 6, 8, 9, 10, and 12) who are asymptomatic at a mean 7-year follow-up (range, 1 to 16). However, 3 of them have persistent short-coupled VPBs (isolated, coupled, and triplets) documented by 24-hour ECG recordings. In 1 of the 12 patients initially treated with verapamil, the treatment was stopped because this arrhythmia was supposed to be bradycardia dependent (patient 13). Among our 14 patients, 7 experienced a probable arrhythmia recurrence: 3 on verapamil, shocked by the ICD in 2 cases and fatal in 1 case; 2 on β-blockers, resulting in death in both cases; and 2 without drug treatment, shocked by the ICD in 1 case and resulting in death in 1 case. The mean time between the first ventricular arrhythmia and the recurrence was 34.4 months (range, 6 to 54 months).

Discussion

We report a group of 14 patients presenting with remarkably consistent clinical and ECG patterns that should be identified in the setting of idiopathic, potentially lethal ventricular tachyarrhythmias. These young adults of either sex with no detectable structural heart disease experienced syncope caused by severe ventricular tachyarrhythmias. The ECG displayed typical torsade de pointes, with an unusually short coupling interval (always less than 300 milliseconds) of the first beat of the torsade de pointes or of the isolated VPBs, a characteristic that seems to be specific to this new ECG entity in the absence of any acute disease. There was no long QT interval at any time; there was a familial history of sudden death in 30% of the cases, and the natural history of sudden death was accounted for by the tendency of torsade de pointes to deteriorate into VF (10 of 14).

This arrhythmia fulfills the ECG criteria of torsade de pointes, a term that was coined to differentiate the
ECG pattern of particular tachyarrhythmias from either VF or polymorphic VT. The pattern in a single lead may be suggestive and even sufficient to make the diagnosis, although its absence in a single lead does not permit rejection of the diagnosis. However, an important difference compared with classic torsade de pointes is the unusually short rather than long coupling interval of the first beat of the torsade. This is why we call this entity the short-coupled variant of torsade de pointes.

**Clinical and ECG Features**

To our knowledge, only a limited number of similar cases with sufficient information to recognize the major features of the short-coupled variant of torsade de pointes have been published8-13 (Table 2). Almost all them were qualified as “idiopathic paroxysmal VF” (not polymorphic VT). This term in fact may well cover various entities that have in common their catastrophic outcome but may begin in different ways.

A familial history of unexplained sudden death was present in 4 patients (2 deaths in the family of patient 6) and in Strasberg’s case.12 The mean age at first symptom was not different in our experience (34 years; range, 15 to 49) and in the literature (31 years; range, 16 to 52).

No underlying cardiac disease was detectable. Although we cannot formally exclude the possibility of a latent cardiomyopathy in the absence of endomyocardial biopsy, it is unlikely since with a follow-up now exceeding 5 years in 7 of them, clinical parameters and echocardiograms remain normal.

The ECG pattern was uniform, including a normal QT interval. The attacks did not consistently relate to any environment of emotional or psychological stress, any form of adrenergic stimulation, or, on the contrary, any metabolic factor or bradycardia. All torsade de pointes started with a very short coupling interval (mean, 245 milliseconds). The proper rate of the tachyarrhythmia was slightly faster (mean, 240 beats min⁻¹) than in classic torsade de pointes (200 to 220 beats min⁻¹). A reason might be that Deseretenne’s descriptions mainly concerned torsade de pointes in the acquired long QT syndrome, thus frequently implicating older patients with diseased hearts further depressed by the responsible drug or metabolic disorder. Torsade de pointes degenerated into VF in 10 of our 14 cases and in 4 of the 9 cases in the literature (14 of 23). Only 1 sudden death15 was reported during a relatively limited follow-up compared with ours. Isolated VPBs had also a very short coupling interval that we believe is specific to the syndrome: We are not aware of any other chronic situation in which a value of less than 300 milliseconds is constantly observed. The morphology of isolated VPBs and the initial beat of the torsade de pointes was homogeneous in 9 of our patients and also present in Belhassen’s case.11

The electrophysiological studies are usually negative, not a surprising finding in the setting of torsade de pointes. In only 1 of our patients was the torsade de pointes inducible. This has also been reported by 2 other groups.11,12 Other artificially induced tachyarrhythmias are occasionally observed after aggressive stimulations, including VF or nonsustained polymorphic VT14,15: The results are inconsistent, and the arrhythmias are probably not specific. This also applies to the effect of pharmacological maneuvers. If, however, in our experience there was no interpatient reproducibility, the significant effect of any drug (isoproterenol, atropine, calcium, or verapamil), once obtained, was highly reproducible.

In the long term, the spontaneous behavior of the arrhythmia is unpredictable. Various drugs including β-blockers, amiodarone, and even quinidine have been used, some of them being apparently successful in the short term. In our experience, however, and with limited support from the literature,13 verapamil is the only drug that consistently although not constantly suppresses the arrhythmia on the ECG. However, this beneficial effect of verapamil does not prevent sudden death. Therefore, we strongly suggest the use of ICD therapy.

**ECG Diagnosis**

From the ECG point of view, the identity of torsade de pointes is now well established. The completely desynchronized, non–self-limited electrical activity of a VF and the still-organized, self-terminating torsade de pointes cannot be considered in the same way. It must be remembered that an important characteristic of torsade de pointes is the pattern of the beat that heralds the end of the episode: At variance from self-terminating VF and polymorphic VT, its amplitude is always larger than that of the normal QRS complex. On the other hand, a short-coupled variant of torsade de pointes can degenerate into VF within a few seconds, so no conclusion should be made when the whole document, starting from the last sinus beat, is not available. Therefore, many patients with the short-coupled variant of torsade de pointes may have died suddenly because of VF, and our series may constitute a subgroup of selected patients who survived because of recurrent episodes of torsade de pointes preceding VF.

Some polymorphic VT also may be difficult to distinguish from torsade de pointes, a problem that arises mainly when one does not take into account the context of severely diseased hearts that are further depressed by drugs or metabolic disorders. Such ECG data16,17 should be interpreted with some caution before claiming that torsade de pointes has a limited specificity.

In fact, the real problem is to progress in the knowledge of the varieties of syndromes that may be responsible for sudden death in the absence of any evidence of structural heart disease and acute illness. Primary VF was recently reported by Brugada and Brugada18 in the setting of a syndrome including a right bundle branch block, a persistent ST-segment elevation with no long QT, but the coupling interval of the VPB was not short. An unusually short coupling interval is observed in acute ischemia but not in chronic, stable diseases of the heart. Only in a single patient with mild hypertrophic cardiomyopathy and a familial history of sudden death did we recently observe such an extremely short coupling interval.

Of course, this characteristic is in sharp contrast with torsade de pointes of the long QT syndrome, whether congenital or acquired. However, this does not exclude any relations between the long QT syndrome and the presently described entity.19 A familial history of unexplained sudden death was present in 4 patients; patient 1 developed a long QT with sotalol, and the first
syncope occurred in patient 8 as she had an acute potassium deficit. One should also recall that Straessberg's case\cite{12} was presented as a doxepin-induced accident, thus putting this drug on the blacklist of torsade de pointes-generating causes.

**Pathophysiology**

The pathogenetic mechanism of torsade de pointes has not been established. The hypotheses proposed are either reentry caused by dispersion of repolarization or triggered activity following afterdepolarizations.\cite{20,21}

Torsade de pointes are often supposed to be secondary to early afterdepolarizations (EADs).\cite{22} However, EADs have the prerequisite of a prolonged cellular action potential and are bradycardia dependent. This fits very well with the long QT syndrome but not with the normal QT interval, the short coupling interval, and the rarity of pause-induced arrhythmias in the short-coupled variant of torsade de pointes. EADs are also known to be slow-channel dependent; therefore, the effect of verapamil, which mainly inhibits the slow inward calcium current,\cite{23,24} would be consistent. A recent study\cite{25} reported its efficacy in suppressing torsade de pointes in patients with atrioventricular block, which could be explained by a direct membrane effect by inhibition of EADs. Intracellular calcium overload is more characteristically a key feature in the occurrence of delayed afterdepolarizations (DADs). Verapamil also has been demonstrated as effective in suppressing DADs and triggered activity.\cite{26} Therefore, DADs might also be proposed as the mechanism of the first beat of the torsade, although the short coupling interval would not be easy to explain.

Although difficult to define, the relations between the autonomic nervous system and short-coupled VPBs and torsade de pointes are not nil. Ventricular arrhythmias predominate at daytime. In some cases they are consistently preceded by a dramatic sinus acceleration over a few beats, possibly because of a vagally deprived favoring effect also suggested by the occasional arrhythmogenic effect of atropine. A low day/night ratio of the heart rate and an overall decreased HRV with a vagal activity more depressed than the sympathetic activity are indeed unusual in young adults without structural heart disease. This observation should, however, be cautiously interpreted because of the relative imprecision that remains in the distinction between the sympathetic and vagal components of the HRV.

Verapamil partially corrected these abnormalities, and a vagotonic action of this drug is further suggested by the reversibility by atropine of its effect on the sinus and the AV nodes. These observations support the favoring role of a low parasympathetic drive. An increased sympathetic drive would be much less likely, and the β-blockers had no effect, in our experience.

**Conclusions**

The short-coupled variant of torsade de pointes forms a new ECG entity that may be responsible for sudden death in the absence of any evidence of structural heart disease and acute illness. There is a familial history of sudden death in 30% of the cases. This arrhythmia is observed in the context of a particular profile of the autonomic nervous system with a low HRV and a high sympathetic to parasympathetic ratio. We have found no efficacy of class I antiarrhythmic agents as well as β-blockers and amiodarone. Only verapamil displays an ECG and clinical efficacy but does not prevent sudden death. Therefore, we strongly suggest widespread use of ICD therapy.

**Note Added in Proof.** Since the submission of this article, patient 9 died suddenly after a follow-up of 24 months. He had refused the implantation of an ICD and was treated with verapamil combined with amiodarone. No autopsy was performed.

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