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Quantitative Analysis of T Wave Abnormalities and Their Prognostic Implications in the Idiopathic Long QT Syndrome

GABRIELLA MALFATTO, MD,*† GABRIELLA BERIA, MD,*‡ SERGIO SALA, MD,*†
OSCAR BONAZZI, MD,* PETER J. SCHWARTZ, MD, FACC*§

Milan and Pavia, Italy

Objectives. **We evaluated the diagnostic and prognostic value of morphologic abnormalities of the T wave (mainly notched or biphasic T waves) in patients affected by the idiopathic long QT syndrome.**

Background. **In the long QT syndrome, these abnormalities in T wave morphology are often observed and are of uncertain significance.**

Methods. **The T wave abnormalities in the electrocardiogram (ECG) of 53 patients with the long QT syndrome and 53 control subjects of similar age and gender were analyzed, and their association with major cardiac events was defined.**

Results. **Notched or biphasic T waves were defined according to morphologic criteria. They were present in 33 (62%) of 53 patients with the long QT syndrome and in 8 (15%) of 53 control subjects ($p < 0.001$). Moreover, among patients with the long QT syndrome they were much more frequent in symptomatic (history of syncope or cardiac arrest) than in asymptomatic subjects (30 [81%] of 37 vs. 3 [19%] of 16, $p < 0.001$). The same distribution was observed within families with the long QT syndrome, in which symptomatic members had more pronounced T wave abnormalities than did their asymptomatic siblings or parents. In symptomatic patients, the occurrence of T wave abnormalities was independent of the length of repolarization (corrected QT). These T wave abnormalities were associated with the presence of a specific pattern of abnormal left ventricular wall motion.**

Conclusions. **This study has quantified an ECG pattern typical of the long QT syndrome and provides the first evidence that morphologic analysis of T wave abnormalities may contribute to the diagnosis of the long QT syndrome and the identification of patients at higher risk for syncope or cardiac arrest.**

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Despite considerable progress in research (1–7), several aspects of the idiopathic long QT syndrome are not understood. One feature that has attracted clinical attention since its first description is the bizarre morphology of the T wave. Physicians who had the opportunity of examining several patients with the long QT syndrome could not help noticing that, in addition to the prolongation of the QT interval, unusual T wave configurations were frequently present in this uncommon familial syndrome. Indeed, this finding was repeatedly mentioned in several early reports (8–10).

Notched and biphasic T waves constitute the most striking of these abnormalities, and they were included in the diagnostic criteria proposed in 1985 (2) and revised in 1993 (11). A computer-assisted quantification of several rate-dependent and rate-independent components of the T wave in patients with the long QT syndrome was recently performed (12). However, the various T wave patterns that any general practitioner can easily observe and identify on the standard electrocardiogram (ECG) in the long QT syndrome have not yet been analyzed in detail, nor have they been correlated with clinical history. Recognition of markers of high risk for the occurrence of cardiac arrest is of major practical importance in a disease such as the long QT syndrome, which is characterized by a high mortality rate in untreated patients and by a relatively large number of affected subjects (disease carriers) who may remain asymptomatic throughout their life (2,5,7). The availability of effective therapies (2,13) emphasizes the importance of an early identification of patients likely to develop syncope or cardiac arrest.

In 1991, we described a previously unsuspected abnormality in the left ventricular posterior wall motion that was correlated with a higher risk for syncope or cardiac arrest (14). Relevant here, most of the patients with echocardiographic abnormalities also had a notched T wave (14). To investigate whether this specific ECG abnormality might have diagnostic and prognostic value, we have characterized the T wave patterns and correlated them with the clinical history and the echocardiographic pattern. Preliminary data have been reported elsewhere (15).

From the *Clinica Medica Generale e Terapia Medica, Università di Milano, †Centro Auxologico Italiano IRCCS and ‡Divisione di Cardiologia, Policlinico di Milano, IRCCS, Milan; and §Dipartimento di Medicina, Università di Pavia, Pavia, Italy. This study was supported in part by Grant HL-33843 from the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland and by Grant 396 from Telethon-Italy.

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Address for correspondence: Dr. Peter J. Schwartz, Clinica Medica Generale e Terapia Medica, University of Milan, Via F. Sforza, 35, 20122 Milan, Italy.

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Methods

Study patients. The study involved 53 patients referred to the University of Milan because they were affected by the idiopathic long QT syndrome and 53 healthy control subjects. Patients and control subjects were similar in gender and age. Patients with the long QT syndrome were admitted either for the occurrence of syncope or cardiac arrest or for periodic follow-up visits. They were predominantly female subjects (70%), relatively young (mean age 21 years, range 10 to 40), with a prolonged ventricular repolarization as measured in lead D_2 (corrected QT [QTc] interval 495 ± 41 ms). The majority (42 [79%] of 53) were affected by the familial type of the long QT syndrome. A history of documented syncope or cardiac arrest was present in 37 patients (69%) hitherto defined as "symptomatic." The state of therapy at the time of the study was as follows: beta-adrenergic blocking agents (mainly propranolol, 2 to 3 mg/kg body weight per day) in 16 patients; beta-blockers and left cardiac sympathetic denervation in 6 patients, and no therapy in 31 patients. For 13 of the latter 31 patients, in the ECGs were also available after institution of antiadrenergic therapy: beta-blockers (10 patients) or left cardiac sympathetic denervation (3 patients). All patients receiving antiadrenergic therapy had a history of syncope or cardiac arrest. There were four families with two to four affected members each. They included one symptomatic subject, the proband, and some asymptomatic family members (siblings or parents) with a long QTc. The participants in the control group had a normal 12-lead ECG and negative findings by clinical history and complete clinical examination.

Data and statistical analysis. The ECG variables taken into account were heart rate, QTc in lead D_2 and T wave morphology. To define the latter, we distinguished five different patterns (numbered 1 to 5 in Fig. 1). Within this classification, patterns 4 and 5, indicating a biphasic and a notched T wave, describe an abnormal repolarization. Specifically, a T wave was defined as *biphasic* when two distinct components of opposite polarity were present. It was defined as *notched* when a second positive deflection interrupted its descending phase ("camel hump" configuration). An ECG was judged *abnormal* if T wave pattern 4 or 5 was present. We calculated the frequency by which any of these T wave patterns were present in the control group and the group with the long QT syndrome. The latter group was further classified into patients with and without symptoms. To quantify the different lead distribution of T wave abnormalities in the various groups, we used the "lead prevalence index" developed by Watanabe and Nishimura (16). The lead number (e.g., 1 for lead V_1) is multiplied by the number of cases showing biphasic or notched T waves in that lead, for all six leads. The product is then divided by the total number of leads in which abnormal T waves were seen. This index represents the average location of biphasic and notched T waves in precordial leads. For example, an index of 2 indicates that the abnormality is confined to lead V_2, whereas an index of 3.5 indicates that it is mainly evident between leads V_3 and V_4.

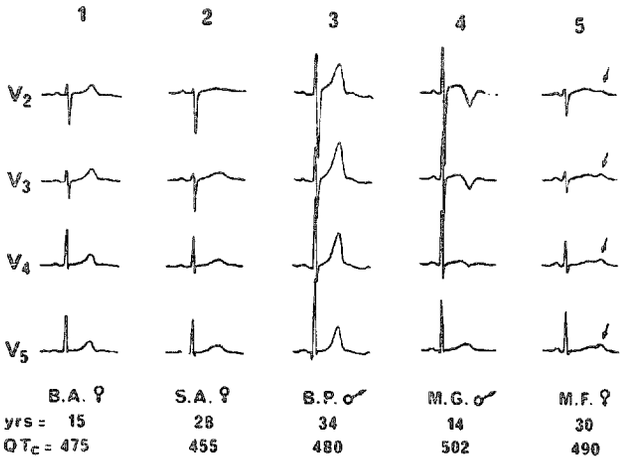

Figure 1. Examples of the five different T wave patterns. The numbers 1 to 5 represent, respectively: 1) a normal T wave; 2) a broad T wave; 3) a peaked T wave; 4) a biphasic T wave; 5) a notched T wave (the notch is indicated by the arrow). Patterns 4 and 5 were classified as "abnormal" throughout the study. QTc = corrected QT interval.

The morphology of the T wave was also related to the length of repolarization, expressed as QTc, and subdivided into four subgroups: 1) QTc <440 ms; 2) borderline QTc (between 441 and 470 ms); 3) QTc between 471 and 500 ms; and 4) QTc >500 ms. The prevalence of an abnormal T wave (biphasic or notched) was also considered in these subgroups with regard to control subjects and symptomatic and asymptomatic patients with the long QT syndrome.

Because of the potential for a similar pathogenetic and electrophysiologic substrate (14) and to obtain a better definition of the risk for cardiac events, the association between T wave and specific abnormalities in left ventricular wall motion was analyzed in 36 patients whose M-mode echocardiogram was also available. The abnormalities included two aspects: an increased rate of thickening in the early phase and a slow rate of thickening in the late systolic phase, with a plateau morphology (14).

Statistical analysis. Data are expressed as mean value ± 1 SD. Frequency comparison was performed by the chi-square test with the Yates correction. A two-tailed p value < 0.05 was considered the limit for significance.

Results

The patients with the long QT syndrome and control subjects had a similar mean age (21 ± 11 and 19 ± 8 years, respectively). As expected by the characteristic pathophysiology of the long QT syndrome (4–6), and after the obvious exclusion of patients receiving beta-blocker therapy, mean heart rate was significantly slower in patients with the long QT syndrome than in control subjects (64 ± 11 vs. 73 ± 8 beats/min, $p < 0.01$). The QTc measured in lead D_2 was

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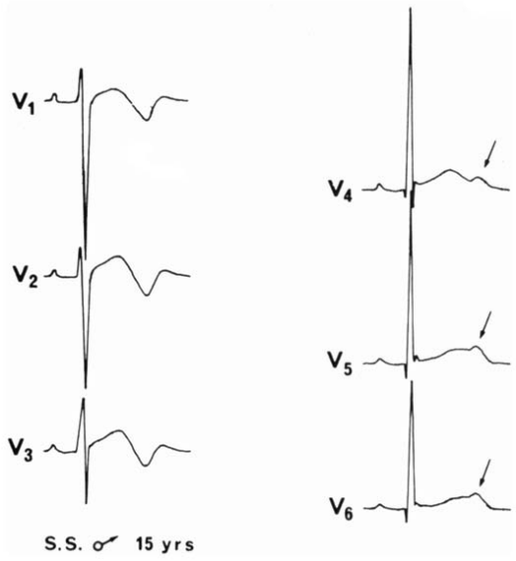

Figure 2. Example of a shift in T wave morphology across the precordial leads. In leads V_2 to V_4, the T wave is distinctly biphasic, whereas in leads V_5 and V_6, a clear notch is visible, as indicated by the arrow, which produces a TU complex. When this behavior was observed, the T wave pattern was classified as pattern 5.

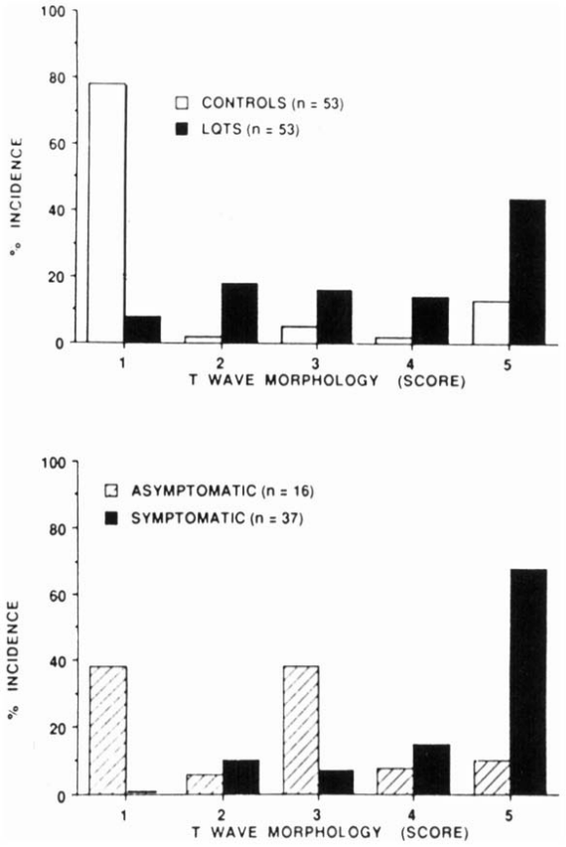

Figure 3. Frequency distribution of the five T wave patterns in the study groups. **Top,** In normal subjects, the prevalent T wave morphology was a smooth, normal T wave (pattern 1), whereas in patients with the long QT syndrome (LQTS), a morphology between patterns 2 and 5 was more commonly observed. This was particularly evident in symptomatic patients (**bottom**).

markedly longer in patients with the long QT syndrome than in control subjects (495 ± 41 vs. 398 ± 19 ms, $p < 0.001$). There was a trend for a longer QTc in symptomatic compared with asymptomatic patients (502 ± 47 vs. 485 ± 37 ms, respectively, $p = 0.10$).

Electrocardiographic analysis. The ECGs of the patients with the long QT syndrome were analyzed with regard to the presence and type of T wave abnormalities and the relation of T wave abnormalities with the length of repolarization. T wave abnormalities were more evident in precordial than in limb leads. They tended to be more widespread in patients with the long QT syndrome than in control subjects and were visible in leads V_2 to V_5, with a prevalence in leads V_3 and V_4. In control subjects, when present, they were confined to leads V_2 and V_3. This visual impression was quantified by the significantly different "lead prevalence index" in the two groups (2.21 in control subjects and 3.57 in patients, $p < 0.01$), whereas there was no difference between symptomatic and asymptomatic patients (3.61 vs. 3.35). In some instances, the T wave morphology shifted from one abnormal pattern to another across the precordial leads (Fig. 2). In this case, the abnormality with the highest score was considered for the quantitative analysis.

The prevalence of a T wave abnormality (biphasic or notched T wave in Fig. 1) was higher in the long QT syndrome group than in the control group (33 [62%] of 53 vs. 8 [15%] of 53, $p < 0.001$). Because a biphasic or notched T wave can be found in the ECG of normal young subjects (16–18), we considered separately the prevalence of these T wave abnormalities in subjects <15 or >15 years of age. Among those <15 years old, T wave abnormalities were present in 8 (23%) of 35 control subjects and in 22 (63%) of 35 patients with the long QT syndrome ($p < 0.001$). Among those >15 years old, biphasic or notched T waves were observed in none of 18 control subjects but were present in 11 (61%) of 18 patients with the long QT syndrome ($p < 0.001$). In the long QT syndrome, irrespective of age, these abnormalities were more prevalent in symptomatic (30 [81%] of 37) than in asymptomatic (3 [19%] of 16) patients ($p < 0.001$).

The frequency distribution of the various T wave patterns was found to be significantly different between patients and control subjects (Fig. 3). In patients with the long QT syndrome, the prevailing T wave patterns were between morphologies 2 and 5 (broad, peaked, biphasic, notched), whereas the control subjects had a prevalence of morphology 1 (smooth T wave, i.e., normal).

The relation between the presence of T wave abnormalities and the length of repolarization was complex. In asymptomatic patients with the long QT syndrome, abnormal T waves were infrequent and more likely to be observed when repolarization was longer (in none for a QTc <470 ms; in two of two for a QTc >500 ms). On the other hand, in symptom-

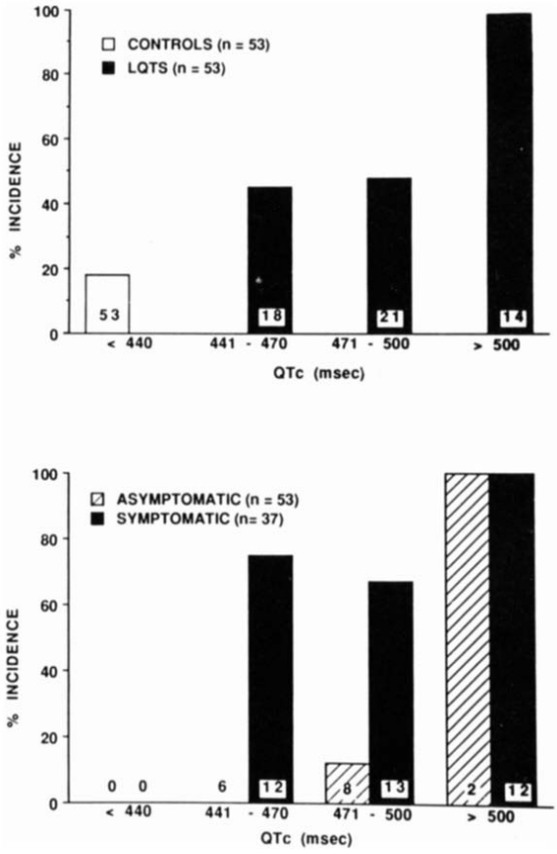

Figure 4. Relation between the frequency distribution of T wave abnormalities (patterns 4 and 5) in the study groups and the duration of corrected QT (QTc) interval. In normal subjects with a normal QTc, few T wave abnormalities were seen. In patients with the long QT syndrome (LQTS), there was a higher prevalence of biphasic or notched T waves with increasing QTc (top). However, this was the case for only the asymptomatic patients. The symptomatic patients had a high prevalence of T wave abnormalities irrespective of the duration of repolarization (bottom). The number of patients in each group is shown at the bottom of each bar.

atic patients, T wave abnormalities had a high prevalence regardless of QTc (Fig. 4).

For the correct identification of patients with the long QT syndrome with a history of syncope or cardiac arrest, or both, the sensitivity and specificity of finding a T wave abnormality were 91% and 65%, respectively (positive predictive value 86%).

Effect of beta-blockade and of left cardiac sympathetic denervation. In 13 patients the ECG was analyzed both before and after long-term therapy with beta-blockers (10 patients) or after left cardiac sympathetic denervation (3 patients). In the absence of therapy, T wave abnormalities were present in 10 (85%) of these 13 patients. With antiadrenergic treatment, the incidence of abnormal T wave configuration decreased to 6 (46%) of 13 (chi-square = 2.67, $p = 0.10$) because in some patients the T wave abnormalities disappeared with therapy (Fig. 5). We then considered separately these two small groups. In patients receiving beta-blocker therapy, the T wave abnormalities, observed in

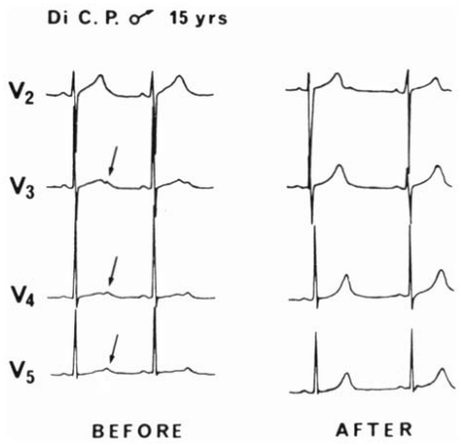

Figure 5. Effect of beta-adrenergic blocking agents on T wave morphology. In this patient, beta-blockade is accompanied by "normalization" of the T wave pattern. This was observed in a minority of patients (two of the eight who had an abnormal T wave in the absence of treatment).

8 of 10 during washout, were still present in 6 of 10 after treatment. In the three patients who underwent left cardiac sympathetic denervation, an abnormal T wave was present in two before denervation and in none afterward.

Familial distribution of T wave morphology. Four families, with a total of 12 subjects, had both symptomatic and asymptomatic members with the long QT syndrome. Biphasic or notched T waves were observed in three of four symptomatic patients. Conversely, none of the eight asymptomatic family members with the long QT syndrome (brothers, sisters and mothers) showed biphasic or notched T waves. In this group of affected and asymptomatic family members, the prevalent morphology was a peaked or a broad T wave (Fig. 6).

Relation with echocardiographic abnormalities. As previously suggested (14), the alterations in the morphologic abnormality of the T wave and those in left ventricular wall thickening were correlated. We analyzed both the ECG and the M-mode echocardiogram in 36 patients. An abnormal T wave was present in 24 patients (67%), and the typical echocardiographic pattern was found in 22 (63%). Again, these two findings were more frequent in the subgroup of 26 symptomatic patients than in the 10 asymptomatic patients: Peaked or notched T waves occurred in 85% and 20%, respectively, and the echocardiographic abnormality in 77% and 20%, respectively. Abnormal T waves were seen in 19 (89%) of the 22 patients with and in 5 (35%) of the 14 patients without the echocardiographic abnormality ($p < 0.001$). For identifying subjects with a history of syncope and cardiac arrest, the sensitivity and specificity of finding either abnormal T waves or the echocardiographic pattern were similar (88% and 86% and 63% and 50%, respectively). However, when the association of an abnormal T wave with the echocardiographic abnormality was taken into account, the sensitivity and specificity for a correct identification in-

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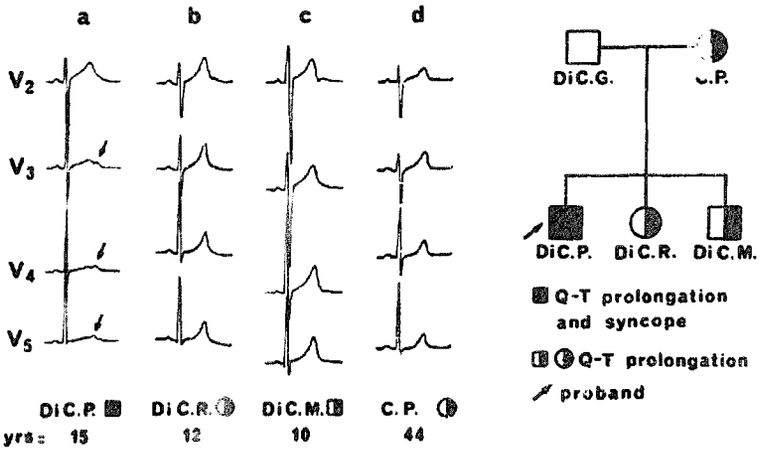

Figure 6. Different patterns of T wave morphology across family members. A notched T wave is evident in the patient with a history of syncope (DiC. P.), whereas his brother, sister and mother, who remain asymptomatic despite a prolonged QT interval, have peaked, broad or normal T waves. The family tree is shown at right.

creased to 95% and 77%, respectively (positive predictive value 90%).

Discussion

This study demonstrates that notched T waves are frequent in patients affected by the long QT syndrome and that they are associated with a greater probability of having syncope or cardiac arrest. The electrophysiologic mechanism underlying this phenomenon is likely to be closely related to the pathogenesis of the long QT syndrome itself. This finding also has clear diagnostic and prognostic implications.

Electrophysiologic mechanisms. Experimental and clinical evidence suggests that early afterdepolarizations may be present in the long QT syndrome (19–24). Prominent notches on the T wave have been described in both the acquired and the congenital long QT syndromes by Jackman et al. (22,23). They also observed that the behavior of the notches after changes in heart rate and during adrenergic stimulation was consistent with that of early afterdepolarization–related phenomena (23). On the basis of the effects of left cardiac sympathetic denervation, a link between early afterdepolarizations, the notches on the T wave and alpha-adrenergic mechanisms has been recently suggested (24). Early afterdepolarizations can prolong the duration of the QT interval and also influence T wave morphology. Their contribution to the shape and duration of the T wave would vary according to their extension and distribution across the myocardium (22–24).

Nishimura et al. (25) experimentally reproduced a notched T wave in the intact heart by creating an imbalance in cardiac action potential duration (right vs. left ventricle or anterior vs. posterior ventricular wall). Watanabe and Nishimura (16) extended this experimental observation clinically and suggested that "bifid" (or notched) T waves might reflect a delayed right ventricular repolarization. De Ambroggi et al. (26), by body surface mapping, demonstrated that patients with the long QT syndrome often have a large area of negativity in the anterior wall, a finding that indicates delayed repolarization. It is of interest for the pathogenetic mechanisms of the long QT syndrome (2,4) that the right anterior ventricle is primarily innervated by the right cardiac sympathetic nerves.

The biphasic or notched T waves exemplified by patterns 4 and 5 have been traditionally interpreted as a "juvenile" form of repolarization (16–18). With due caution for the relatively small numbers, we found, in agreement with a large study (18), that these T waves occurred in our healthy control group only in subjects <15 years old.

Diagnostic implications. The diagnosis of typical cases of the long QT syndrome is easy if the physician is aware of the disease. However, the clinical presentation is sometimes less straightforward. For these patients, a set of diagnostic criteria was provided in 1985 (2) and updated in 1993 (11). Additional and characteristic abnormalities have also been described. These include sinus pauses >1.2 s (27), a large area of anterior negativity and a multipolar configuration on body surface mapping (26), dispersion of repolarization (28,29), specific echocardiographic abnormalities (14), abnormal behavior of the QTc during exercise (30,31) and alterations in the duration of various ECG components in the digitized ECG (12). Despite such progress, the diagnosis in patients with stress-induced syncope, no family history and borderline QT interval prolongation requires caution and experience. Moreover, body surface mapping and computer analysis of the digitized ECG are seldom available even in academic centers. The present results allow the practicing cardiologist to draw clinically important inferences from a simple ECG analysis. The T wave pattern described here points strongly to the diagnosis of the long QT syndrome in borderline cases and particularly when the pattern is associated with the specific echocardiographic abnormality (14).

Within the same family, different morphologies of the T wave do exist and are correlated with symptoms. This observation suggests that these T wave patterns may reflect more the degree of severity of the disease within affected persons than a genetic trait (32). A more extensive study in several large pedigrees is warranted to define this issue.

Prognostic implications. The prognostic value of the T wave abnormalities discussed in the present study applies only to the long QT syndrome and should be not extrapolated to other conditions. The main data available for risk stratification in the long QT syndrome are from the International Prospective Registry and Study (3,5). The importance of the actual duration of the QT interval has not yet been clearly defined, even though a QTc >500 ms seems to be associated with a greater probability of syncope (5,7,32). The present morphologic analysis of the T wave contributes to prognostic stratification. Patterns 4 and 5 are linked to syncope and cardiac arrest significantly more than are the other patterns. Because T wave abnormalities were not related to QTc duration in symptomatic patients with the long QT syndrome, prolonged repolarization and abnormal T waves may represent two independent prognostic indexes. This is important because it allows the identification of high risk patients even in the group with only modest QT prolongation (QTc 440 to 470 ms).

The association of T wave and echocardiographic abnormalities correctly identifies the majority of symptomatic patients with high sensitivity and specificity. The practical implication of this new information is in suggesting that it may be wise to initiate therapy in a patients with the long QT syndrome who has T wave notches and the specific echocardiographic abnormality but is still asymptomatic.

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References

1. Schwartz PJ, Periti M, Malliani A. The long QT syndrome. Am Heart J 1975;89:378–90.
2. Schwartz PJ. Idiopathic long QT syndrome. Progress and questions. Am Heart J 1985;109:399–411.
3. Moss AJ, Schwartz PJ, Crampton RS, Locati E, Carleen E. The long QT syndrome: a prospective international study. Circulation 1985;71:17–21.
4. Schwartz PJ, Locati E, Priori SG, Zaza A. The idiopathic long QT syndrome. In: Zipes DP, Jalife J, editors. Cardiac Electrophysiology. From Cell to Bedside. Philadelphia: Saunders, 1989:589.
5. Moss AJ, Schwartz PJ, Crampton RS, et al. The long QT syndrome: prospective longitudinal study of 328 families. Circulation 1991;84:1136–44.
6. Schwartz PJ, Bonazzi O, Locati EH, Napolitano C, Sala S. Pathogenesis and therapy of the idiopathic long QT syndrome. Ann N Y Acad Sci 1992;644:112–41.
7. Vincent GM, Timothy K, Leppert M, Keating M. The spectrum of symptoms and QT interval in long QT syndrome gene carriers. N Engl J Med 1992;327:846–52.
8. Jervell A, Lange-Nielsen F. Congenital deaf-mutism, functional heart disease with prolongation of the QT interval. Am Heart J 1957;54:59–68.
9. Romano C, Gemme G, Pongiglione R. Aritmie cardiache rare in eta' pediatrica. Clin Pediatr 1963;45:656–83.
10. Fraser GR, Froggatt P, James TN. Congenital deafness associated with ECG abnormalities, fainting attacks and sudden death. Q J Med 1964;33:361–8.
11. Schwartz PJ, Moss AJ, Vincent GM, Crampton RS. Diagnostic criteria for the long QT syndrome: an update. Circulation 1993;88:782–4.
12. Benhorin J, Merri M, Alberti M, et al. Long QT syndrome: new electrocardiographic characteristics. Circulation 1990;82:521–7.
13. Schwartz PJ, Locati E, Moss AJ, Crampton RS, Trazzi R, Ruberti U. Left cardiac sympathetic denervation in the therapy of the congenital long QT syndrome. A worldwide report. Circulation 1991;84:503–11.
14. Nador F, Beria G, De Ferrari GM, et al. Unsuspected echocardiographic abnormality in the long QT syndrome: diagnostic, prognostic and pathogenetic implications. Circulation 1991;84:1530–42.
15. Malfatto G, Beria G, Sala S, Bonazzi O, Schwartz PJ. Prognostic significance of T wave abnormalities in the idiopathic long QT syndrome (LQTS) [abstract]. Circulation 1990;82 Suppl III:III-54.
16. Watanabe Y, Nishimura M. Clinical electrocardiographic studies of bifid T waves. Br Heart J 1984;52:201–14.
17. Lepeschkin E, Surawicz B. The duration of the QU interval and its components in electrocardiograms of normal persons. Am Heart J 1953;46:9–20.
18. Ishikawa K, Ohonuma H. The clinical significance of a notch on the T wave. Jpn Circ J 1979;43:539–46.
19. Gavrilescu S, Luca C. Right ventricular monophasic action potentials in patients with long QT syndrome. Br Heart J 1978;40:1014–8.
20. Bonatti V, Rolli A, Botti G. Recording of monophasic action potentials of the right ventricle in long QT syndromes complicated by severe ventricular arrhythmias. Eur Heart J 1983;4:168–79.
21. Brachmann J, Scherlag BJ, Rosenshtraukh LV, Lazzara R. Bradycardia-dependent triggered activity: relevance to drug-induced multiform ventricular tachycardia. Circulation 1983;68:846–56.
22. Jackman WM, Friday KJ, Anderson JL, Aliot EM, Clark M, Lazzara R. The long QT syndrome. A critical review, new observation and a unifying hypothesis. Prog Cardiovasc Dis 1988;2:115–72.
23. Jackman WM, Szabo B, Friday KJ, et al. Ventricular tachyarrhythmias related to early afterdepolarizations and triggered firing. Relationship to QT interval prolongation and potential therapeutic role for calcium channel blocking agents. J Cardiovasc Electrophysiol 1990;1:170–93.
24. Malfatto G, Rosen MR, Foresti A, Schwartz PJ. Idiopathic long QT syndrome exacerbated by beta adrenergic blockade and responsive to left cardiac sympathetic denervation. Implications regarding electrophysiologic substrate and adrenergic modulation. J Cardiovasc Electrophysiol 1992;3:295–305.
25. Nishimura M, Watanabe Y, Toda H. The genesis of bifid T waves: experimental demonstration in isolated perfused rabbit hearts. Int J Cardiol 1984;6:1–14.
26. De Ambroggi L, Bertoni T, Locati E, Stramba-Badiale M, Schwartz PJ. Mapping of body surface potentials in the idiopathic long QT syndrome. Circulation 1985;74:1334–45.
27. Schwartz PJ. The long QT syndrome. In: Kulbertus HE, Wellens HJJ, editors. Sudden Death. The Hague: Martinus Nijhoff, 1980:358.
28. De Ambroggi L, Negroni MS, Monza E, Bertoni T, Schwartz PJ. Dispersion of ventricular repolarization in the long QT syndrome. Am J Cardiol 1991;68:614–20.
29. Priori SG, Napolitano C, Diehl L, Schwartz PJ. Dispersion of repolarization as a marker to predict efficacy of antiadrenergic therapy [abstract]. J Am Coll Cardiol 1993;21:94A.
30. Sala S, Malfatto G, Locati EH, De Ferrari GM, Schwartz PJ. Diagnostic value of exercise-induced T wave abnormalities in the idiopathic long QT syndrome [abstract]. Circulation 1992;78 Suppl I:I-392.
31. Vincent GM, Jaiswal D, Timothy KW. Effects of exercise on heart rate, QT, QTc and QT/QS2 in the Romano-Ward inherited long QT syndrome. Am J Cardiol 1991;68:498–503.
32. Moss AJ, Robinson JL. Clinical aspects of the idiopathic long QT syndrome. Ann N Y Acad Sci 1992;644:103–11.