

## T-Peak to T-End Abnormality in Pediatric Patients with Syncope

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**Abstract**

**Objective:** The purpose of this study was to examine the relationship between T-peak-to-T-end interval and its dispersion in children with syncope to detect possible repolarization abnormalities in these patients.

**Methods:** We enrolled 19 patients with a positive tilt test for syncope (7 boys, 12 girls) and 35 participants with normal results on the test.

**Findings:** Mean age was  $11.4 \pm 3.1$  years in patients and  $10.0 \pm 5.1$  years in controls ( $P = 0.27$ ). The T-peak-to-T-end interval in lead V1 was significantly longer in patients with a positive tilt test ( $0.36 \pm 0.062$  vs.  $0.32 \pm 0.071$ ,  $P = 0.007$ ). T-peak-to-T-end interval dispersion was significantly greater in the group of patients ( $0.15 \pm 0.07$  vs.  $0.11 \pm 0.04$ ,  $P = 0.003$ ).

**Conclusion:** The T-peak-to-T-end interval in lead V1 and T-peak-to-T-end dispersion were significantly larger in patients with a positive tilt test. Our findings suggest a depolarization abnormality in children with syncope.

*Iranian Journal of Pediatrics, Volume 22 (Number 3), September 2012, Pages: 375-381***Key Words:** Electrocardiogram; Ventricular Repolarization; T-end; Syncope; Vasovagal Test; Tilt-table Test**Introduction**

Syncope is a disabling condition, and patients with this problem frequently seek medical attention. In the Framingham Study the incidence of adults reporting at least one syncopal episode during their lifetime was estimated at 3%<sup>[1]</sup>. The incidence of syncope is higher in females than in males, with a peak frequency at 15 to 19 years.

The most common cause of syncope in children is a disturbance in arterial baroreflex. Abnormal reflex activity is caused by excessive vagal tone and sympathetic withdrawal, which leads to a critical decrease in cerebral blood flow<sup>[2]</sup>. During the initial paraclinical evaluation for syncope, a

12-lead electrocardiogram is advisable to exclude arrhythmia as the cause.

Transmural, transseptal or apicobasal dispersion of repolarization creates voltage gradients that affect the J wave and T wave of the electrocardiogram. Amplification of this repolarization underlies the development of life-threatening ventricular arrhythmias associated with various inherited or acquired ion channelopathies, which can give rise to the long QT, short QT, and Brugada syndrome<sup>[3-8]</sup>. The sympathetic withdrawal and excessive vagal tone in syncope may cause repolarization abnormality in electrocardiogram. In this study we evaluated the T-peak-to-T-end interval and its dispersion in

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children with syncope to detect possible repolarization abnormalities in these patients.

### Subjects and Methods

In a prospective study, between November 2009 and November 2010 we enrolled 54 children with possibility of syncope referred consecutively to Motahari Clinic affiliated with Shiraz University of Medical Sciences in Shiraz, Iran for tilt table test. The patients receiving any medication or with any cardiac or seizure disorder were excluded from the study. The study was approved by Ethic Committee of Shiraz University of Medical Sciences and informed consent was deemed unnecessary by the board because no intervention in any form was administered by the researchers. We recorded clinical history, tilt test results and electrocardiogram findings for all participants.

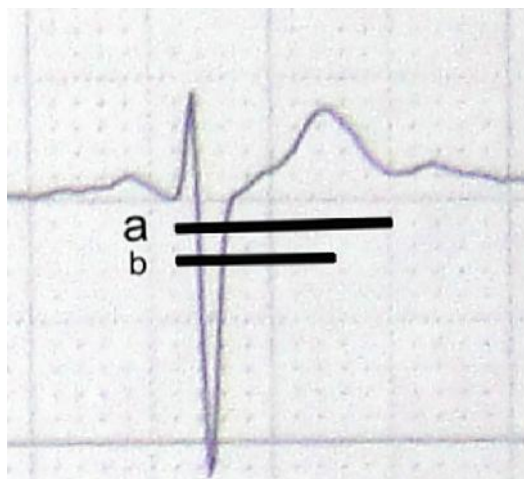
All participants were tilted on a tilt table to a 60-degree position for 45 min (Westminster protocol)<sup>[9]</sup>. At the onset of orthostatic weakness or syncope, the patients were immediately placed in the recumbent position and closely monitored until full recovery. For each participant with negative tilt table test, the tilt protocol was repeated after 10 min rest in the supine position and after the participant was given oral nitroglycerin to increase sensitivity of tilt table

test (0.2 mg for <10 year and 0.4mg for >10 year olds).

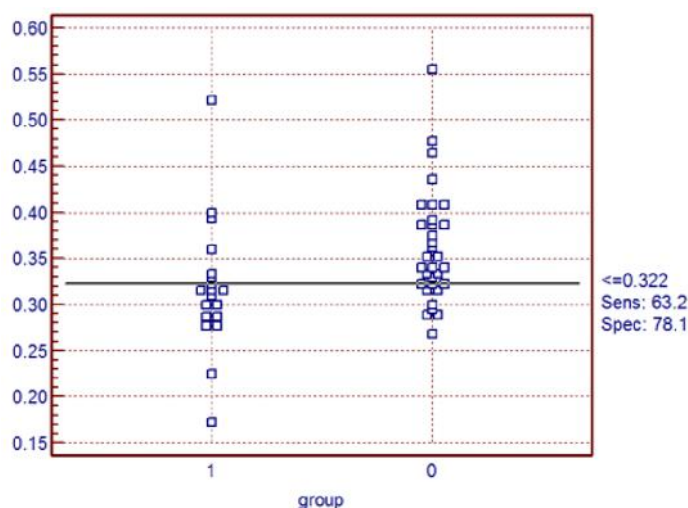
All electrocardiograms were recorded with the participant in the supine position before starting the tilt test. Recordings were made with a digital electrocardiogram machine (Alicia Diagnostics, Sanford, FL, USA). The digitally recorded electrocardiogram tracings were evaluated with a digital clipper in Corel Photo Paint v.13 software (Ottawa, Canada). Magnification of electrocardiogram made a fine determination of measurement points. T-peak-to-T-end interval and T-peak-to-T-end dispersion (defined as the difference between the maximum and minimum T-peak-to-T-end interval in precordial leads V1 to V6 during a single beat) were measured. The T-peak-to-T-end was measured in each precordial lead and obtained from the difference between QT interval and QT peak interval, measured from the beginning of the QRS until the peak of the T-wave (Fig. 1).

The patients with positive tilt table test result were considered as case group and the patients with negative test as control group. T-peak-to-T-end interval and T-peak-to-T-end dispersion were compared in cases and controls.

SPSS statistical software (SPSS Inc., Chicago, IL, USA) (version 15) and MedCalc 8.0 software (Mariakerke, Belgium) were used for data analysis. To examine the prognostic value of T-peak-to-T-end interval and T-peak-to-T-end dispersion and determine cutoff values, receiver



**Fig. 1:** The T-peak-to-T-end was measured from the difference between QT interval (line a) and QT peak interval (line b), measured from the beginning of the QRS until the peak of the T-wave



**Fig. 2:** Receiver operating characteristic curve shows the hot point of T-peak-to-T-end interval in lead V1 for detection of patients with and without syncope

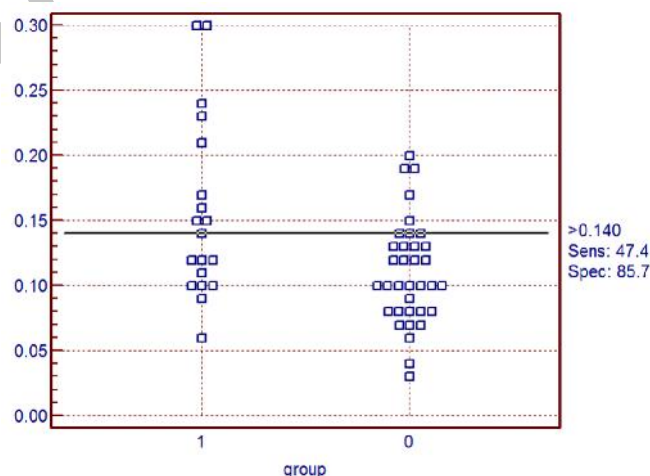
operating characteristic curves were plotted according to standard procedures. We used the Mann-Whitney test to compare the results between cases and controls. The intraobserver and interobserver variability were assessed in 10 patients with negative test for syncope using intraclass correlation and coefficients of variation, respectively. A value of  $P$  less than 0.05 was considered statistically significant.

## Findings

Tilt table test was positive in 19 patients (7 boys,

12 girls) and 35 patients had negative tilt test. Mean age was  $11.4 \pm 3.1$  years in the patients with positive tilt test and  $10.0 \pm 5.1$  years in the patients with negative tilt test ( $P=0.27$ ). According to the European Task Force on Syncope classification, 18 patients had type 1 syncope (mixed type), in which heart rate fell at the time of syncope but did not fall to less than 40 beats per minute for longer than 10 seconds with or without asystole for less than 3 seconds, in this type of syncope, blood pressure fell before heart rate did. One patient had type 2B syncope (cardioinhibition with asystole).

In this type asystole occurred for longer than 3 seconds and the fall in blood pressure coincided with or preceded the fall in heart rate<sup>[10]</sup>. Five



**Fig. 3:** Receiver operating characteristic curve shows the hot point of T-peak-to-T-end dispersion for detection of patients with and without syncope

patients developed syncope after using nitroglycerin, but there was no statistically significant difference in the frequency of T-peak-to-T-end between patients who received medication and those without medication ( $P=0.68$ ). The T-peak-to-T-end interval in lead V1 was statistically longer in patients with a positive tilt test ( $0.36\pm0.062$  vs  $0.32\pm0.071$ ,  $P=0.007$ ). Table 1 shows the T-peak-to-T-end dispersion in precordial leads. Analysis of the receiver operating characteristic curve (Fig 2) showed that a T-peak-to-T-end interval larger than 0.32 in lead V1 had a sensitivity of 68.2%, a specificity of 78.1% and a positive likelihood ratio of 3.13 for the detection of syncope. T-peak-to-T-end dispersion was significantly larger in the case group ( $0.15\pm0.07$  vs  $0.11\pm0.04$ ;  $P=0.003$ ). Analysis of the ROC curve (Fig 3) showed that a T-peak-to-T-end dispersion larger than 0.14 had a sensitivity of 47.4 %, a specificity of 85.7 % and a positive likelihood ratio of 3.32 for detecting patients with syncope.

There was good agreement between the two independent observers' measurements for the duration of the QT interval, the time interval between the onset to peak of T wave; and the T-peak-to-T-end was  $r=0.94$ ,  $r=0.93$ , and  $r=0.91$ , respectively. Interobserver variability for the time interval between the QT interval, the time interval between the onset and peak of T wave, and the T-peak-to-T-end was  $5\pm3\%$ ,  $4\pm3\%$ , and  $3\pm3\%$ , respectively. Reproducibility for the QT interval,

the time interval between the onset and peak of T wave, and the T-peak-to-T-end were  $7\pm4\%$ ,  $5\pm3\%$ , and  $6\pm3\%$ , respectively. The reproducibility of measurements was not affected by the heart rate (range, 110–160).

## Discussion

This study found a statistically significant increase in T-peak-to-T-end interval in lead V1 and T-peak-to-T-end dispersion in patients with a positive tilt test, compared to children with a negative tilt test. These findings reveal presence of repolarization abnormality in patient with syncope. Currently, upright tilt testing is a widely accepted diagnostic test for evaluating patients with syncope<sup>[10-14]</sup>. This test provides diagnostic evidence of the susceptibility to neurally-mediated syncope and it is considered the "gold standard" for establishing this diagnosis.

In this study also 94% (18 from 19) patients had type 1 syncope (mixed type). Type I syncope is the most common type of syncope. According to a new classification which has been proposed by the European Task Force on Syncope, four types of syncope have now been described.

Type 1: Mixed type. Heart rate falls at the time of syncope but does not fall to  $<40$  beats per

**Table 1:** T-peak to T-end dispersion measured in the precordial leads in the patients with negative tilt test result (0) and patients with a positive tilt test (1).

Parameter	Group	Mean (SD)
T-peak to T-end dispersion	0	0.11 (0.04)
	1	0.16 (0.07)
T-peak to T-end in V1	0	0.36 (0.06)
	1	0.32 (0.07)
T-peak to T-end in V2	0	0.37 (0.09)
	1	0.42 (0.14)
T-peak to T-end in V3	0	0.36 (0.08)
	1	0.39 (0.14)
T-peak to T-end in V4	0	0.38 (0.08)
	1	0.39 (0.09)
T-peak to T-end in V5	0	0.37 (0.05)
	1	0.40 (0.09)
T-peak to T-end in V6	0	0.37 (0.06)
	1	0.39 (0.08)

SD: standard Deviation; The patients with negative tilt test result (0) and patients with a positive tilt test (1)

minute for >10 seconds with or without asystole for <3 seconds. Blood pressure falls before heart rate falls.

Type 2A: Cardioinhibition without asystole. Heart rate falls to a ventricular rate <40 beats per minute for >10 seconds but asystole of >3 seconds does not occur. Blood pressure falls before the heart rate falls. Type 2B: Cardioinhibition with asystole. Asystole occurs for >3 sec. Blood pressure fall coincides with or occurs before the heart rate fall.

Type 3: Vasodepressor. Heart rate does not fall >10 % from its peak at the time of syncope<sup>[10]</sup>.

The electrocardiogram is another important component in the work-up of patients with syncope; this study establishes a definite diagnosis in approximately 5 percent of patients and is suggestive of the diagnosis in another 5 percent. Some findings that may identify the probable cause of syncope include prolonged QT interval (long QT syndrome), the presence of a delta wave (Wolff-Parkinson-White syndrome), the presence of a right bundle branch block pattern with ST segment elevation (Brugada syndrome), heart block, or the presence of T-wave inversion in the right precordial leads (arrhythmogenic right ventricular dysplasia). However, most patients with syncope have normal electrocardiogram results. This fact suggests that cardiac anomalies are an unlikely cause of syncope, which accordingly is often associated with a good prognosis, particularly in young patients. In spite of the low diagnostic yield of electrocardiogram, it is inexpensive and risk-free. For these reasons, an electrocardiogram is considered a standard part of the evaluation for virtually all patients with syncope<sup>[10]</sup>.

The interval from the peak of the T wave to the end of the T wave in the electrocardiogram tracing has been referred to as the T-peak-to-T-end interval. This parameter is an indicator of transmural dispersion of surface electrocardiogram, which evaluates ventricular repolarization, and also is an indicator of the risk of arrhythmia.

Three electrophysiological types of cells - endocardial, epicardial, and M cells -, have been identified in the ventricular myocardium. Differences in the course of repolarization of these

three myocardial cell types contribute to the inscription of the T-wave on the electrocardiograph<sup>[15]</sup>. The peak of the T-wave coincides with epicardial repolarization and the end of the T-wave with repolarization of the M cells, so that T-peak-to-T-end interval is an indicator of the transmural dispersion of repolarization<sup>[5]</sup>. Measuring T-peak-to-T-end dispersion provides an indicator of the maximum dispersion of repolarization: this indicator reflects variations of the transmural dispersion of repolarization among different regions of the ventricular myocardium. This interval can be a helpful predictor of the development of life-threatening arrhythmias<sup>[16,17]</sup>, as shown in studies that found it to be a risk factor for sudden cardiac death or ventricular arrhythmias in patients with Brugada syndrome and hypertrophic cardiomyopathy<sup>[18,19]</sup>. However, other studies showed that prolonged T-peak-to-T-end interval was not associated with increased arrhythmic risk in patients with long QT syndrome<sup>[20]</sup>, or in post-myocardial infarction patients treated with amiodarone<sup>[21,22]</sup>. Takenaka et al showed that exercise can accentuate T-peak-to-T-end interval in patients with the form of congenital long-QT syndrome type 1 caused by a functional defect in the slow component of the delayed rectifier potassium current, but not in those with the type 2 form of congenital long-QT syndrome caused by a functional defects in the rapid component of the delayed rectifier potassium current<sup>[23]</sup>. Topilski et al found that QT, corrected QT and T-peak-to-T-end intervals were strong predictors of torsade de pointes<sup>[24]</sup>. Watanabe et al demonstrated that prolonged T-peak-to-T-end interval was associated with the development of ventricular tachycardia in high-risk patients with organic heart disease<sup>[25]</sup>. A study also showed relationship between the T-peak to T-end interval, ventricular tachyarrhythmia, and death<sup>[26]</sup>.

Current recommendations are to measure the T-peak-to-T-end interval in the precordial leads. If biphasic or triphasic T waves occur, the recommendation is to measure the interval from the first components nadir of the T wave to the end of the T wave<sup>[27,28]</sup>. To our knowledge, no studies have evaluated the relationship between T-peak-to-T-end and syncope, but a study by



Kula S et al showed that corrected QT dispersion measured in patients with neurally-mediated cardiac syncope showed circadian variations, with peak values in the late night and morning hours. They observed that corrected QT dispersion peaked in the morning hours, which coincides with the time of the peak number of episodes in these patients<sup>[29]</sup>. A study by Benatar and Carbonez showed that the T-peak-to-T-end interval lengthened with increasing age as the heart rate decreased<sup>[30]</sup>, and another report found no gender differences in T-peak-to-T-end interval between boys and girls<sup>[31]</sup>.

Patients with catecholaminergic polymorphic ventricular tachycardia and the *RyR2* mutation show increased T-peak-to-T-end interval at high heart rates, which improves with beta-blocker treatment<sup>[32]</sup>. The T-peak-to-T-end interval cannot be used to distinguish symptomatic from asymptomatic patients with congenital long QT syndrome. The T-peak-to-T-end to QT interval ratio has been shown to be an electrocardiographic indicator of arrhythmogenesis for both congenital and acquired ion channel diseases that lead to ventricular arrhythmias.

Small sample size was the major limitation of our study which may preclude generalization of this study.

## Conclusion

Our study of a sample of children with syncope shows that T-peak-to-T-end interval in lead V1 and T-peak-to-T-end dispersion were significantly larger in patients with a positive tilt test, and we suggest that this parameter may be useful in diagnosing pediatric patients with syncope.

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**Conflict of Interest:** None

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