

Prolongation of ventricular depolarization and repolarization in patients with cardiac surgery

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ARTICLE INFORMATION

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Competing interests

The authors declare no competing interests

Acronyms

CABG: coronary artery bypass graft surgery
ECG: electrocardiogram
QT: QT interval
QTc: corrected QT interval
QTd: QT interval dispersion
T_{PE}: T_{PEAK}-T_{END} interval
T_{PEd}: T_{PEAK}-T_{END} interval dispersion

ABSTRACT

Introduction: Cardiac surgery involves a series of aggressive mechanical and chemical elements that affect the cardiac muscle; which may be shown by the electrocardiogram.

Objectives: To evaluate whether electrocardiographic measurements reflecting ventricular depolarization and repolarization are prolonged after cardiac surgery.

Method: We studied 51 patients with cardiac surgery who underwent an electrocardiogram before and after surgery. The difference between QT, QTc, QT dispersion, T_{PEAK}-T_{END} interval (T_{P-T_E}), T_{P-T_E} dispersion and QRS duration, before and after surgery was compared using the T test.

Results: Electrocardiogram after surgery showed significantly higher QTc values, QT dispersion, T_{P-T_E}, T_{P-T_E} dispersion and QRS duration (p<0.006). The uncorrected QT interval was greater in the postoperative electrocardiogram, without statistically significant difference (p=0.49).

Conclusions: Myocardial aggression during cardiac surgery modifies the ventricular electrical activity and is verified by the significantly prolonged depolarization and repolarization measurements. These variables could be used in future studies as predictors of adverse events in this procedure.

Keywords: Cardiac surgery, Myocardial aggression, Electrocardiogram

Prolongación de la despolarización y la repolarización ventriculares en pacientes operados de cirugía cardíaca

RESUMEN

Introducción: La cirugía cardíaca establece una serie de elementos mecánicos y químicos de agresión al músculo cardíaco, que pudiese verse reflejada en el electrocardiograma.

Objetivo: Evaluar si las medidas electrocardiográficas que reflejan la despolarización y la repolarización ventriculares se prolongan posterior a la cirugía cardíaca.

Método: Se estudiaron 51 pacientes con cirugía cardíaca, a quienes se les realizó electrocardiograma antes y después del procedimiento. Se comparó, mediante la prueba T, la diferencia de los valores de intervalo QT, QTc, dispersión del QT, intervalo T_{PICO}-T_{FINAL} (T_{P,F}), dispersión del T_{P,F} y duración del QRS, antes y después de la intervención quirúrgica.

Resultados: Los valores del QTc, dispersión del QT, T_{P,F}, dispersión del T_{P,F} y duración del QRS fueron significativamente mayores (p<0,006) en el electrocardio-

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grama posterior a la cirugía. El intervalo QT sin corregir fue mayor en el electrocardiograma posquirúrgico, sin diferencia estadísticamente significativa ($p=0,49$).

Conclusiones: La agresión al músculo cardíaco durante la cirugía cardíaca modifica la actividad eléctrica ventricular y se constata en la prolongación significativa de las mediciones que reflejan la despolarización y repolarización ventriculares. Estas variables pudieran utilizarse en futuros estudios como predictores de eventos adversos de este procedimiento.

Palabras clave: Cirugía cardíaca, Agresión miocárdica, Electrocardiograma

INTRODUCTION

Cardiac tissue damage is known to occur following cardiac surgery due, in part, to a series of chemical and metabolic changes related to the surgical technique, as well as to the effects produced by the drugs used in the procedure¹. The present study was designed to demonstrate the electrical alterations after cardiac surgery by comparing the differences between pre and post-surgical electrocardiogram (ECG) measures that reflect ventricular depolarization and repolarization, such as: QT interval, corrected QT interval (QTc), QT interval dispersion (QTd), T_{PEAK}-T_{END} interval (T_{P-E}), T_{P-E} dispersion (T_{P-Ed}) and QRS duration.

METHOD

Between August and November 2017, patients who underwent surgery at the Instituto de Cardiología y Cirugía Cardiovascular from Havana, Cuba, were studied. All patients underwent 12-lead ECGs prior to surgery and immediately upon arrival in the post-surgical intensive care unit. Those with previous arrhythmias, permanent pacemakers or with external pacemaker-dependent rhythm placed during surgery were excluded.

The QT, QTc, QTd, T_{P-E}, T_{P-Ed} and QRS duration were measured manually. Twelve-lead electrocardiograms were recorded at a paper speed of 25 mm per second. QTc was calculated using the Bazett formula². QT interval was measured from the beginning of the QRS complex to the end of the T wave, defined as the intercept between the isoelectric line and a tangent line drawn to the steepest part of the T wave³. QTd was defined as the difference between the maximum and minimum QT interval in the 12-lead ECGs⁴. T_{P-E} was obtained from the highest value obtained in the precordial leads, by the difference between the QT interval and the peak QT interval

(measured from the beginning of the QRS complex to the peak of the T wave). In the case of negative or biphasic T waves, the Q-T peak interval was measured until the first nadir of the T wave. T waves less than 1.5 mm in amplitude were not measured. T_{P-Ed} was obtained from the difference between the maximum and minimum T_{P-E} obtained in the precordial leads⁵. Measurements were made by two independent observers, in case of a difference of >20 ms a third measurement was made by another observer (**Figure 1** and **Figure 2**).

Numerical variables were first compared with the F test for two variances and, according to the result, the two sample t-test was applied for equal or unequal variances according to the first analysis.

RESULTS

Fifty-one patients (60±11 years), predominantly males (78%), who underwent cardiac surgery were studied. A total of 27 patients underwent coronary artery bypass graft surgery (CABG), 21 valvular surgery, 2 combined surgeries, and 1 case of atrial myxoma excision.

QTc, QTd, T_{P-E}, T_{P-Ed} values and QRS duration were significantly higher in the postoperative ECG ($p<0.006$). QT interval was also higher in this ECG, but there was no significant difference ($p=0.49$) (**Table 1**).

When the two main study-groups (CABG vs. valvular surgery), were analyzed, we found that both groups similarly showed prolonged values in the different electrocardiographic measurements (**Table 2**). However, it is striking that, although there was an increase in the QTd and T_{P-E} values in the group of CABG-patients, such increase was not statistically significant; unlike the valvular surgery group (where it did occur). It should be noted that, as was observed in the general group (**Table 1**), the QT interval had practically no variation in such groups.

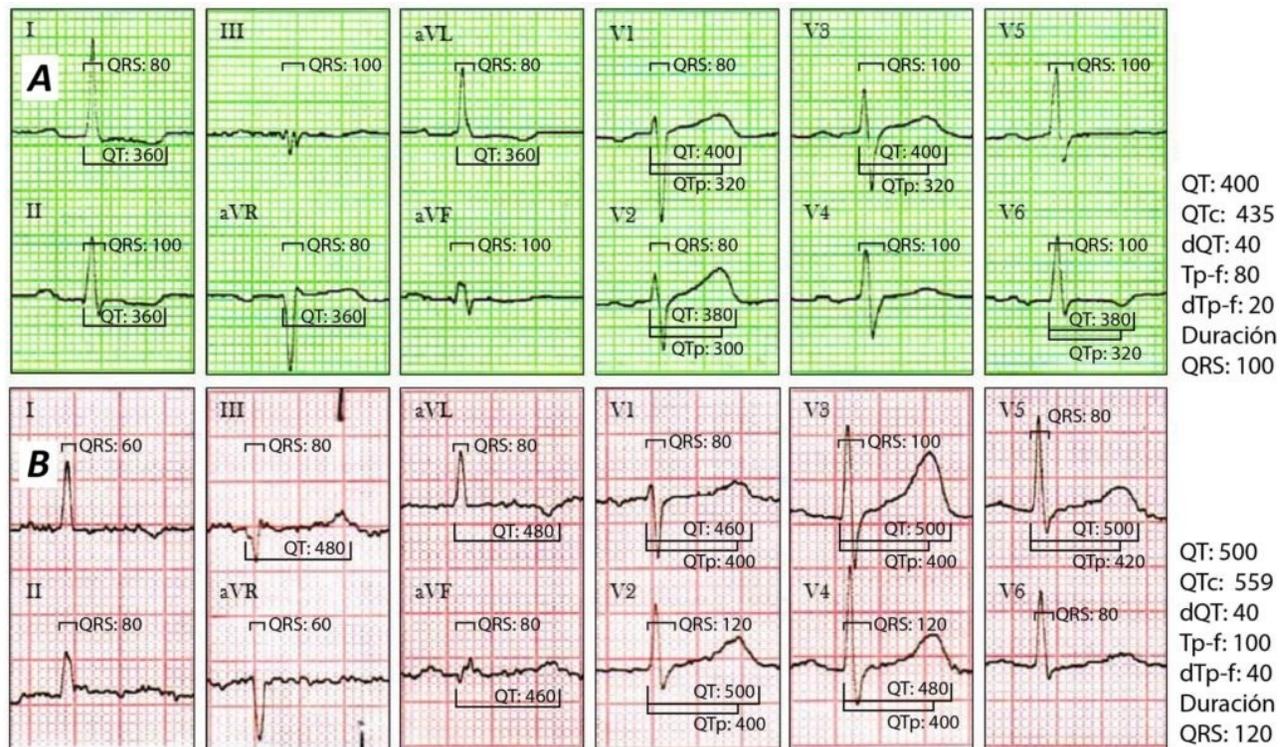


Figure 1. Electrocardiograms of a 74-year-old woman who underwent aortic valve replacement surgery. **A.** Preoperative. **B.** Postoperative. All values are in milliseconds, T waves < 1.5 mm were not measured. ECGs standardized at 25 mm/s and 10 mm/mV.

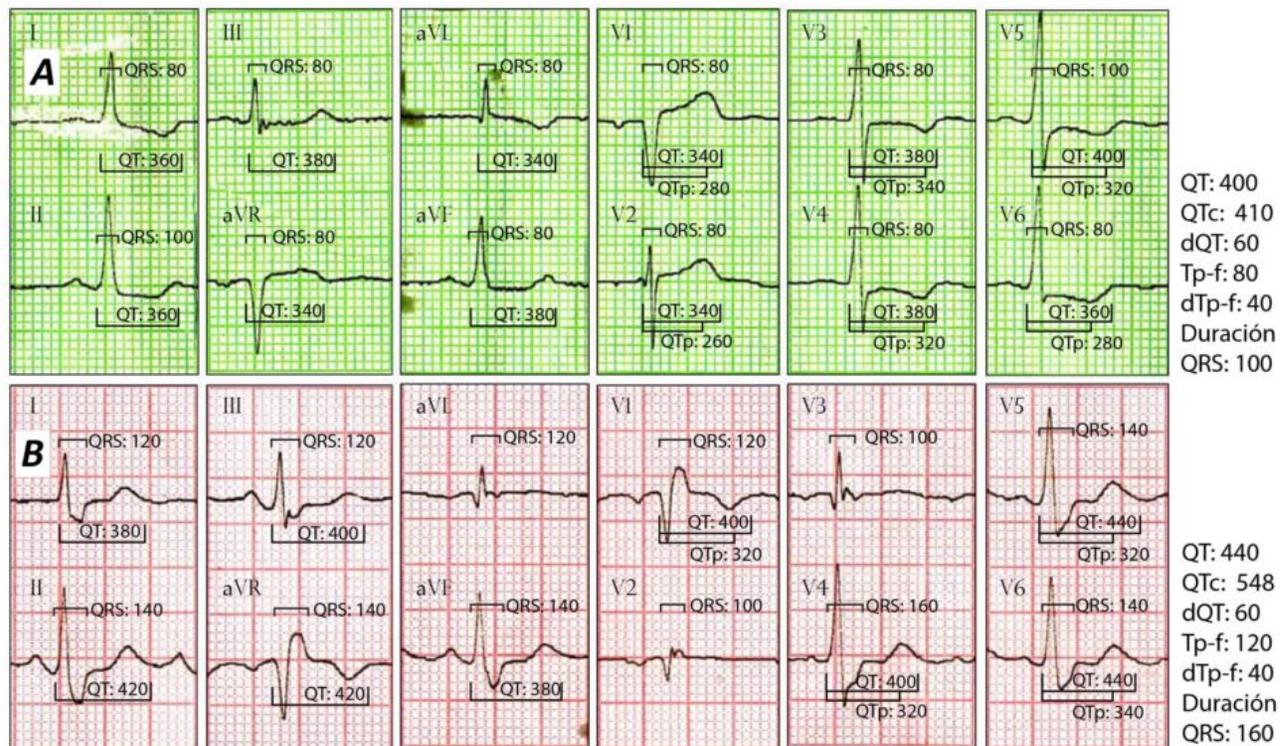


Figure 2. Electrocardiograms of a 64-year-old man who underwent coronary artery bypass graft surgery. **A.** Preoperative. **B.** Postoperative. All values are in milliseconds, T waves < 1.5 mm were not measured. ECGs standardized at 25 mm/s and 10 mm/mV.

Table 1. Comparison of pre and postoperative electrocardiographic measurements in patients who underwent cardiac surgery (n=51).

| Parameter | Electrocardiogram | | p |
|-------------------|-------------------|---------------|--------------------|
| | Preoperative | Postoperative | |
| QT | 382 ± 40 | 388 ± 46 | 0.490* |
| QTc | 414 ± 32 | 462 ± 41 | 0.000 ^Ω |
| QTd | 36 ± 22 | 49 ± 25 | 0.006* |
| T _{P-E} | 80 ± 15 | 93 ± 23 | 0.002 ^Ω |
| T _{P-Ed} | 25 ± 12 | 41 ± 19 | 0.006 ^Ω |
| QRS width | 85 ± 12 | 97 ± 17 | 0.000 ^Ω |

The values are in milliseconds and express mean ± standard deviation.

* T test for two samples with equal variances.

^Ω T test for two samples with unequal variances.

DISCUSSION

The prolongation of electrocardiographic measurements that reflect ventricular depolarization and repolarization may be due to congenital or acquired causes^{6,7}. Our study demonstrated that the measurements of QTc, QTd, T_{P-E}, T_{P-Ed} and QRS duration are prolonged in the ECG after cardiac surgery with respect to the baseline. The QT interval reflects both depolarization and ventricular repolarization. The PROLOQIT results showed that both mechanical and pharmacological aggression to the myocardium during cardiac surgery affects depolarization and ventricular repolarization, which prolongs QTc. This

study included 259 patients and found a postoperative QTc of 462±43 ms, results similar to our findings⁶.

Biry *et al*⁸ also showed prolongation of QTc by assessing 82 patients with cardiac surgery and found that 25% of them had very long QTc (>500 ms), while the majority had moderate QTc prolongation (>440 ms in men and >460 ms in women)⁸. The impact of QTc prolongation in cardiac surgery is still under discussion, as there are studies such as that of Pasquier *et al*⁹ which did not show an increase in mortality related to QTc prolongation, in contrast to that of Tisdale *et al*¹⁰, demonstrating the contrary.

It should be noted that in our study the QT interval did not show any significant variation, however the QTc interval did. This is due to the fact that the RR interval was significantly lower in the postoperative ECG (869±183 vs. 713±136 ms; p<0.0001), which indicates the importance of correcting the above-mentioned interval.

The dispersion of ventricular repolarization can be assessed by QTd, in such a way that its prolongation is related to a marked heterogeneity of transmural refractoriness¹¹. Normal values range between 30 and 65 ms and its prolongation has been related to congenital long QT and acute ischemic heart disease¹².

We did not find data regarding QTd and cardiac surgery. We observed in our study that although the values of both pre and postoperative QTd were normal, the difference was statistically significant (36±22 vs. 49±25 ms, p<0.0001), which reflects alteration in the homogeneity of ventricular repolarization.

Table 2. Comparison of measurements between pre and postoperative electrocardiograms in patients with coronary artery bypass graft surgery and cardiac valvular surgery.

| Parameter | Coronary artery bypass graft surgery (n=27) | | p | Valvular surgery (n=21) | | p |
|-------------------|---------------------------------------------|---------------|--------------------|-------------------------|---------------|--------------------|
| | Preoperative | Postoperative | | Preoperative | Postoperative | |
| QT | 380 ± 33 | 384 ± 47 | 0.689 ^Ω | 384 ± 49 | 391 ± 47 | 0.611* |
| QTc | 404 ± 27 | 455 ± 44 | 0.000* | 427 ± 35 | 471 ± 40 | 0.000* |
| QTd | 36 ± 25 | 45 ± 26 | 0.207* | 39 ± 18 | 53 ± 23 | 0.003* |
| T _{P-E} | 78 ± 13 | 86 ± 22 | 0.104 ^Ω | 85 ± 18 | 113 ± 21 | 0.004* |
| T _{P-Ed} | 26 ± 13 | 42 ± 20 | 0.002 ^Ω | 26 ± 11 | 42 ± 18 | 0.001 ^Ω |
| QRS width | 86 ± 12 | 96 ± 18 | 0.015 ^Ω | 85 ± 12 | 98 ± 18 | 0.007* |

The values are in milliseconds and express mean ± standard deviation.

* T test for two samples with equal variances.

^Ω T test for two samples with unequal variances.

Prolonged T_{P-E} is also related to alterations in ventricular repolarization, and has been associated with an increase in cardiovascular mortality and heart failure, according to the Copenhagen study¹³. In addition, the prolongation of T_{P-E} is a marker associated with increased arrhythmogenic risk in Brugada and long QT syndromes, hypertrophic cardiomyopathy and structural heart disease^{5,14-18}.

In our study, T_{P-E} considerably increased after cardiac surgery (80 ± 15 vs. 93 ± 23 ms $p=0.002$), which demonstrates the transmural instability of the heart muscle after this surgical procedure. But we did not find previous published reports in this type of patients.

The T_{P-Ed} was proposed by Castro Hevia *et al*¹⁴, as a predictor of malignant arrhythmias in Brugada syndrome. It was then applied in other conditions and proved to be useful as a predictor of malignant arrhythmias and sudden cardiac death¹⁹. We have not seen data on this marker in patients with cardiac surgery and found a significantly increased postoperative value (T_{P-Ed} 25 ± 12 vs. 41 ± 19 ms, $p=0.006$), which reflects an alteration in the transmural dispersion of repolarization in different areas of the heart.

Conduction delays reflected in the increase in QRS duration has been assumed to be an arrhythmogenic risk factor in various disorders such as the J wave syndrome²⁰⁻²². We have not found data in patients with cardiac surgery. In our study, however, patients had an increase in QRS duration after surgery (88 ± 12 vs. 97 ± 17 ms, $p<0.0001$), which may reflect a postoperative intraventricular conduction disorder.

CONCLUSIONS

The electrocardiographic measurements analyzed (QTc, QTd, T_{P-E} , T_{P-Ed} , QRS duration) may represent, from the electrical point of view, the aggression inflicted on the heart muscle during surgery. Whether these measurements predict adverse events in the patients deserves further study.

REFERENCES

1. Desborough JP. The stress response to trauma and surgery. *Br J Anaesth.* 2000;85(1):109-17.
2. Bazett HC. An analysis of the time-relations of electrocardiograms. *Ann Noninvasive Electrocardiol.* 1997;2(2):177-194.
3. Rautaharju PM, Surawicz B, Gettes LS, Bailey JJ, Childers R, Deal BJ, *et al.* AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram. Part IV: The ST segment, T and U waves, and the QT interval: A scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. *Circulation.* 2009;119(10):e241-250.
4. Day CP, McComb JM, Campbell RW. QT dispersion: an indication of arrhythmia risk in patients with long QT intervals. *Br Heart J.* 1990;63(6):342-4.
5. Maury P, Sacher F, Gourraud JB, Pasquié JL, Raczka F, Bongard V, *et al.* Increased Tpeak-Tend interval is highly and independently related to arrhythmic events in Brugada syndrome. *Heart Rhythm.* 2015;12(12):2469-76.
6. Toma M, Marstrand P, Holmenlund K, Umar S, Wanscher M, Pehrson S, *et al.* QT interval prolongation after cardiac surgery; an interesting biological phenomenon or a clinical problem? Data from the Prolongit Study. *J Clin Toxicol [Internet].* 2014 [citado 30 Ener 2018];4(3):195. Disponible en: <https://www.omicsonline.org/open-access/interesting-biological-phenomenon-or-a-clinical-problem-data-from-the-prolongit-study-2161-0495.1000-195.pdf>
7. Yan GX, Shimizu W, Antzelevitch C. Characteristics and distribution of M cells in arterially perfused canine left ventricular wedge preparations. *Circulation.* 1998;98(18):1921-7.
8. Biry M, Schurr U, Ritter S, Baenziger K, Zollinger A, Genoni M. High incidence of severely prolonged QT interval after cardiac surgery. *Crit Care.* 2010;14(Supl 1):P134 [Resumen].
9. Pasquier M, Pantet O, Hugli O, Pruvot E, Buclin T, Waeber G, *et al.* Prevalence and determinants of QT interval prolongation in medical inpatients. *Intern Med J.* 2012;42(8):933-40.
10. Tisdale JE, Wroblewski HA, Overholser BR, Kingery JR, Trujillo TN, Kovacs RJ. Prevalence of QT interval prolongation in patients admitted to cardiac care units and frequency of subsequent administration of QT interval-prolonging drugs: a prospective, observational study in a large urban academic medical center in the US. *Drug Saf.* 2012;35(6):459-70.
11. Antzelevitch C, Shimizu W, Yan GX, Sicouri S. Cel-

- ular basis for QT dispersion. *J Electrocardiol.* 1998;30(Supl 1):168-75.
12. Zayas Molina R, Díaz Garriga RE, Dorantes Sánchez M. Dispersión del intervalo QT: un predictor de arritmias ventriculares malignas. *Rev Cubana Cardiol Cir Cardiovasc.* [Internet]. 2000 [citado 30 Ene 2018];14(2):116-23. Disponible en: <http://revcardiologia.sld.cu/index.php/revcardiologia/article/view/496/423>
 13. Bachmann TN, Skov MW, Rasmussen PV, Graff C, Pietersen A, Lind B, et al. Electrocardiographic Tpeak-Tend interval and risk of cardiovascular morbidity and mortality: Results from the Copenhagen ECG study. *Heart Rhythm.* 2016;13(4):915-24.
 14. Castro Hevia J, Antzelevitch C, Tornés Bázquez F, Dorantes Sánchez M, Dorticós Balea F, Zayas Molina R, et al. Tpeak-Tend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the Brugada syndrome. *J Am Coll Cardiol.* 2006;47(9):1828-34.
 15. Rosenthal TM, Stahls PF, Abi Samra FM, Bernard ML, Khatib S, Polin GM, et al. T-peak to T-end interval for prediction of ventricular tachyarrhythmia and mortality in a primary prevention population with systolic cardiomyopathy. *Heart Rhythm.* 2015;12(8):1789-97.
 16. Panikkath R, Reinier K, Uy-Evanado A, Teodorescu C, Hattenhauer J, Mariani R, et al. Prolonged Tpeak-to-Tend interval on the resting ECG is associated with increased risk of sudden cardiac death. *Circ Arrhythm Electrophysiol.* 2011;4(4):441-7.
 17. Barbhaiya C, Po JR, Hanon S, Schweitzer P. Tpeak - Tend and Tpeak - Tend/QT ratio as markers of ventricular arrhythmia risk in cardiac resynchronization therapy patients. *Pacing Clin Electrophysiol.* 2013;36(1):103-8.
 18. Haarmark C, Hansen PR, Vedel-Larsen E, Pedersen SH, Graff C, Andersen MP, et al. The prognostic value of the Tpeak-Tend interval in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. *J Electrocardiol.* 2009;42(6):555-60.
 19. Castro-Torres Y, Carmona-Puerta R, Katholi RE. Ventricular repolarization markers for predicting malignant arrhythmias in clinical practice. *World J Clin Cases.* 2015;3(8):705-20.
 20. Smits JP, Eckardt L, Probst V, Bezzina CR, Schott JJ, Remme CA, et al. Genotype-phenotype relationship in Brugada syndrome: electrocardiographic features differentiate SCN5A-related patients from non-SCN5A-related patients. *J Am Coll Cardiol.* 2002;40(2):350-6.
 21. Yokokawa M, Noda T, Okamura H, Satomi K, Suyama K, Kurita T, et al. Comparison of long-term follow-up of electrocardiographic features in Brugada syndrome between the SCN5A-positive probands and the SCN5A-negative probands. *Am J Cardiol.* 2007;100(4):649-55.
 22. Watanabe H, Nogami A, Ohkubo K, Kawata H, Hayashi Y, Ishikawa T, et al. Electrocardiographic characteristics and SCN5A mutations in idiopathic ventricular fibrillation associated with early repolarization. *Circ Arrhythm Electrophysiol.* 2011;4(6):874-81.