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The Correlation between QT Dispersion and Severity of Pulmonary Valve Stenosis

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Abstract

Background: The heart rate-corrected QT interval (QTc) and QTc dispersion (QTcd) are prolonged and associated with ventricular arrhythmia and an increase in sudden death in a variety of diseases such as coronary heart disease, heart failure, hypertension and diabetes mellitus.

Objective: Study of the relation between QTcd, QT interval and QTc and severity of pulmonary stenosis.

Methods: A prospective observational cohort single center study in a period of 10 months starting from June 2016 to March 2017 at Cardiovascular Medicine Department, Tanta University Hospitals in Gharbia Governorate, Egypt. The study enrolled 50 subjects of both genders; 40 patients who were diagnosed with pulmonary stenosis & 10 subjects matched in age, sex, weight and body surface area as a control group. Resting 12-lead electrocardiogram was recorded. QT interval was measured manually and corrected using Bazett's formula. Patients were divided into groups with mild, moderate and severe pulmonary valve stenosis and a control group according to peak pressure gradient across pulmonary valve.

Results: In all observed cases, mean QTc was higher in severe pulmonary valve stenosis than in controls (448.67±28.0 ms vs. 404.0± 19.55ms, p=0.001) and QTcd was higher in mild, moderate (51.75±2.18 & 69.23±6.07ms respectively) and severe pulmonary valve stenosis (79.27±6.73ms) than in controls (46.20±5.49ms) (p=0.001).

Conclusion: In patients with pulmonary valve stenosis, mean QTc and QTcd are positively correlated to peak pressure gradient across pulmonary valve and are significantly increased in patients with severe pulmonary valve stenosis.

Key Words: *Pulmonary valve stenosis – QT dispersion – QT interval – Electrocardiogram – Peak pulmonary pressure gradient.*

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Introduction

THE valvular Pulmonary Stenosis (PS) has been reported at 0.6 to 0.8 per 1000 live births, and when associated with other congenital cardiac lesions, it may occur in as many as 50% of all patients with congenital heart disease [1]. It may interfere with the growth and development of the lung and cause pressure overload on the right heart. This may predispose the patient to cardiac failure, limited exercise tolerance, and arrhythmias [1].

Pulmonary valvular stenosis can be divided into mild, moderate, and severe according to the Right Ventricle Systolic Pressure (RVSP) and the gradient between the pulmonary artery systolic pressure and the right ventricle systolic pressure: mild, the pressure gradient 25-40mmHg; moderate, the pressure gradient 40-60mmHg; and severe, the pressure gradient ≥60mmHg [2].

The QT interval is the duration between onset of the QRS complex and the end of the T wave in an Electrocardiogram (ECG) and reflects the repolarization time of the myocardium. QT dispersion (QTcd) is the difference in repolarization duration among several electrocardiographic leads and reflects local differences in recovery time of the myocardium [3].

Studies have shown that the heart rate-corrected QT interval (QTc) and QTcd are prolonged and associated with ventricular arrhythmia and an increase in sudden death in a variety of diseases such as coronary heart disease, heart failure, hypertension and diabetes mellitus [4]. It has been reported that QTcd is significantly increased in patients with isolated right ventricular hypertrophy [5].

The aim of this work was to study the relation between QTcd, QT interval and QTc and severity of PS.

Patients and Methods

The study was conducted as a prospective observational cohort study from June 2016 to March 2017 at Cardiovascular Medicine Department, Tanta University Hospitals in Gharbia Governorate, Egypt. The study included 50 subjects of both genders; 40 patients who were diagnosed with PS and 10 subjects matched in age, sex, weight and body surface area as a control group. Patients were divided into two groups based on peak pressure gradient across pulmonary valve: Group I (patients): Was subdivided into: Mild group: Peak gradient 25-40 mmhg [6,7], Moderate group: Peak gradient 40-60mmhg [6,7], severe group: Peak gradient ≥60mmhg [6,7] and Group II: Control group. An informed consent was taken from all participants.

Exclusion criteria were (1) Other associated congenital heart disease. (2) Irregular rhythm (3) Patients on medications affecting QT interval, QTc & QTcd e.g. (amiodarone).

All included patients were subjected to full history taking, full clinical examination, twelve-lead surface Electrocardiogram (ECG), plain chest X-ray, lab investigations and full transthoracic 2D echocardiograph assessment.

Each patient was subjected for twelve-lead surface ECG. An ECG was recorded after the patient had rested for about 10min in the supine position: 12-lead recording on a MAC 1200 ST ECG machine with 10mm/mv amplitude, paper speed 25mm/s and standard lead positions. Only ECGs with sinus rhythm were used in the study. The measurements were performed manually with a calibrator by an experienced observer blinded to the clinical data of the patients. The QT intervals were measured from the onset of the QRS complex to the end of the T wave, defined as the return to TP isoelectric baseline [8]. Only monophasic well-defined T waves were accepted for measurement. If U waves were present, the QT was measured to the nadir of the curve between the T and U waves with the aid of a tangent. If the end of the T wave could not be reliably determined, or if T waves were isoelectric or of very low amplitude (<0.05 Mv), the lead was not included in the analysis. At least two consecutive cycles were measured in each of the 12 leads, and the mean value of the consecutive cycles of each lead was calculated [8]. The QTcd was defined as the difference between the maximum and minimum QT values, and mean QT interval was calculated from the mean value of the consecutive cycles of each lead. Bazett's formula ($QTc=QT/\sqrt{RR}$) was used to obtain heart rate-corrected (c) values of QT intervals and dispersions [9]. To estimate intra-observer variability, two copies of a random sample of ten ECGs were taken and the QT interval was measured again [9].

Echocardiographic examinations were done for every patient with (Vivid 7 dimension; General Electric Medical Systems, Horten, Norway) equipped with a MHz phased array transducer, which is selected according to patient's age. Standard views (parasternal long and short axis, apical four, five and two chamber, subcostal and suprasternal views) with ECG tracing were obtained in 2D and colour modes. For data acquisition, three complete three cardiac cycles were collected and stored in a cine-loop format. Pulsed wave Doppler across the pulmonary valve measuring peak and mean pressure gradient to detect the severity of PS [10].

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, the Receiver Operating Characteristic (ROC) curve and chi-square test by SPSS V. 20. Numerical data was presented as mean and Standard Deviation (SD) and categorical data was presented as number and percentage. Chi-squared test was used for statistical analysis. When the chi-squared test was not appropriate, the Monte Carlo Exact test was applied. The level of significance was adopted at $p<0.05$.

Subjects were informed about the purpose and procedure of the study and benefits of sharing in it. Ethical considerations of the study were carried out according to that of Declaration of Helsinki.

Results

A total of 50 subjects were enrolled into this study. There were 10 cases in the control group, 12 patients with mild PS, 13 with moderate PS and 15 patients with severe PS. The final study group comprised 21 males and 19 females, mean age 12.30±5.39 years and mean body surface area 1.29±0.44m^2 (Table 1).

Regarding ECG, there was a statistically significant difference among studied groups regarding Axis (p-value=0.001) (Table 2). In the control group, all had normal axis.

There was a statistically significant difference among studied groups regarding QT interval, QTC and QTcd as they increased with increasing degree of severity of PS. It was more in moderate group than in mild and in severe group than in mild and moderate groups (p-value=0.001) (Table 3).

There was a positive correlation between the QTcd and degree of PS as QTcd increased with increasing degree of severity of pulmonary stenosis, r=0.778 and p<0.001 (Table 4) Fig. (1).

There was a statistically significant difference among studied groups regarding QTcd and symptoms of PS as when QTcd was increased there was an increase in the incidence of symptoms of PS. The ROC Curve analysis was performed for QTcd to diagnose cases with symptoms of PS. The Area Under Curve (AUC) was 0.801 (p-value=0.001) as illustrated in Fig. (2). The sensitivity was 90%, the specificity 55%, PPV=66.7% and NPV=84.6 with cut off value >57 (Table 5).

Table (1): Comparison between the studied groups according to demographic data.

		Patients (group I)						Control (group II) (n=10) No.	p
		Mild (n=12)		Moderate (n=13)		Severe (n=15)			
		No.	%	No.	%	No.	%		
Sex:									
Male		41.7	7	53.8	9	60.0	5	50.0	$\chi^2 p$=0.818
Female		58.3	6	46.2	6	40.0	5	50.0	
$p_{control}$	FE 1.000	FE 1.000		FE 1.000		FE 0.697			
p-value		p_1=0.543, p_2=0.343, p_3=0.743							
Age (years):									
Min.-max.		15.0-19.0		4.0-19.0		4.0-18.0		5.0-19.0	H p<0.001 *
Mean ± SD.		17.25±1.48		13.38±4.72		7.40±3.50		11.40±4.95	
$p_{control}$	MW 0.652	MW 0.006*		MW 0.366		MW 0.036*			
p-value		p_1=0.020*, p_2<0.001 *, p_3=0.003 *							
Weight (kg):									
Min.-max.		50.0-70.0		16.0-73.0		14.0-60.0		18.0-67.0	H p<0.001*
Mean ± SD.		61.67±5.50		47.38± 19.05		23.87± 11.73		41.20± 18.79	
$p_{control}$	MW 0.856	MW 0.037*		MW 0.456		MW 0.005 *			
p-value		p_1=0.050, p_2<0.001 *, p_3=0.002*							
BSA:									
Min.-max.		1.46-1.80		0.66-1.88		0.62-1.69		0.73-1.80	H p<0.001*
Mean ± SD.		1.69±0.11		1.39±0.40		0.88±0.28		1.34±0.43	
$p_{control}$	MW 0.5 19	MW 0.149		MW 0.803		MW 0.004*			
p-value		p_1=0.079, p_2<0.001 *, p_3=0.002*							

H : p-value for Kruskal Wallis test.
MW : p-value for Mann Whitney test.
FE : p-value for Fisher Exact test.
p : p-value for comparing between mild.
Moderate : Sever and control group.
$p_{control}$: p-value for comparing between control and total cases.
p_1 : p-value for comparing between mild and moderate group.
p_2 : p-value for comparing between mild and severe group.
p_3 : p-value for comparing between moderate and severe group.
* : Statistically significant at $p \leq 0.0$.

Table (2): Comparison between the different studied groups according to ECG findings.

ECG			Patients (group I) Mild (n=12)		Moderate (n=13)		Severe (n=15)		Control (group II) (n=10)		p
			No.	%	No.	%	No.	%	No.	%	
Rhythm:											
Sinus	40	100	12	100.0	13	100.0	15	100.0	10	100.0	–
Axis:											
Normal			11	91.7	7	53.8	5	33.3	10	100.0	^{MC}p<0.001 *
Left axis			1	8.3	1	7.7	0	0.0	0	0.0	
Right axis			0	0.0	5	38.5	10	66.7	0	0.0	
$p_{control}$	^{MC}0.042*		^{FE}1.000		^{MC}0.024*		^{FE}0.001 *				
p-value	$^{MC}p_1$=0.037*, $^{MC}p_2$<0.001*, $^{MC}p_3$=0.184										
Rate (bpm):											
Min.-max.			75.0-90.0		75.0-110.0		75.0-120.0		90.0-110.0		^{H}p<0.001 *
Mean ± SD.	^{MW}0.158		80.83±5.97		90.0±10.61		105.0±12.10		99.0±8.76		
$p_{control}$			^{MW}<0.001 *		^{MW}0.052		^{MW}0.120				
p-value	p_1=0.026*, p_2<0.001 *, p_3=0.003 *										

H : p-value for Kruskal Wallis test.
MW : p-value for Mann Whitney test.
MC : p-value for Monte Carlo.
FE : p-value for Fisher Exact test.
bpm : Beat per minute.
p : p-value for comparing between Mild.
Moderate : Sever and control group.
$p_{control}$: p-value for comparing between control and total cases.
p_1 : p-value for comparing between mild and moderate group.
p_2 : p-value for comparing between mild and severe group.
p_3 : p-value for comparing between moderate and severe group.
* : Statistically significant at $p \leq 0.05$.

Table (3): Comparison between the different studied groups according to QT interval, QTc & QTcd.

QT			Patients (group I) Mild (n=12)	Moderate (n=13)	Severe (n=15)	Control (group II) (n=10)	F_p
Interval (m sec.):							
Min.-max.			320.0-360.0	320.0-380.0	320.0-380.0	320.0-440.0	0.030*
Mean ± SD.			341.67±18.01	338.46±19.08	357.33±16.68	370.0±50.11	
$p_{control}$	#0.177		@0.088	@0.042*	@0.671		
p-value	p_1=0.991, p_2=0.458, p_3=0.277						
QTc:							
Min.-max.			390.0-450.0	390.0-460.0	390.0-480.0	380.0-440.0	<0.001 *
Mean ± SD.			427.50±16.03	437.69±20.06	448.67±28.0	404.0±19.55	
$p_{control}$	#<0.001*		@0.072	@0.004*	@<0.001 *		
p-value	p_1=0.653, p_2=0.074, p_3=0.554						
Dispersion:							
Min.-max.			48.0-55.0	58.0-76.0	57.0-87.0	39.0-56.0	<0.001 *
Mean ± SD.			51.75±2.18	69.23±6.07	79.27±6.73	46.20±5.49	
$p_{control}$	#<0.001*		@0.102	@<0.001 *	@<0.001 *		
p-value	p_1<0.001*, p_2<0.001*, p_3<0.001*						

p : p-value for ANOVA test for comparing between mild.
Moderate : Sever and control group.
: p-value for Student t-test.
@ : p-value for Post Hoc Test (Tukey).
$p_{control}$: p-value for comparing between control group and total cases or sub groups.
p_1 : p-value for Post Hoc Test (Tukey) for comparing between mild and moderate group.
p_2 : p-value for Post Hoc Test (Tukey) for comparing between mild and severe group.
p_3 : p-value for Post Hoc Test (Tukey) for comparing between moderate and severe group.
* : Statistically significant at $p \leq 0.05$.

Table (4): Correlation between QTcd and peak gradient in cases group (n=40).

	QT dispersion	
	r	*p*
Peak gradient	0.778*	<0.001 *

r: Pearson coefficient.
*: Statistically significant at $p \leq 0.05$.

Table (5): Agreement (sensitivity, specificity) for QTcd to predict cases with symptoms (dyspnea) (n=40).

	Cut off	Sensitivity	Specificity	PPV	NPV
QT dispersion	>57	90.0	55.0	66.7	84.6

AUC : Area Under a Curve.
p-value : Probability value.
CI : Confidence Intervals.
* : Statistically significant at $p \leq 0.05$.

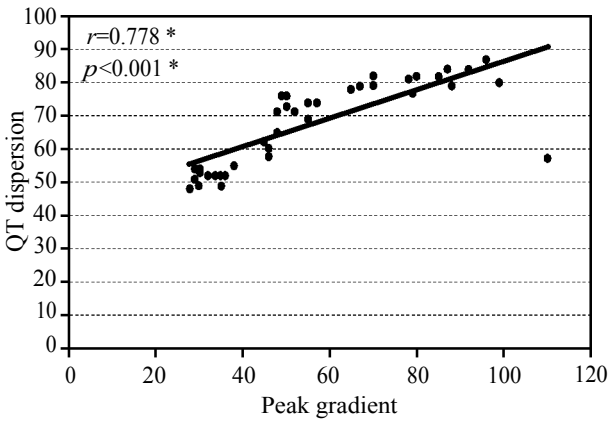
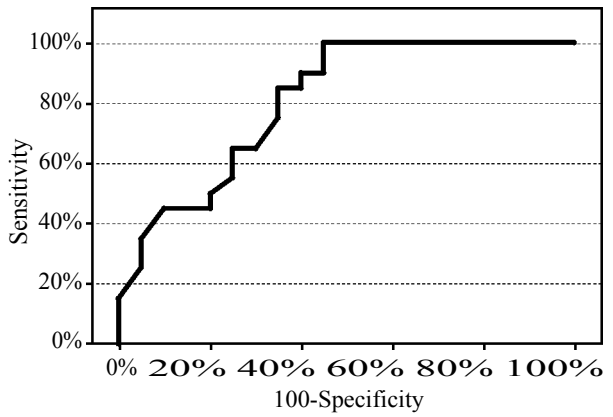


Fig. (1): Correlation between QTcd and peak gradient in patients group (n=40).



	QT dispersion
AUC	0.801 *
p	0.001*
95% C.I	0.671-0.941

Fig. (2): ROC curve for QTcd to diagnose cases with symptoms (dyspnea) (n=40).

Discussion

In this study QTc was found to increase with increasing degree of severity of PS (*p*-value=0.001).

QTcd also was found to increase with increasing degree of severity of PS, as it is increased in moderate group more than mild group and in severe group more than mild and moderate groups (*p*-value=0.001). QTc and QTcd in mild, moderate and severe PS were higher than in control group. Thereby we believe that increase pressure gradient across pulmonary valve may contribute to the increase in QTc (*p*-value=0.001) and QTcd (*p*-value=0.001).

So, QTc and QTcd were positively correlated with severity of PS as it increased with increasing degree of severity of PS (peak gradient across the pulmonary valve) (*p*-value=0.001).

QTcd reflects inhomogeneity of repolarization and delayed cardiac repolarization leading to increase the QTcd is a well-characterized precursor of arrhythmias [11]. Thus, the degree of increase in pressure gradient across pulmonary valve might be associated with increased inhomogeneity in repolarization, probably predisposing the patients to arrhythmias.

Up to our knowledge there is no previous studies discussing the correlation between QTc and QTcd and severity of PS but many studies discussing the relation between QTc and QTcd and Pulmonary Hypertension (PH).

Zhang Hong-Liang et al., [12] studied 201 patients who had undergone right heart catheterization for a preliminary diagnosis of pulmonary hypertension and found that mean QTc and QTcd were positively correlated to mean Pulmonary Artery Pressure (PAP) in women with pulmonary hypertension and were significantly increased in women with severe pulmonary hypertension.

Tuncer et al., [5] studied 25 patients with right ventricular hypertrophy without coexisting systemic hypertension, Chronic Obstructive Pulmonary Disease (COPD) or pulmonary hypertension who had emigrated from a high-altitude region to a low-altitude region 25 years previously and found that QTcd was significantly higher than in a normal control group.

Martin et al., [13] found that QTc was prolonged (defined as ›_0.45s) in two of 25 patients with right ventricular hypertrophy without other coexisting disorders but was not statistically significant in comparison with a normal control group.

Akgül et al., [14] found that among patients with sickle cell disease, those with pulmonary hypertension had significantly higher mean QTc and QTcd than patients without pulmonary hypertension. This is the only report of the effect of pulmonary hypertension on QTc and QTcd; however, the patients all had sickle cell disease-induced pulmonary hypertension. So, RV loading by any factor may affect QTc and QTcd.

Conclusion:

In patients with pulmonary valve stenosis, mean QTc and QTcd are positively correlated to peak pressure gradient across pulmonary valve and are significantly increased in patients with severe pulmonary valve stenosis.

References

1- HOFFMAN J.I. and KAPLAN S.: The incidence of congenital heart disease. J. Am. Coll. Cardiol., 39: 1890-900; 2002.

2- KIM D.H., PARK S.J., JUNG J.W., KIM N.K. and CHOI J.Y.: The Comparison between the Echocardiographic Data to the Cardiac Catheterization Data on the Diagnosis, Treatment, and Follow-Up in Patients Diagnosed as Pulmonary Valve Stenosis. J. Cardiovasc. Ultrasound, 21: 18-22, 2013.

3- FELTES T.F., BACHA E., BEEKMAN III R.H., CHEATHAM J.P., FEINSTEIN J.A., GOMES A.S., HIJAZI Z.M., ING F.F., De MOOR M., ROBERT MORROW W., MULLINS C.E., TAUBERT K.A. and ZAHN E.M. : AHA Scientific Statement Indications for Cardiac Catheterization and Intervention in Pediatric Cardiac Disease A Scientific Statement from the American Heart Association. Council on Clinical Cardiology, and Council on Cardiovascular Radiology and Intervention. Circulation, 123: 2607-52, 2011.

4- LARSEN B.S., ENGSTROM G.E., KUMARATHURAI P.K., NILSSON P.N., WENDELBOE NIELSEN O.W., JUHLIN T.J., JOHNSON L.J. and SAJADIEH A.S.: Prognostic value of excessive atrial ectopy in relation to atrial fibrillation and ischemic stroke in a large pooled scandinavian holter cohort. Journal of the American College of Cardiology, 66: 232-41, 2015.

5- TUNCER M., GUNES Y., GUNTEKIN U., ASLAN S., GUMRUKCUOGLU H.A., ERYONUCU B. and ERMIS C.: Association of increased QTc dispersion and right ventricular hypertrophy. Med. Sci. Monit., 14: CR102-105, 2008.

6- BAUMGARTNER H., HUNG J., BERMEJO J., CHAMBERS J.B., EVANGELISTA A., GRIFFIN B.P., IUNG B., OTTO C.M., PELLIKKA P.A. and QUIÑONES M.: Echocardiographic Assessment of Valve Stenosis: EAE/ASE Recommendations for Clinical Practice. J. Am. Soc. Echocardiogr., 22: 1-23, 2009.

7- BAUMGARTNER H., BONHOEFFER P., De GROOT N.M.S., De HAAN F., DEANFIELD J.E., GALIE N., GATZOULIS M.A., GOHLKE-BAERWOLF C., KAEMMERER H., KILNER P., MEIJBOOM F., MULDER B.J.M., OECHSLIN E., OLIVER J.M., SERRAF A., SZATMARI A., THAULOW E., VOUHE P.R. and WALMA E.: Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC) A, Association for European Paediatric Cardiology (AEPC) A, ESC Committee for Practice Guidelines (CPG) J, Ceconi C., Dean V., Filippatos G., Funck-Brentano C., Hobbs R., Kearney P., McDonagh T., Popescu B.A., Reiner Z., Sechtem U., Sirnes P.A., Tendera M., Vardas P., Widimsky P., McDonagh T., Swan L., Andreotti F., Beghetti M., Borggrefe M., Bozio A., Brecker S., Budts W., Hess J., Hirsch R., Jondeau G., Kokkonen J., Kozelj M., Kucukoglu S., Laan M., Lionis C., Metreveli I., Moons P., Pieper P.G., Pilossoff V., Popelova J., Price S., Roos-Hesselink J., Uva M.S., Tornos P., Trindade P.T., Ukkonen H., Walker H., Webb G.D., Westby J.: ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). Eur. Heart J., 31: 2915-57, 2010.

8- POSTEMA P.G. and WILDE A.A.M.: The measurement of the QT interval. Curr. Cardiol. Rev., 10: 287-94, 2014.

9- MOZOS I. and SERBAN C.: The relation between QT interval and T-wave variables in hypertensive patients. J. Pharm. Bioallied. Sci., 3: 33 9-44, 2011.

10- LOPEZ L., COLAN S.D., FROMMELT P.C., ENSING G.J., KENDALL K., YOUNOSZAI A.K., LAI W.W. and GEVA T.: Recommendations for Quantification Methods During the Performance of a Pediatric Echocardiogram: A Report From the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. J. Am. Soc. Echocardiogr., 23: 465-95, 2010.

11- KIANI A., RAFIEYIAN S., ROODPEYMA S., SEFIDGARNIA M.: The Relationship between Coronary Artery Aneurysm and QT Interval Dispersion in Acute Phase of Kawasaki Disease. Iran J. Pediatr., 21: 220-4, 2011.

12- HONG-LIANG Z., QIN L., ZHI-HONG L., ZHI-HUI Z., CHANG-MING X., XIN-HAI N., JIAN-GUO H., YING-JIE W. and SHU Z.: Heart rate-corrected QT interval and QT dispersion in patients with pulmonary hypertension. Wien Klin Wochenschr., 121: 33 0-33, 2009.

13- MARTIN A.B., GARSON A. and PERRY J.C.: Prolonged QT interval in hypertrophic and dilated cardiomyopathy in children. Am. Heart J., 127: 64-70, 1994.

14- AKGÜL F., SEYFELI E., MELEK I., DUMAN T., SEYDALIYEVA T., GALI E. and YALÇIN F.: Increased QT dispersion in sickle cell disease: Effect of pulmonary hypertension. Acta Haematol., 118: 1-6, 2007.

العلاقة بين تشتت ال "كيو تى" فى رسم القلب الكهربائى ومدى ضيق الصمام الرئوى

أجريت هذه الدراسة على أربعين مريضا تم إستقبالهم بقسم القلب بمستشفيات كلية الطب جامعة طنطا بالإضافة إلى عشرة أشخاص متطابقين فى السن والعمر والوزن مع المرضى كمجموعة قياس فى الفترة من يونيو ٢٠١٦ حتى مارس ٢٠١٧.

وقد أظهرت الدراسة وجود علاقة مؤثرة بين تشتت فترة كيو تى فى رسم القلب الكهربائى وشدة ضيق الصمام الرئوى حيث يزداد التشتت مع إزدياد ضيق الصمام الرئوى.