ORIGINAL ARTICLE

Assessment of electrocardiographic parameters in adult patients undergoing extracorporeal shockwave lithotripsy

Ekstrakorporal şok dalga litotripsi uygulanan erişkin hastalarda elektrokardiyografik parametrelerin değerlendirilmesi

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ABSTRACT

Objective: Extracorporeal shock wave lithotripsy (ESWL) is a safe and effective treatment for urinary tract calculi. While serious side effects are rare, transient cardiac arrhythmias may occur. New electrocardiographic (ECG) parameters, such as P wave dispersion (PWD), QT dispersion (QTd), T peak to T end (Tp-e) interval, Tp-e interval/QT ratio, and Tp-e interval/corrected QT ratio have been defined to help predict atrial and ventricular arrhythmias. However, effect of ESWL on these ECG parameters has not been previously investigated. The present study was an examination of the effect of ESWL on ECG parameters.

Methods: Total of 40 consecutive patients who underwent ESWL were prospectively enrolled in the study. Pre-procedure ECG parameters were compared with post-procedure ECG parameters.

Results: PWD values were significantly longer on post-procedure ECG compared with pre-procedure ECG (p=0.017). Corrected QT duration and QTd were significantly longer on post-procedure ECG compared with pre-procedure ECG (p=0.046 and p=0.008, respectively). In addition, Tp-e interval, Tp-e interval/QT ratio, and Tp-e interval/QTc ratio were significantly longer post procedure (p=0.035, p=0.045, and p=0.022, respectively). In univariate correlation analysis, duration of procedure was significantly correlated with post-procedure PWD, QTc, and QTD values.

Conclusion: Clinical use of ECG parameters may be helpful in monitoring of patients receiving ungated ESWL in order to detect cardiac dysrhythmia.

ÖZET

Amaç: Ekstrakorporal şok dalga tedavisi (ESWL) üriner sistem taşlarının güvenli ve etkili bir tedavi yöntemidir. Ciddi yan etkiler nadir olmakla birlikte, geçici kardiyak aritmiler tedavi sırasında görülebilmektedir. P dalga dispersiyonu (PWD), QT dispersiyonu (QTd), T dalga piki ve T dalga sonu intervali (TPe), Tp-e aralığı / QTd oranı ve Tp-e intervali / düzeltilmiş QT oranı gibi yeni elektrokardiyografik parametrelerin atriyal ve ventriküler aritmileri öngördüğü bildirilmiştir. Ancak, bu EKG parametreleri üzerine ESWL şok dalgasının etkisi daha önce araştırılmamıştır. Bu çalışmada, ESWL tedavisinin EKG parametreleri üzerine etkisini araştırmayı amaçladık.

Yöntemler: Çalışmaya ESWL tedavisi uygulanan 40 hasta alındı. İşlemden hemen önce ve sonrasında EKG parametreleri değerlendirildi.

Bulgular: PWD değerleleri; QT süresi ve düzeltilmiş QT sürelerinin işlem öncesi EKG örneklerine göre anlamlı şekilde daha uzun olduğu saptandı (sırasıyla, p=0.017, p=0.046 and p=0.008). Buna ek olarak, Tp-e intervali, Tp-e intervali/QTd oranı ve Tp-e intervali/QTc oranı işlem sonrası çekilen EKG örneğinde anlamlı derecede uzun bulundu (sırasıyla, p=0.035, p=0.045 ve p=0.022). Tek değişkenli korelasyon analizinde, işlem süresinin işlem sonrası PWD, QTc ve QTd değerlerinde uzama ile anlamlı şekilde ilişkili olduğu saptandı.

Sonuç: Klinik pratikte EKG parametrelerinin kullanımı ungated ESWL tedavisi gören hastalarda aritmik komplikasyonların monitörizasyonunda faydalı olabilir.

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Extracorporeal shock wave lithotripsy (ESWL) is considered safe and effective treatment modality for upper urinary tract calculi in adult patients. ESWL may be performed in 2 ways: gated (shock waves synchronized to R waves on electrocardiogram [ECG]) or ungated (unsynchronized to R waves on ECG). According to the literature, cardiac dysrhythmia (CD) caused by ESWL is not uncommon during the procedure, especially in patients undergoing ungated ESWL. Ungated ESWL has been found to be associated with CD, which is usually minor, unifocal ventricular premature beats, in up to 21% of adult patients. Incidence of arrhythmia has been greatly reduced by use of gated ESWL, which involves coupling the shock wave with ECG and release of discharges during refractory period.[1–3]

ECG is an important diagnostic tool for arrhythmia, and novel detailed ECG parameters, such as P wave dispersion (PWD), QT dispersion (QTD), T peak to T end (Tp-e) interval, Tp-e interval/QT ratio, and Tp-e interval/corrected QT ratio have been defined to predict atrial and ventricular arrhythmia.[4–8] However, effect of ESWL on detailed ECG parameters has not been investigated. This study was an examination of effect of ESWL on ECG parameters.

METHODS

Study population

Total of 40 consecutive patients who underwent ungated ESWL between October 2014 and December 2014 were prospectively enrolled. Patients younger than 18 years of age, those who used antiarrhythmic drugs, and those with previous diagnosis of coronary artery disease, congestive heart failure, severe valvular heart disease, chronic obstructive pulmonary disease, or end-stage renal insufficiency were excluded. In addition, patients who had ECG indicating left/right bundle branch block pattern, pacemaker rhythm, pre-excitation syndromes, or atrial fibrillation, or whose ECGs were not suitable for calculation of study parameters were excluded from the study. This study was approved by the local ethics committee. Written informed consent was obtained from study participants according to the Declaration of Helsinki.

Study protocol

Demographic and clinical features, admission laboratory parameters, and echocardiographic characteristics were recorded. ECGs obtained immediately before and after ESWL were collected for evaluation. Cardiac monitoring was performed on all patients during procedure.

Abbreviations:

CD	*Cardiac dysrhythmia*
ECG	*Electrocardiogram*
ESWL	*Extracorporeal shock wave lithotripsy*
PWD	*P wave dispersion*
QTd	*QT dispersion*
TDR	*Total dispersion of repolarization*
Tp-e	*T wave peak to T wave end*

Hypertension was defined as systolic pressure >140 mmHg and/or diastolic pressure >90 mmHg, or if the individual was taking antihypertensive medication. Diabetes mellitus was defined as fasting glucose level >126 mg/dL and/or if the patient was taking anti-diabetic medication. Hyperlipidemia was defined as total serum cholesterol level >240 mg/dL. Body mass index was calculated by dividing weight by square of height. Echocardiographic study was performed using Vivid 3 system (GE Healthcare, Inc. Chicago, IL, USA) in accordance with American Society of Echocardiography guidelines.

Electrocardiogram assessment

Twelve-lead surface ECG (50 mm/s, 10 mm/mV, Cardiofax GEM; Nihon Kohden Corp., Tokyo, Japan) was recorded at rest in supine position. An electronic digital caliper was used to minimize error measurements on surface ECGs. All ECG recordings were analyzed by an independent clinician who was blinded to clinical data of the patients. Three measurements were taken for each ECG parameter on the 12 leads (except for Tp-e interval, which was measured on precordial leads), and mean of 3 measurements was recorded. Longest value of each ECG parameter in any single lead was used in statistical analysis.

P max was defined as longest and P min as shortest P wave duration measured from 12-lead electrocardiogram. P wave dispersion (PWd) was defined as difference between P max and P min. PR interval was measured from onset of P wave to onset of QRS complex. QRS complex duration was defined as duration from initiation of Q wave to end of S wave. QT interval was measured from first deflection of QRS complex to end of T wave, defined as meeting point of descending branch of T to isoelectric line, and was corrected for heart rate using Bazett formula: QTc = QTd$\sqrt{}$ (R–R interval). QTd was defined as difference between maximum and minimum QT intervals of 12 leads.

Tp-e interval was defined as interval from peak of T wave to end of T wave, and was corrected for heart rate. Measurements of Tp-e interval were performed from precordial leads. Tp-e interval/QT and Tp-e interval/QTc ratios were calculated from these measurements.

Lithotripsy operation

Ungated ESWL was performed using E-1000 lithotripsy machine with electrohydraulic lithotripter (EMD Medical Technologies, Ankara, Turkey) without sedation or anesthesia. All patients underwent lithotripsy with gradual, incremental energy increase from 14kV to 18 kV. Maximum shock energy and duration of procedure were recorded. Patients did not receive any medication during procedure. Management of procedure was left to discretion of the attending urologist.

Statistical analysis

All data are presented as mean±SD or median [interquartile range] for parametric variables, and as percentage for categorical variables. Continuous variables were assessed for normal distribution assumption using Kolmogorov-Smirnov statistics. Categorical variables were tested with Pearson's chi-squared test and Fisher's exact test. Pre- and post-procedure ECG data were compared using paired t-test (for parameters with normal distribution) or Wilcoxon signed-ranks test (for parameters without normal distribution). Pearson's correlation analysis was used to investigate correlations between variables. P values were 3-sided: 3-digit value of p, such as 0.001, and value <0.050 was deemed statistically significant. All statistical studies were performed using SPSS for Windows, Version 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Demographic, clinical, laboratory, and echocardiographic characteristics of the study group are summarized in Table 1. Study population consisted of 40 patients with mean age of 40.1±11.8 years. Seventy-five percent (n=30) of the patients were male.

No ventricular or atrial extrasystole was observed on pre-procedure ECGs of study population. Atrial extrasystole developed in 4 (10%) patients and ventricular extrasystole developed in 3 (8%) patients during periprocedural period.

Comparison of pre- and post-procedure ECG parameters is provided in Table 2. While P min and P max values were similar, PWD values were significantly longer on post-procedure ECGs compared with pre-procedure ECGs (p=0.017). PR interval and QRS complex duration did not vary between pre- and

Table 1. Demographic, clinical, laboratory, and echocardiographic characteristics of the study population

Characteristics	Study group (n=40)		
	n	%	Mean±SD
Age (years)			40.1±11.8
Male gender	30	75	
Body mass index (kg/m^2)			25.9±1.9
Hypertension	5	13	
Diabetes mellitus	4	10	
Hyperlipidemia	8	20	
Admission heart rate (beats per minute)			79.6±13.9
Follow-up heart rate (beats per minute)			67.7±10.9
Systolic blood pressure (mmHg)			127±19.3
Left ventricle ejection fraction (%)			60±5
Atrial extrasystole	4	10	
Ventricular extrasystole	3	8	

SD: Standard deviation.

Table 2. Comparison of admission and after-discharge electrocardiographic parameters

ECG parameters	Pre-procedure	Post-procedure	*p*
	Mean±SD	Mean±SD	
Heart rate (bpm)	79.6±13.9	81.7±10.9	0.440
Pmax (ms)	108.7±19.7	115.3±14.1	0.083
Pmin (ms)	76.6±14.8	74.3±15.2	0.398
PWD (ms)	32.1±19.1	40.9±15.1	0.017*
PR duration (ms)	146.3±32.1	152.3±25.1	0.172
QRS duration (ms)	99.2±9.2	99.1±9.9	0.910
QTc (ms)	396.3±17.6	409.3±32.4	0.046*
QTd (ms)	38.3±10.6	46.9±14.4	0.008*
Tp-e interval (ms)	76.7±14.3	82.2±10.6	0.035*
Tp-e/QT	0.21±0.03	0.23±0.05	0.045*
Tp-e/QTc	0.19±0.03	0.22±0.05	0.022*

ECG: Electrocardiographic; Pmax: Maximum duration of P wave; Pmin: Minimum duration of P wave; PWD: P wave dispersion; QTc: Corrected QT duration; QTd: QT dispersion; Tp-e: T peak to T end; SD: Standard deviation.

post-procedure ECGs (p=0.172 and p=0.910, respectively). Corrected QT duration and QTd were significantly longer on post-procedure ECGs compared with pre-procedure ECGs (p=0.046 and p=0.008, respectively). In addition, Tp-e interval, Tp-e interval/QT ratio, and Tp-e interval/QTc ratio were significantly longer on post-procedure ECGs (p=0.035, p=0.045, and p=0.022, respectively). Post-procedure heart rate was higher than pre-procedure heart rate, but difference did not reach statistical significance (p=0.440).

In univariate correlation analysis, duration of ESWL was significantly correlated with post-procedure PWD (r=0.399, p=0.011), QTc (r=0.367, p=0.020), and QTd (r=0.383, p=0.015) (Figure 1). Significant correlation was not found between duration of procedure and other ECG parameters. Univariate correlation analysis was also performed to investigate relationship between ESWL shock energy and ECG parameters. Significant correlation between shock energy and post-procedure QTc (r=0.298, p=0.047), Tp-e interval (r=0.515, p=0.001), Tp-e interval/QT ratio (r=0.334, p=0.035), and Tp-e interval/QTc ratio (r=0.413, p=0.008) was observed. Other ECG parameters did not correlate with shock energy.

DISCUSSION

Primary finding of this study was that values of PWD, QTd, Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio were significantly higher on follow-up ECG compared with admission ECG in patients who underwent ESWL. These changes in ECG parameters secondary to ESWL may be associated with increased risk of arrhythmia in patients who undergo ungated ESWL.

CD during ESWL is not uncommon. Although underlying mechanisms of dysrhythmia are not fully understood, proposed mechanisms are direct mechanical stimulation of the myocardium and/or a neurohumoral response to treatment.[9,10] It has been reported that younger patients have been shown to have increased risk of experiencing CD during ESWL than older patients due to change in neurohumoral regulation over time and decrease in norepinephrine synthesis and level with age.[9] Experimental evidence of association between propensity for lethal arrhythmia and either enhanced sympathetic or reduced vagal activity has led to development of quantitative and qualitative markers of autonomic activity.[11] Autonomic nervous system has important role in development of CD. It has been proposed that neurohormonal activation and elevated epinephrine level in response to ESWL play role in association between ESWL and CD.[9–12]

Furthermore, in an animal study, CD has been induced by focusing shockwaves at apex of the heart with direct mechanical stimulation of the myocardium.[13] It has also been reported that individuals treated for right-sided renal stones rather than left-sided[9,14]

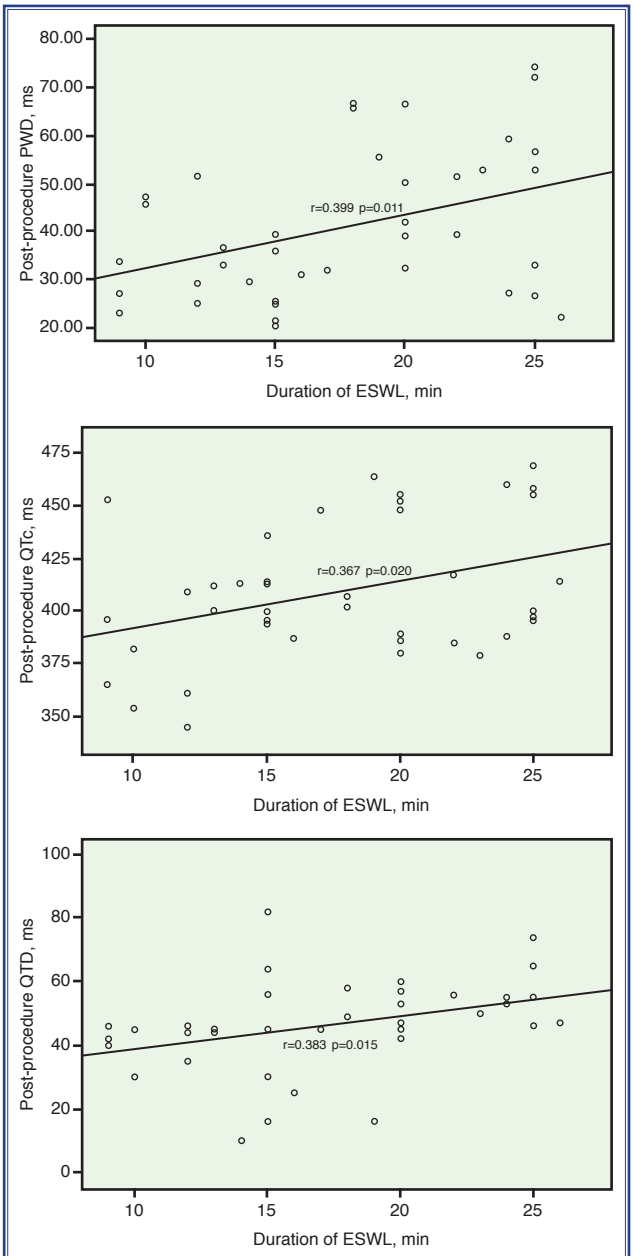

Figure 1. Duration of extracorporeal shock wave lithotripsy was significantly correlated with some post-procedure electrocardiographic parameters. ESWL: Extracorporeal shock wave lithotripsy; PWD: P wave dispersion; QTc: corrected QT duration; QTd: QT dispersion.

and renal stones rather than ureteric stones are more likely to develop CD.[9,15] Therefore, it was supposed that location and/or side of stone is important predisposing factor in development of CD, and that direct mechanic stimulation of the myocardium contributes to CD during ESWL.[16] In our study, because of small sample size, we did not analyze effect of location or side of stone in our study population. This is limiting factor for our study.

Studies investigating new ECG parameters to predict cardiac arrhythmia have been published recently.[17] One of these novel parameters is PWD. Increased PWD has been found to be associated with heterogeneous atrial repolarization favoring reentry mechanisms. PWD has also been found to be associated with inhomogeneous and discontinuous propagation of sinus impulses and presence of intraatrial conduction abnormalities. In recent studies, PWD has been proven to be a predictor of supraventricular arrhythmias and atrial fibrillation.[8,17–19] In our study, while P max and P min were similar, PWD values were significantly greater in patients who underwent ESWL. Autonomic tone may have modulatory effect on PWD, which includes changing velocity of impulse propagation.[19] Tukek et al.[20] proposed that increased sympathetic activity may cause significant increase in PWD. Thus, neurohormonal activation and higher epinephrine level may cause increased PWD, leading to atrial arrhythmia in patients who undergo ESWL, as correlated with previous reports.

Increased QTD is an ECG parameter that represents inhomogeneous ventricular repolarization and electrical instability, which may predispose patient to ventricular arrhythmia.[7] It has been reported that changes in autonomic neural tone may influence ventricular depolarization and repolarization, leading to prolongation of QTD.[21] Autonomic nervous system also has important role in electrophysiological heterogeneity. It has also been reported that there is a correlation between QTD and autonomic imbalance.[22,23] In our study, post-procedure QTD values were significantly higher than admission QTD values. We assume that this finding is related to neurohumoral activation and autonomic dysfunction in ESWL patients.

Tp-e interval, Tp-e interval/QT, and Tp-e interval/QTc ratios are also new ECG parameters that reflect increased dispersion of ventricular repolarization. Previous studies reported that Tp-e interval is used as index of total dispersion of repolarization (TDR), which reflects heterogeneity rather than total duration of repolarization.[24,25] It has also been observed that variations in cardiac autonomic neural tone and elevated sympathetic activity on the ventricular myocardium are associated with TDR, which increases risk of developing ventricular arrhythmia.[26,27] Tp-e

interval and Tp-e/QT ratio are valuable ECG indexes of arrhythmic risk as well, and may be indexes for dispersion of ventricular repolarization.[5,6] So, previous studies have demonstrated that increased Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio are associated with malignant ventricular arrhythmic risk.[8,28,29] In our study, Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio were significantly higher on post-procedure ECGs compared with pre-procedure ECGs.

We also demonstrated correlation of some ECG parameters with ESWL duration and shock energy. As result of these correlations, it can be speculated that increased effect of ESWL may yield more arrhythmic complications.

Limitations

A few limitations of our study deserve mention. This was single-center, prospective study with relatively small sample size. Lack of technical equipment at our hospital prevented use of 24-hour Holter monitoring. We also performed all ECG measurements manually; software-based computer measurements may have provided more accurate results. Although surface ECG parameters described in this study may provide considerable amount of useful information regarding arrhythmic substrate, especially in the healthy heart, any single test is unlikely to be powerful enough to adequately risk-stratify patients regarding arrhythmia and sudden cardiac arrest.

Conclusion

This is the first study to demonstrate greater PWD, QTc, QTD, Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio values on surface 12-lead ECGs in patients who underwent ESWL. We assume that ESWL may alter the function of the cardiac autonomic nervous system via neurohumoral activation in patients with urolithiasis, leading to related ECG changes. In addition, it should be kept mind that, alone or in combination with neurohumoral response, direct mechanical effect may be underlying mechanism in development of CD. Our findings may support clinical use of ECG parameters as useful tools in monitoring of patients receiving ungated ESWL in order to detect CD. These findings may lead to more comprehensive studies.

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Disclosures

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Keywords: Arrhythmia; electrocardiography; extracorporeal shock wave lithotripsy.

Anahtar sözcükler: Aritmi; elektrokardiyografi; ekstrakorporal şok dalga tedavisi.