Gastroesophageal reflux disease is associated with abnormal ventricular repolarization indices

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ABSTRACT

Background/Aims: Gastroesophageal Reflux Disease (GERD) is a clinical entity affecting the upper gastrointestinal tract. The pathophysiology of GERD has been associated with autonomic nervous system disorders. Autonomic nervous system disturbances in GERD patients have been shown to lead to fatal ventricular arrhythmias (VAs) that result in electrical and ventricular repolarization anomalies. The maximum to terminal electrocardiographic T wave (Tpe) has been associated with repolarization of transmural dispersion. In addition, a higher Tpe interval (TpeI) and Tpe/QT ratio correspond with VAs. The goal of this report was to assess ventricular repolarization, by TpeI and Tpe/QT ratio, in GERD patients.

Materials and Methods: The study was comprised of 46 GERD subjects and 43 healthy volunteers. TpeI, cTpe, and Tpe/Q ratios were determined from electrocardiograms and associations of the groups were compared.

Results: The clinical characteristics were similar between the two groups. TpeI, corrected Tpe (cTpe) interval, and Tpe/QT ratio were higher in subjects with GERD in comparison to the control group (P<0.001, P=0.018, and P<0.001, respectively).

Conclusion: TpeI and Tpe/QT ratio were higher in GERD patients. Patients with GERD may have an increased risk for VAs

Keywords: Gastroesophageal reflux, Tpe interval, Tpe/QT ratio, ventricular arrhythmia

INTRODUCTION

Gastroesophageal reflux disease (GERD) is characterized by acid regurgitation and epigastric burning that occur as the result of reflux of gastric content into the esophagus (1). GERD is the most common gastrointestinal disorder, with an increasing prevalence in developed countries (2,3). Disturbances in the autonomic nervous system (ANS) were observed in patients with GERD, and they were related to the pathophysiology of the disease. The relationship between GERD and cardiac dysrhythmia was documented as gastrocardiac syndrome (4,5). GERD, and its effects on the cardiac system represent a showcase the complexity between the heart and the ANS. The evidence suggests that chronic GERD can cause an autonomic response, which results in VAs (6). Disturbed autonomic nervous functions may trigger VAs through electrical and ventricular changes in anomalies. Repolarization of the myocardium can be assessed using several techniques. In addition, recent reports have demonstrated that TpeI, the interval between the peak to the end of the electrocardiographic Tpe, is an index for the repolarization of transmural dispersion (7,8). TpeI and the Tpe/QT ratio has been documented as significant in terms of electrocardiographic indexes for arrhythmic risk, corresponding to spatial transmural dispersion (9,10).

In this report, we examined the ventricular arrhythmia potential in patients with GERD by calculating TpeI and the Tpe/QT ratio, which are the indexes of ventricular repolarization.

MATERIALS AND METHODS

Study population

Forty-five patients diagnosed with GERD upon an endoscopic examination performed at the gastroenterology clinic were enrolled in the study. In addition, 43 healthy volunteers were enrolled during a routine control check-up in the cardiology clinic. Approval was obtained from the ethics committee (Ethics Committee of Adıyaman University, 2017/9-18), and every subject in the study provided informed consent. An electrocardiogram (ECG) was applied in all cases. Left ventricular measurements were done following the American Society of Echocardiography criteria (11). The cases who had left ventricular hypertrophy and dysfunction and/or left bundle branch

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block in ECG, rheumatoid heart disease, heart valvular disease, thyroid dysfunction, chronic lung disease, chronic kidney disease, anemia, electrolyte disturbance, chronic liver disease, chronic infection, atrioventricular conduction disturbance, non-sinus rhythm in ECG, systemic rheumatoid disease, or who used antidepressants and antipsychotic or antihistaminic drugs, were excluded from the study.

Electrocardiography

All ECGs were performed with a recording device adjusted to the 1 mV/cm standardization and 50 mm/sec paper speed (Nihon Kohden, Tokyo, Japan), with the patient resting in the supine position. The patient heart rate was recorded at rest during the ECG. To avoid erroneous calculations, the QT and TpeI analyses were made in duplicate measurements. Subjects that had U waves and negative T waves were excluded. Whenever possible, QT interval (QTI) was assessed in all 12 leads, while TpeI was examined from precordial derivations (12). The QTI was calculated at the QRS complex beginning at the T wave end, and it was the corrected for heart rate using Bazett's formula (QTc=QT/RR-2) (13). The QTd was calculated using the difference from the maximum and minimum QTI of the 12 leads. The TpeI was calculated from the peak of the T wave to the end of the T wave. Then, the TpeI was corrected for the heart rate. The end of the T wave was determined to be at the intersection of the tangent and the T-wave downslope and isoelectric line. The Tpe/QT ratio was calculated from these measurements.

Statistical analysis

All analyses were performed using the Statistical Package for Social Sciences, v 22.0 (IBM Corp.; Armonk, NY, USA). Variables were expressed as the mean±standard deviation, whereas categorical variables were expressed as percentage. For numerical variables, statistical analyses were made with independent samples using the t-test/Mann-Whitney U-test. For categorical variables, Fisher's exact test or chi-square test was used. A p-value <0.05 was considered statistically significant.

RESULTS

The patient demographics and clinical outcomes are presented in Table 1. All demographics were similar between the two groups (for all, p>0.05).

The ECG measurements of both groups are presented in Table 2. The QTd and cQTd were higher in patients with GERD in comparison to controls (p=0.002 and P=0.09, respectively). Moreover, TpeI, cTpeI, and the Tpe/QT ratio were increased in patients with GERD in comparison to controls (p<0.001, p=0.018, and p<0.001, respectively).

DISCUSSION

The study results showed a significantly increased TpeI and the Tpe/QT ratio in patients with GERD in comparison to the controls.

Several previous studies reported that increased dispersion in ventricular repolarization is a predisposing factor

Table 1. Clinical characteristics and echocardiographic findings of groups.

Variables	Patients with GERD (n=46)	Control group (n=43)	p
Age (years)	51.0 ± 8.9	51.1 ± 5.0	0.961
Gender, male, n %	38 (82.6)	31 (72.0)	0.425
BMI (kg/m^2)	26.4 ± 3.0	25.2 ± 2.7	0.059
Diabetes mellitus, n, (%)	6 (13.0)	1 (2.32)	0.065
Smokers, n, (%)	19 (41.3)	15 (34.8)	0.588
Heart rate (beats/min)	71.9. ± 8.3	75.7 ± 9.7	0.052
Systolic BP (mmHg)	126.7 ± 7.0	127.0. ± 5.4	0.792
Diastolic BP (mmHg)	72.3 ± 5.0	71.6 ± 6.0	0.544
IVS (mm)	10.7 ±0.8	10.5 ± 0.7	0.434
PW (mm)	8.3 ± 1.0	8.0 ± 1.3	0.244
LVEF (%)	61.0 ± 2.9	61.9 ± 3.6	0.184

BMI: body mass index; BP: blood pressure; IVS: interventricular septum; PW: posterior wall; LVEF: left ventricle ejection fraction.

Table 2. Electrocardiographic findings of the groups.

	Patients with GERD (n=46)	Control group (n=43)	p
QTd (ms)	28.1±8.8	22.8±6.7	0.002
cQTd (ms)	30.3±10.5	25.2±6.9	0.009
Tpe (ms)	88.1±14.1	79.2±4.6	<0.001
cTpe (ms)	94.3±15.00	88.4±5.9	0.018
Tpe/QT	0.24±0.02	0.22 ±0.01	<0.001

QTd: QT dispersion; cQTd: corrected QT dispersion; Tpe: Tpe intreval; cTpe: corrected Tpe interval.

for VAs (14,15). Moreover, an association has been shown between a prolonged TpeI and VAs (16). The duration of action potential is longer in M-cells of the myocardium in comparison to the other myocardial cells. Repolarization is first completed at the epicardial cells. The peak of the T wave is reflective of the epicardial action potential end, whereas the T-wave end is comparable to the endocardial action potential. Therefore, the TpeI demonstrates the transmural dispersion. A prolonged TpeI was shown to be related to sudden cardiac death (17). However, TpeI was shown to be affected by the variations of heart rate and body weight. Presently, the Tpe/QT ratio is a more precise index for the ventricular dispersion compared to QTd, corrected QTd, and TpeI, and it is independent of heart rate alterations (18). In a recent study, Yayla et al. showed that TpeI and Tpe/QT were increased in patients with aortic stenosis, and this increase was correlated with the severity of the disease (19). In another study, it was shown that myocardial fibrosis may cause changes in myocardium in patients with systemic sclerosis, and these changes may cause heterogeneity in ventricular repolarization and may increase the TpeI and Tpe/QT (20). TpeI and the Tpe/QT ratio were also evaluated in celiac disease, which is an autoimmune disease, and these indexes were reported to increase in patients with celiac disease (21). Inflammation can have an artymogenic effect by creating autoimmune dysfunction and myocardial damage. Esophageal inflammation resulting from GERD increases the vagal modulation of cardiac functions (22). The esophageal mucosa inflammation impacts reflex cardiac rhythm mechanisms, which can result in secondary cardiac dysrhythmia complications (23). Furthermore, the relationship between neurocardiac dysfunction and esophageal acid exposure was shown, and the treatment of esophageal symptoms was reported to result in an improvement of cardiac functions (24). It has been reported that disturbances in the ANS can increase the frequency of lower esophageal sphincter relaxation by reducing the muscular control at the lower esophageal sphincter (25). Several previous studies have found a reduced sympathetic activity in GERD (26,27).

On the other hand, a study by Milovanovic et al. showed an increased activity in both the sympathetic and parasympathetic systems in GERD (28). In our study, we found a significantly increased TpeI and the Tpe/QT ratio in patients with GERD compared to controls. Possible causes for the higher TpeI and Tpe/QT ratio may be related to changes in the autonomic neural tonus and an increased sympathetic activity in patients with GERD. These changes have been associated with increased VAs, along with the changes in transmural dispersion of repolarization (29,30). Our results are quite significant as, to the best of our knowledge, no other study in the literature has examined TpeI and the Tpe/QT ratio as highly sensitive gauges of ventricular repolarization anomalies and VAs potential in patients with GERD. Major limitations to this study are the lack of follow-up of patients regarding ventricular arrhythmia and the size of the patient cohort. Large scale, multi-centered prospective studies are required to document and evaluate ventricular arrhythmias occurring in patients with GERD with an increased TpeI and the Tpe/QT ratio.

In summary, patients with GERD may have an increased risk for VAs, and the VAs risk in patients with GERD can be predicted by measuring TpeI and the Tpe/QT ratio, which are the indicators of ventricular repolarization anomalies. Nonetheless, further studies with a greater number of patients are required.

Ethics Committee Approval: Ethics committee approval for this study was received from the Ethics Committee of Adıyaman University (Decision Date/Number: 2017/9-18).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

Peer-review: Externally peer-reviewed.

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