

Alterations in QT dispersion in the surface electrocardiogram of female adolescent inpatients diagnosed with bulimia nervosa

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Abstract

Increased QT dispersion (QTd) reflects cardiac autonomic imbalance and indicates elevated risk for cardiac arrhythmias. In the present study, we assessed heart rate, QT and corrected QT intervals, and QTd in 20 acutely ill bulimia nervosa adolescent inpatients on admission and discharge. A significant decrease in QTd was found between admission and discharge (67 ± 13 milliseconds vs 55 ± 12 milliseconds, respectively; $P = .0005$). The decrease in QTd values correlated significantly with the decrease in the frequency of bingeing/purging behaviors ($r = 0.51$, $P = .022$). No significant correlations were found between the electrocardiographic indices and other clinical and laboratory measures. The elevated QTd in malnourished bulimia nervosa patients might indicate a cardiac autonomic imbalance that is most likely corrected after symptomatic improvement.

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1. Introduction

Anorexia nervosa (AN) is a psychiatric disorder associated with particularly high mortality and morbidity rates [1]. These are mostly attributed to cardiac complications, primarily ventricular arrhythmias that are related to various conduction abnormalities, including prolonged QT interval and elevated QT dispersion (QTd) [1–3].

QT dispersion, defined as the maximal interlead difference in QT intervals, has been found to serve as a measure of myocardial repolarization inhomogeneity [4]. QT dispersion has been found to be positively correlated with heart rate variability, suggesting that increased QTd may indicate the likelihood of increased sympathetic tone and/or decreased vagal tone [5,6]. Accordingly, elevated QTd values (in the

range of 60–80 milliseconds in comparison with values between 20 and 50 milliseconds in healthy subjects) may represent a predisposing factor for arrhythmic events and sudden death [7–9].

Several studies have found that the QT interval and QTd are greater in AN female patients compared with non-eating disorder (ED) controls, with the QTd in these patients being inversely correlated with the left ventricular mass [10,11]. Furthermore, a significant decrease in QTd may occur after weight restoration [12,13].

Previous research has also found that higher QTd values may be found in normal-weight physically healthy patients diagnosed with psychiatric disorders such as major depression and social anxiety disorder in comparison with healthy controls [14,15]. This suggests that reduced vagal modulation, potentially lowering the threshold of lethal arrhythmias, may occur also in normal-weight psychiatric patients.

The findings in emaciated malnourished AN patients and in normal-weight patients with psychiatric disorders that are often comorbid with EDs led us to examine whether these electrocardiographic (ECG) changes would be found also in bulimia nervosa (BN). Reviewing the literature, we found

The study was conducted at the Pediatric Psychosomatic Department, The Edmond and Lily Safra Children's Hospital, The Chaim Sheba Medical Center, Tel Hashomer, Israel.

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that only one group analyzed QTd in BN patients [11,16]. In their earlier study, Takimoto et al showed increased QT interval and QTd in both AN and BN patients compared with healthy controls [11]. Later on, this group found that BN patients with elevated depression or anxiety had significantly longer QT intervals and increased QTd compared with patients with lower mood disturbance [16]. These findings suggested that mood disturbances might increase the risk for arrhythmias in BN. From a different perspective, late potentials, a predictor of ventricular arrhythmias, measured from the signal-averaged electrocardiogram were reported to be more common in BN patients with a history of AN, suggesting the likelihood of increased risk for cardiac morbidity in these conditions [17].

The aim of the present study was to assess the QT interval, its rate-corrected value (QT_c), and QTd in female adolescent BN inpatients in the acute condition of their illness on admission and upon achieving symptomatic stabilization at discharge. We hypothesized that these indices would be elevated in acutely ill BN patients, but decrease to reference range after clinical improvement.

2. Method

2.1. Patients

We studied 20 consecutive BN female adolescent (age, 16.2 ± 0.8 years) inpatients that fulfilled the study's criteria. All were hospitalized in the adolescent inpatient ED department at the Chaim Sheba Medical Center, Tel Hashomer, Israel. Bulimia nervosa diagnosis (according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV]* criteria) was established independently by 2 senior child and adolescent psychiatrists (DS and AY) using the Eating Disorders Family History Interview [18,19]. This is a structured clinical interview designed to gather detailed information on weight and eating history that has been extensively used in the study of ED patients, including in our previous electrographic study in AN [13,20]. Other *DSM-IV* Axis I psychiatric disorders were similarly established with the Structured Clinical Interview for *DSM-IV* Axis I Disorders—Patient Edition (Version 2.0) [21]. The data collected in the interviews were analyzed in regular meetings of the research team, and only those participants for whom there was a unanimous agreement as to the diagnosis of BN were included in the study. Bulimia nervosa inpatients were excluded from the study if they ever had a bipolar disorder, schizophrenic spectrum disorder, organic brain syndrome, substance use disorder, or any lifetime or current cardiovascular, pulmonary, or neurologic disorder. One patient was diagnosed with hypothyroidism before the development of BN and was treated with thyroid hormone supplements. Nevertheless, the dosage of the medication was stable throughout the study period. None of the patients was smoking before the study (as indicated by

self-report) or during the study (it is the policy of this department not to allow smoking while hospitalized).

Requirements for discharge for all BN patients included the cessation of bingeing, vomiting, and use of laxatives for at least 2 consecutive weeks as recorded with daily food monitoring using the cognitive-behavioral therapy design of Fairburn et al [22].

2.2. Measurements and procedure

Demographic and clinical variables, including age, duration of hospitalization, and use of medications before hospitalization, were recorded using a structured interview.

A complete medical and neurologic evaluation was performed on admission and, thereafter, monthly until discharge. Samples for routine laboratory examinations, including sodium, potassium, calcium, phosphorous, urea, creatinine, complete blood count, free thyroxin index, triiodothyronine, thyroid-stimulating hormone, cortisol, iron, folic acid, vitamin B-12, and urinalysis, were collected between 8:00 and 9:00 AM, after an overnight fast, at baseline (within the first week after hospitalization) and, thereafter, monthly until discharge. Weight and height were evaluated during the early morning hours at baseline and, thereafter, monthly until discharge by a single investigator (AT) using standardized procedures [23]. Body mass index was calculated as weight in kilograms divided by height in meters squared [24].

Severity of BN was assessed on admission and discharge. This was done with the 7-item self-rating bulimia subscale of the Eating Disorders Inventory–2 (EDI-2) [25] and with the per-week bingeing/purging episodes rate, assessed with the Eating Disorders Family History Interview on admission and with the daily food monitoring at discharge.

All participants and their parents or other legal guardians, in the case of minors under the age of 18 years, agreed to participate in the study by signing a written informed consent after the nature of the study was explained to them. The study was approved by the Helsinki Committee of the Chaim Sheba Medical Center.

2.3. Medications

Upon admission, 13 patients were medication-free (according to self-reports and medical records) for at least 2 weeks before entering the study; and 7 patients were treated with selective serotonin reuptake inhibitors (SSRIs). Two patients were also treated at admission with mood stabilizers. Upon discharge, 18 patients were treated with SSRIs. Five patients were additionally treated with atypical antipsychotics (either risperidone or olanzapine), 7 were treated with mood stabilizers (mostly topiramate, and also lamotrigine and carbamazepine), and 1 patient received methylphenidate in addition to the SSRIs. As noted earlier, 1 patient was treated with thyroid supplementation because of hypothyroidism. The drug regimen was kept constant for at least 4 weeks before the discharge ECG examination. Vasoactive

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