Cardiac Disorders in Young Women With Anorexia Nervosa

Margarita Vázquez, José L. Olivares, Jesús Fleta, Isaac Lacambra, and Mariano González

Introduction and objectives. The objective of this study was to compare heart abnormalities in young women with anorexia nervosa and in a control group of the same age and sex.

Patients and method. We report a matched case-control study of 30 adolescents with anorexia nervosa and 30 healthy women of the same age with normal weight. An electrocardiogram and echocardiogram were done. Heart parameters were measured on the electrocardiographic tracings, and QT dispersion was defined as the difference between maximum QT and minimum QT in any of the 12 leads. Diameter, mass and left ventricular mass index were measured.

Results. QT and corrected QT intervals were significantly greater in patients with anorexia nervosa than in the control group. QT dispersion and corrected QT dispersion were significantly greater in anorexia nervosa than in the control group (QTd, 59.3 ± 23.0 vs 38.4 ± 8.0 ms; p = 0.000; QTcd, 56.5 ± 24.2 vs. 40.3 ± 21.8 ms; p = 0.011). Left ventricular mass was significantly lower in young women with anorexia nervosa. We found a significant relationship between body mass index and left ventricular mass index, and between the former and corrected QT dispersion.

Conclusions. Adolescents with anorexia nervosa show significant cardiac disorders in comparison to healthy women of the same age. This finding may be a useful indicator of the risk of arrhythmia and sudden death in patients with anorexia nervosa.

Key words: Anorexia nervosa. QT interval. QT interval dispersion. Left ventricular mass.

INTRODUCTION

Anorexia nervosa is an eating disorder characterized by voluntary restriction of food intake, leading to marked loss of weight, and which may even result in severe malnutrition and death. It mostly affects women...
between the ages of 12-25 years, with adolescence being
the period of greatest risk. Almost 80% of patients have
cardiovascular abnormalities, mainly bradycardia,
hypotension, arrhythmias and repolarization disorders;
sudden death has been reported in 10% of patients.1-6
Special attention has been given over recent years to
changes in the QT interval7,8 and modifications of the
myocardial mass and heart function detected by
echocardiography.9,12 The aim of this study was to
compare heart abnormalities in young women with
anorexia nervosa and a control group of healthy women
matched for age.

PATIENTS AND METHODS

Patients and controls

This case-control study included 30 patients, all
women, with anorexia nervosa, who had been referred
by the psychiatry outpatient service of the hospital and
who were admitted between 1 January 2001 and 30
August 2002. Their ages ranged from 12.1-18.5 years
(mean, 15.5±1.6 years). Anorexia nervosa was defined
according to DSM-IV of the American Academy of
Psychiatry.13

The control group was composed of 30 matched
healthy adolescents, mean age 15.5±1.6 years, of normal
weight, who had been referred to the hospital for
evaluation of an innocent murmur or functional chest
pain. Controls were excluded from the study if they had
a chronic disease, a family history of arrhythmia14 or
were receiving pharmacological therapy.15

Electrocardiographic study

Standard 12-lead ECGs were obtained at a paper
speed of 25 mm/s. Heart rate was calculated from the
average RR interval of the tracings. Manual
measurement of the QT interval was made in all leads
from the start of the QRS complex to the end of the T
wave on the iso-electric line. In the presence of a U
wave, the end of the QT interval was considered to be
the nadir between the T and U waves. Patients with
bundle branch block were excluded. The corrected QT
interval (QTc) was adjusted with Bazett’s formula.16 QTc
was considered to be increased if it was greater than 440
ms. QT dispersion was defined as the difference
between the maximum QT interval and the minimum
QT interval in all leads. The QTc interval dispersion was
the difference between the maximum and the minimum
QTc intervals measured in the 12 leads.17,20 Based on
previous studies21 and our own control group, the cut-off
value was set at a dispersion of 60 ms. Holter
monitoring was carried out according to the guidelines
of the Spanish Society of Cardiology.22

Echocardiographic study

All patients and controls underwent two-dimensional
M mode echocardiogram and Doppler study, with the
subject at rest in the left lateral decubitus position.
Quantitative evaluation was made of the left ventricular
diastolic diameter, the left ventricular end-diastolic diameter, the interventricular septum thickness, the left
ventricular posterior wall, the shortening fraction, the
ejection fraction, the left ventricular mass and the heart
mass index. Measurements were determined with
standard techniques in accordance with the
recommendations of the American Society of
Echocardiography.23-25

Statistical study

Data are expressed as the mean±standard deviation.
The Kolmogorov-Smirnov test, with Lilliefors
modification, was used to verify normality of the
variables, and Student t test and Mann-Whitney U to
compare differences between means with independent
data, together with Spearman correlation index and
regression line. Categorical variables were expressed as
percentages and compared by χ² test and odds ratios
(OR) were calculated with 95% confidence intervals
(95% CI). Data were analyzed with the SPSS statistical
software for Windows 10.0 (SPSS Inc.) and differences
were considered significant if the P<.05.

RESULTS

Patient characteristics

Table 1 shows the main clinical characteristics, age,
weight, body mass index (BMI) and heart rate of the
young women with anorexia nervosa and the matched
controls. Though there was no difference in age, the
weight, BMI and heart rate were all significantly lower
in the patients with anorexia nervosa than the controls.

Electrocardiographic and echocardiographic
results

Table 2 shows the electrocardiographic (QT interval,
QTc, QT dispersion, QTc dispersion) and
echocardiographic measurements (left ventricular end-
TABLE 1. Clinical characteristics of the young women with anorexia nervosa and the control group of matched healthy women

<table>
<thead>
<tr>
<th></th>
<th>Anorexia nervosa (n=30)</th>
<th>Control group (n=30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>15.5±1.6</td>
<td>15.1±1.6</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>39.4±6.2</td>
<td>53.1±4.9</td>
<td>.000</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>15.3±2.1</td>
<td>20.3±1.3</td>
<td>.000</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>56.9±12.0</td>
<td>82.9±11.9</td>
<td>.000</td>
</tr>
</tbody>
</table>

The results are expressed as the mean±standard deviation. n indicates number of cases; NS, not significant; BMI, body mass index; bpm, beats per minute.

TABLE 2. Electrocardiographic and echocardiographic measurements in young women with anorexia nervosa and healthy controls matched for age and sex

<table>
<thead>
<tr>
<th></th>
<th>Anorexia nervosa (n=30)</th>
<th>Control group (n=30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>QT, ms</td>
<td>436.6±36.2</td>
<td>360.0±20.0</td>
<td>.001</td>
</tr>
<tr>
<td>QTc, ms</td>
<td>436.3±35.5</td>
<td>391.4±24.3</td>
<td>.001</td>
</tr>
<tr>
<td>QT&gt;440 ms (N)</td>
<td>12/30 (40%)</td>
<td>0/30 (0%)</td>
<td></td>
</tr>
<tr>
<td>QT dispersion, ms</td>
<td>59.3±23.0</td>
<td>38.4±8.0</td>
<td>.000</td>
</tr>
<tr>
<td>QTc dispersion, ms</td>
<td>56.5±24.2</td>
<td>40.3±21.8</td>
<td>.011</td>
</tr>
<tr>
<td>QTc dispersion&gt;60 ms</td>
<td>11/30 (36.7%)</td>
<td>2/30 (6.7%)</td>
<td>.001</td>
</tr>
<tr>
<td>EDD, mm</td>
<td>41.9±4.3</td>
<td>44.9±3.8</td>
<td>.006</td>
</tr>
<tr>
<td>ESD, mm</td>
<td>25.3±2.8</td>
<td>27.8±3.5</td>
<td>.008</td>
</tr>
<tr>
<td>IVST, mm</td>
<td>6.1±1.1</td>
<td>6.9±1.0</td>
<td>.006</td>
</tr>
<tr>
<td>LV PW, mm</td>
<td>6.6±1.2</td>
<td>7.0±0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Shortening fraction,</td>
<td>39.6±4.3</td>
<td>38.4±5.3</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>64.9±4.8</td>
<td>62.8±6.6</td>
<td>NS</td>
</tr>
<tr>
<td>Left ventricular mass, g</td>
<td>76.2±22.6</td>
<td>98.3±21.2</td>
<td>.001</td>
</tr>
<tr>
<td>Cardiac mass index, g/m²</td>
<td>53.9±14.4</td>
<td>64.0±12.4</td>
<td>.015</td>
</tr>
</tbody>
</table>

The results are expressed as the mean±standard deviation.
* Odds ratio=8.11; 95% confidence interval, 1.47-80.65; P=.01.

Fig. 1. Correlation between body mass index and left ventricular mass index.

The left ventricular end-diastolic diameter, left ventricular end-systolic diameter, interventricular septum thickness, left ventricular mass and cardiac mass index were all significantly lower in patients with anorexia nervosa than controls. There were no significant differences in the left ventricular posterior wall, shortening fraction or ejection fraction.

Figure 1 shows the correlation between BMI and left ventricular mass index, which was significantly positive (y=0.08x+13.32; r=+0.378; P<.01). Figure 2 shows the correlation between BMI and QTc dispersion, which was significantly negative (y=−0.07x+21.44; r=−0.4396; P<.001).

DISCUSSION

The process of slimming during anorexia nervosa leads to marked loss of muscle mass. This is further complicated by electrolyte and mineral disturbances induced by habitual use of emetics, laxatives and diuretics, and which result in loss of weight, exercise limitation, arrhythmia and possibly even sudden death. The left ventricular end-diastolic diameter, left ventricular end-systolic diameter, interventricular septum thickness, left ventricular mass and cardiac mass index were all significantly lower in patients with anorexia nervosa than controls. There were no significant differences in the left ventricular posterior wall, shortening fraction or ejection fraction.

Arrhythmias, mainly acute bradycardia, are the best known cardiac disorders, and probably occur in response to the organism attempting to conserve energy by reducing cardiac output. Several different pathogenic mechanisms have been proposed, including electrolyte loss, drugs with adverse cardiovascular effects, reduction in the glycogen content of the heart cell, myofibrillar atrophy, interstitial edema, mitochondrial tumefaction and activation of calcium dependent proteinases.
QT interval and interval dispersion

Most of the patients with anorexia nervosa in this study had arrhythmias in the form of manifest bradycardia, frequent atrial extrasystole, occasional ventricular extrasystole and significantly increased QT and QTc intervals compared to healthy women of the same age. These findings are similar to those reported by others.8,29

An important finding of the study was the fact that young people with anorexia nervosa had a significant increase in QT interval dispersion and a reduction in cardiac chamber size and left ventricular mass compared to the control group, both in absolute figures and relatively after adjusting for body mass. These results are similar to those reported by Galetta et al12 and Swenne and Larsson,8 who showed that weight loss in adolescents with anorexia nervosa and eating disorders is a risk factor for prolongation and dispersion of the QT interval.

Correlation between body mass index, left ventricular mass index and QT interval dispersion

A significant positive correlation was seen between BMI and left ventricular mass index, demonstrating that weight loss is accompanied by a reduction in left ventricular mass, as mentioned by Conri et al.11 There was also a significant negative correlation between the QTc interval dispersion and BMI in patients with anorexia nervosa.

An increase in QT interval dispersion on ECG represents regional differences in myocardial recovery of excitability and may give rise to a greater arrhythmogenic substrate, with the corresponding increased risk of clinically important ventricular arrhythmia and sudden death. In fact, increases in QT interval and QT dispersion have been related to a greater risk of ventricular arrhythmia in patients with coronary heart disease and healthy subjects. The predictive value of increased dispersion of the QT interval as a marker of acute ventricular arrhythmia or sudden death has been demonstrated.5,6

The relation between BMI and left ventricular mass index in anorexia nervosa suggests that the reduction in left ventricular mass may be responsible for the increase in QT interval dispersion. This increase in QT interval dispersion may also be explained by histologic changes and alterations of the cardiac muscle fibers. Indeed, changes in orientation, structure or geometry of the muscle fibers and the collagen network or variations in myocardial blood flow or water content, as described in hypotrophic hearts in states of malnutrition, may be the basis of a non-homogenous repolarization. This is also the case in hypertrophic heart disease.30 An increase in workload may produce ECG changes suggestive of myocardial ischemia and increased duration and dispersion of the QT interval.31

Another possible mechanism influencing increased QT dispersion is alteration of ion channels, active in cardiac repolarization. Alterations have been seen in potassium channels of hypotrophic myocytes with prolongation of the action potential. A further explanation may be the presence of a greater amount of fibrous tissue and an alteration of homogenous ventricular recovery. Autopsy studies have shown myocardial degeneration, myocytolysis, mononuclear infiltrate, fat infiltrate and substitution of muscle tissue for collagen.32,33

Conclusions and clinical implications

Our study suggests that patients with anorexia nervosa have important cardiologic alterations and a greater probability of arrhythmia than healthy adolescents of the same age. Systematic monitoring of the parameters mentioned above may detect the development of acute arrhythmia and the risk of sudden death in these patients.