

Original Article



Cardiac Complications Associated with Eating Disorders in Children: A Multicenter Retrospective Study

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ABSTRACT

Purpose: Eating disorders often result in somatic complications, including cardiac abnormalities. Cardiac abnormalities may involve any part of the heart, including the cardiac conduction system, and can lead to sudden cardiac death. The current study aimed to evaluate the incidence of cardiac complications in pediatric patients with eating disorders and their associated factors.

Methods: We retrospectively analyzed patients aged 10–18 years who were diagnosed with DSM-V (Diagnostic and Statistical Manual of Mental Disorder-V) eating disorders and underwent electrocardiography (ECG) and/or echocardiography between January 2015 and May 2020.

Results: In total, 127 patients were included, of whom 113 (89.0%) were female. The median body mass index (BMI) was 15.05±3.69 kg/m². Overall, 74 patients (58.3%) had ECG abnormalities, with sinus bradycardia being the most common abnormality (91.9%). Patients with ECG abnormalities had significantly lower BMI (14.35±2.78 kg/m² vs. 16.06±4.55 kg/m², *p*<0.001) than patients without ECG abnormalities, as well as lower phosphorus and higher cholesterol levels. Among the 46 patients who underwent echocardiographic evaluation, 23 (50.0%) had echocardiographic abnormalities, with pericardial effusion being the most common (60.9%). The median left ventricular mass (LVM) and ejection fraction were 67.97±21.25 g and 66.91±28.76%, respectively. LVM and BMI showed a positive correlation (*r*=0.604, *p*<0.001). After weight gain, the amount of pericardial effusion was reduced in 3 patients, and 30 patients presented with normal ECG findings.

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Conflict of Interest

The authors have no financial conflicts of interest.

Conclusion: Cardiac abnormalities are relatively frequent in patients with eating disorders. Physicians should focus on this somatic complication and careful monitoring is required.

Keywords: Feeding and eating disorders; Cardiovascular diseases; Pericardial effusion; Bradycardia

INTRODUCTION

Eating disorders are serious psychiatric disorders characterized by abnormal eating and weight control behaviors. Anorexia nervosa (AN) is one of the most common eating disorders; adolescents have a high prevalence of AN (53.6%) and atypical AN (33.9%) [1]. AN often causes serious somatic complications [2,3] and has the highest mortality rate among psychiatric disorders; sudden cardiac death and suicide are the most common causes of death [4].

Starvation induces protein and fat catabolism, which leads to loss of cellular volume and function, thereby resulting in adverse effects and atrophy of the heart, brain, liver, intestines, kidneys, and muscles [5]. Cardiac abnormalities may involve any part of the heart, including the myocardium, pericardium, mitral valve, and/or the cardiac conduction system. Therefore, patients should be closely monitored for left ventricular dysfunction, cardiac hypotrophy, mitral valve prolapse, pericardial effusion, and QT prolongation [6-8]. Recent guidelines for patients with AN recommend routine surveillance using electrocardiography (ECG) and echocardiography [9]. However, these cardiac abnormalities have not been evaluated in children, and studies on their frequency and associated factors are limited. Therefore, in this study, we aimed to evaluate the cardiac complications in pediatric patients with eating disorders and their associated factors. Moreover, as these changes are often reversible after body weight restoration [10,11], we further evaluated the changes in abnormal cardiac abnormalities after treatment.

MATERIALS AND METHODS

In this study, we retrospectively collected the data of patients aged 10–18 years who were diagnosed with eating disorders, such as AN and bulimia nervosa (BN), at 13 centers from January 2015 to May 2020 using codes from the Diagnostic and Statistical Manual of Mental Disorder-V. Among these, those who underwent ECG or echocardiography were included in the analysis. Patients with underlying heart disease, other organic or psychiatric conditions, and those who were prescribed drugs affecting the cardiovascular system were excluded.

Medical data were obtained, including age, sex, body weight, degree of weight loss, and height. Body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters. We further calculated the BMI z-scores. Laboratory values included the white blood cell count and the levels of electrolytes, total cholesterol, thyroid stimulating hormone, and free thyroxine at the time of diagnosis. Cardiovascular complications as well as endocrine, respiratory, and hematological complications were evaluated.

Heart rate and blood pressure were measured with the patient at rest. Bradycardia was defined as a heart rate below the normal range for the patient's age measured in the awake

state (i.e., <70 bpm for school-age children and <60 bpm for adolescents) [12]. Hypotension was defined as blood pressure less than the fifth percentile or less than 90/50 mmHg for children aged 10 years and older [13].

A standard 12-lead ECG was performed with the patient in the supine position at a paper speed of 24 mm/s and an amplitude of 10 mV. The QT intervals were measured manually using a caliper from the beginning of the QRS complex to the end of the T-wave, preferentially in limb lead II. The measurements were obtained in a blinded fashion. For ECG, corrected QT interval (QTc) was calculated using the Bazett formula, considering the extended 460 ms and the boundary between 440 ms and 460 ms [14]. QT dispersion was defined as the difference between the maximum and minimum values, and required at least nine interpretable leads. Abnormal findings such as bradycardia, tachycardia, and arrhythmia were observed.

Echocardiography was performed with the patient lying in the supine or in a left lateral semi-recumbent position. Two-dimensional and M-mode echocardiographic studies were performed by pediatric cardiologists using a commercially available machine. A two-dimensional image was used to obtain the optimum position and angulation of the M-mode line. The standard parasternal, apical, subcostal, and suprasternal views were also obtained. Valve abnormalities, pericardial effusion, left ventricular mass (LVM), LVM per unit body surface area, and ejection fraction were investigated. LVM was calculated using the formula defined by Devereux et al. [15], which has been previously validated for use in children with normal hearts. The ejection fraction, which is a volumetric measure of ventricular fiber shortening, was calculated using the modified Simpson method (biplane disk summation method) [16]. The frequency of cardiac complications and associated risk factors in patients with eating disorders were analyzed. We further re-evaluated the pattern of changes on echocardiography or ECG scans after weight gain in patients with cardiac complications.

For statistical analysis, the Mann–Whitney U-test or Student's *t*-test was used for comparison of continuous variables, and the Fisher exact or chi-square test was used for categorical variables. A *p*-value of <0.05 was considered statistically significant. The statistical program SPSS (ver. 24.0; IBM Co., Armonk, NY, USA) was used for all analyses.

This study was approved by the Institutional Review Boards (IRB number 2021-04-069) of all other participating centers, and the Institutional Review Board of all other participating centers determined that informed consent was not needed, as data were anonymized and analyzed retrospectively.

RESULTS

Clinical characteristics of all patients according to electrographic abnormalities

We included 127 patients with eating disorders, of whom 113 (89.0%) were female. The mean age and BMI were 13.5±2.7 years and 15.05±3.69 kg/m², respectively.

Endocrine complications, such as amenorrhea or thyroid disease, were commonly observed, as were non-cardiac somatic complications. **Table 1** shows the main clinical and biological characteristics of patients with and without ECG abnormalities.

Table 1. Clinical characteristics of all patients according to electrographic abnormalities

Variable	Total (n=127)	Abnormal ECG (n=74)	Normal ECG (n=53)	p-value
Age (yr)	13.52±2.73	13.75±1.99	13.24±3.45	0.297
Female	113 (89.0)	69 (93.2)	44 (83.0)	0.064
BMI (kg/m ²)	15.05±3.69	14.35±2.78	16.06±4.55	<0.001
BMI z-score	-2.89±2.59	-3.46±2.64	-2.06±2.28	0.002
Weight loss (kg)	12.16±3.13	13.82±3.36	9.27±2.70	0.003
Combined complications	108 (85.0)	73 (98.6)	35 (66.0)	0.024
Psychologic	27 (25.0)	13 (17.8)	14 (40.0)	0.163
Endocrine	61 (56.5)	46 (63.0)	15 (42.9)	<0.001
Pulmonary	1 (0.9)	1 (1.4)	0	0.583
Hematologic	19 (17.6)	13 (17.8)	6 (17.1)	0.237
WBC (/mL)	5,874.2±156.8	4,937.8±143.7	6,737.6±129.3	0.006
Hb (g/dL)	12.85±1.56	12.83±1.60	12.88±1.53	0.880
Platelet (10 ³ /μL)	234.58±67.59	215.38±56.18	256.41±78.85	0.002
AST (IU/L)	50.70±5.46	57.29±5.43	36.99±5.29	0.436
ALT (IU/L)	46.80±5.10	58.32±5.51	30.47±5.31	0.274
Albumin (g/dL)	4.62±0.42	4.59±0.43	4.63±0.39	0.652
Na (mmol/L)	141.42±4.84	143.08±3.50	139.09±2.45	0.385
K (mmol/L)	4.53±0.81	4.75±0.98	4.13±0.42	0.378
Cl (mmol/L)	102.62±4.08	102.16±3.36	103.36±2.95	0.091
Ca (mg/dL)	9.35±1.49	9.65±1.58	9.30±1.36	0.213
P (mg/dL)	3.92±0.66	3.75±0.59	4.14±0.68	0.001
Mg (mg/dL)	2.31±0.21	2.33±0.23	2.25±0.16	0.323
Cholesterol (mg/dL)	208.51±50.98	226.63±51.41	180.74±34.35	<0.001

Values are presented as mean±standard deviation or number (%).

ECG: electrocardiography, BMI: body mass index, WBC: white blood cell, Hb: hemoglobin, AST: aspartate aminotransferase, ALT: alanine aminotransferase.

All patients underwent an ECG examination at the time of diagnosis, and 74 (58.3%) presented ECG abnormalities. Patients with ECG abnormalities had a significantly lower BMI than patients without ECG abnormalities (14.35±2.78 kg/m² vs. 16.06±4.55 kg/m²; $p<0.001$) as well as a higher degree of weight loss (11.6±12.36 kg vs. 2.17±14.70 kg, $p=0.011$). The phosphorus level was lower and the cholesterol level was higher in patients with ECG abnormalities than in those without.

Electrocardiographic findings at the time of diagnosis and after treatment

The most commonly observed ECG abnormality was sinus bradycardia, affecting 68 patients (91.9%); among them, seven (10.3%) had severe bradycardia. First-degree atrioventricular block and QTc prolongation were observed in 2 (2.6%) and 12 patients (17.9%), respectively.

Among 74 patients with ECG abnormalities at the time of diagnosis, 44 (59.5%) underwent follow-up ECG examination after weight gain (range: 10 days to 4.1 years; median, 7.2±3.5 months), and ECG abnormalities were no longer observed in 30 (68.2%) patients. The mean BMI increased from 14.35±2.78 kg/m² to 16.25±4.19 kg/m². **Table 2** shows the electrographic findings at the time of diagnosis and after treatment.

Clinical characteristics of patients who underwent echocardiographic evaluation

Echocardiography was performed in 46 patients (36.2%), of whom 23 (50.0%) had abnormalities. There were no significant differences in BMI or other laboratory findings between patients with and without echocardiographic abnormalities (data not shown). As expected, patients with echocardiographic abnormalities had a significantly lower LVM (61.35±18.93 g vs. 79.39±20.93 g, $p=0.022$) and a lower ejection fraction (64.24±9.75% vs. 69.85±7.12%, $p=0.041$) than those without echocardiographic abnormalities.

Table 2. Electrographic findings at the time of diagnosis and post-treatment

Variable	First ECG (n=127)	Follow-up ECG (n=44)
Normal	53 (41.7)	30 (68.2)
Bradycardia	68 (53.5)	13 (29.5)
Severe bradycardia (HR <40)	7 (5.5)	0
QTc prolongation	12 (9.4)	0
First degree AV block	2 (1.6)	1 (2.3)
BMI (kg/m ²)	14.35±2.78	16.25±4.19

Values are presented as number (%), or mean±standard deviation.

ECG: electrocardiography, HR: heart rate, QTc: corrected QT interval, AV: atrioventricular, BMI: body mass index.

Echocardiographic findings at the time of diagnosis and after treatment

Fourteen patients (60.9%) presented with mild-to-moderate pericardial effusion. All patients had a normal ejection fraction, with a mean value of 66.91±28.76%. The mean LVM and LVM index were 67.97±21.25 g and 38.15±28.76 g/m², respectively.

Among the 23 patients with echocardiography abnormalities at the time of diagnosis, 6 (26.1%) underwent follow-up echocardiography examination after weight gain (range: 10 days to 4.1 years; median, 7.2±3.5 months), and 3 patients showed improvement in pericardial effusion. **Table 3** shows the electrographic findings at the time of diagnosis and after treatment. There was a significant positive correlation between LVM and BMI ($r=0.608$, $p<0.0001$; **Fig. 1**).

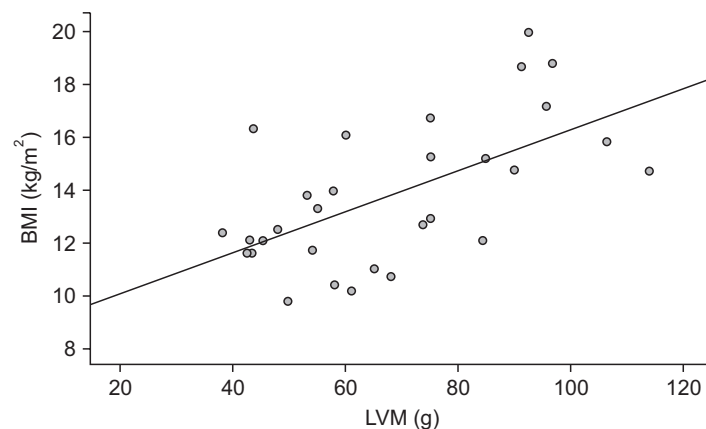


Fig. 1. Positive correlation between LVM and BMI.
LVM: left ventricular mass, BMI: body mass index.

Table 3. Echocardiographic findings at the time of diagnosis and after treatment

Variable	First echocardiography (n=46)	Follow-up echocardiography (n=6)
Normal	23 (50.0)	0
Valve anomaly	12 (26.1)	2 (33.3)
Pericardial effusion	14 (30.4)	No improvement: 3 (50.0) Improvement: 3 (50.0)
LVM (g)	67.97±21.25	70.12±23.25
EF (%)	66.91±28.76	69.78±27.63
BMI (kg/m ²)	13.41±2.56	14.74±2.66

Values are presented as number (%), or mean±standard deviation.

LVM: left ventricular mass, EF: ejection fraction, BMI: body mass index.

DISCUSSION

In this study, we determined the incidence and types of cardiovascular complications in Korean children with eating disorders. The types and severity of cardiovascular complications that commonly occur in patients with eating disorders have been previously shown to vary widely [17,18]. It is important to recognize that cardiovascular complications, if not quickly detected and corrected, can be fatal, leading to sudden death in some patients [19-22].

In the present study, 58.3% of all patients with eating disorders had abnormal ECG findings, and bradycardia accounted for 91.9% of the abnormal findings. These abnormalities were more likely to occur in patients with a lower BMI. Bradycardia has been widely reported in previous studies, with one study reporting bradycardia in up to 95% of patients with AN [23-26]. Similar to the results obtained in previous studies, bradycardia was the most common ECG abnormality observed in the current study. In patients with eating disorders, bradycardia is suspected to be a physiological adaptation to increased vagal tone and decreased metabolism of energy owing to a low caloric intake [27]. However, bradycardia can also result from electrolyte disturbances, especially low potassium, low magnesium, and certain medications.

In the current study, another commonly observed ECG abnormality was prolonged QT interval. Several previous studies have reported QT interval prolongation associated with eating disorders. Cooke et al. [28] observed a prolonged QT interval in 15% of patients with AN as compared to normal controls, and reported that two of these patients died suddenly. Patients who reached their target weight reported a significantly shortened QT interval after refeeding, although it did not completely return to normal. In a study involving adolescents, the mean QT interval was slightly longer in BN than in AN, but the difference was not statistically significant [29]. Prolonged QT intervals on ECG predispose patients to a type of arrhythmia called torsade de pointes, which can worsen into a fatal arrhythmia known as ventricular fibrillation [30]. QT dispersion has also been observed in patients with eating disorders, and patients with these findings appear to be at a higher risk of sudden cardiac death [31]. The prolonged QT interval can result from rapid or severe weight loss [32].

In a previous study in adults, the degree of BMI or weight loss was a factor influencing these abnormal findings; there were more associated complications in these patients [33]. Cardiac arrhythmias have been more commonly observed in patients with a less than ideal body weight [34]. In a multiple regression analysis of a previous study in children, underweight, low BMI, and rapid weight loss just before testing were the most important independent predictors of QTc interval prolongation [35]. In the current study, pediatric patients with ECG abnormalities had a significantly lower BMI than those without ECG abnormalities.

In the current study, patients with ECG abnormalities had significantly higher cholesterol levels and significantly lower phosphorus levels, although potassium and magnesium levels were not significantly different between patients with and without ECG abnormalities. Furthermore, hypercholesterolemia can be caused by an increase in lipolysis and a decrease in cholesterol clearance, thereby leading to cardiovascular complications [36]. The greatest cardiac risk in normal-weight patients with eating disorders, such as BN, is that arrhythmias may occur due to electrolyte abnormalities, including low serum potassium or low serum magnesium. Furthermore, the risks of hypercholesterolemia, hypertension, and diabetes are high in obese patients with eating disorders such as binge eating disorders. All of

these factors can lead to cardiac complications, such as atherosclerotic heart disease and congestive heart failure [18].

In the current study, 50% of patients who underwent echocardiography had abnormalities, and pericardial effusion was observed in approximately 60% of these patients. In a previous study, factors associated with pericardial effusion included low BMI, rapid weight loss, and low T3 and insulin-like growth factor 1 levels [37]. The results of the current study also confirmed a positive relationship between BMI and LVM, similar to the results of many previous studies that showed a significant correlation between BMI and LVM index [38-40].

Most of the above-mentioned issues are reversible, or at least treatable, with proper medical treatment and good nutritional rehabilitation, in consideration of the vascular and electrolyte status of the individual; however, in some cases, emergency procedures, such as cardiac tamponade, are required to prevent sudden death [10]. Although follow-up echocardiography was performed in only 26% of the patients who initially had abnormal echocardiographic findings, pericardial effusion was observed to improve in half of the patients who received follow-up echocardiography in the current study.

The current study has several limitations which should be mentioned. First, as the data used in this study were collected retrospectively, our understanding of the causal relationship between the correlated variables and the factors that influenced them is limited. In addition, the multicenter study design resulted in an inconsistency in the follow-up period for cardiac complications. Second, data on female hormones affecting ECG abnormalities could not be collected. Third, the analysis was conducted without classifying the types of eating disorders, and it was not possible to evaluate whether the mechanisms of cardiovascular disorders were different depending on the underlying eating disorder. However, as almost 90% of the patients had AN, it would be meaningless to analyze this. To overcome these limitations, well-designed prospective studies should be conducted in the future. Despite these limitations, our study is still valuable as it remains the first multicenter study to evaluate cardiovascular complications in Korean children with eating disorders.

In conclusion, cardiac abnormalities are relatively common in patients with eating disorders. Therefore, this somatic complication should be considered and carefully monitored.

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