

Cardiac abnormalities determined by tissue Doppler imaging and arrhythmias in adolescents with anorexia nervosa

Original Article

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Abstract

Background: Anorexia nervosa has a prevalence of 0.5–3% in adolescents, placing this population at increased risk of cardiac anomalies including arrhythmias, pericardial effusion, and myocardial dysfunction. Our objective is to describe cardiovascular anomalies observed by tissue Doppler imaging in patients with anorexia nervosa. **Methods:** We retrospectively reviewed electrocardiogram, Holter, and echocardiography findings in 28 patients diagnosed with anorexia nervosa. **Results:** Electrocardiogram was abnormal in 71% of patients with sinus bradycardia observed in 57%. Holter confirmed sinus bradycardia without significant pauses. Prolonged QTc, low voltage, and ectopic beats were each seen in 14% of patients. Wenckebach atrioventricular block was observed in one patient. Supraventricular or ventricular tachycardia was not observed. Echocardiography showed structurally normal heart in all patients. Pericardial effusion was seen in 7.1% of patients and left ventricular mass was decreased in 10.7%. Mean ejection fraction was 0.73 and mean fractional shortening was 38.4%. Tissue Doppler imaging revealed systolic or diastolic dysfunction in four patients with e', a', and s' velocities in the lateral and septal basal segments more than two standard deviations below the mean. Two patients had decreased left ventricular mass but no significant difference in disease duration from the group. Basal segment velocities below one standard deviation were also observed in an additional seven patients. **Conclusion:** A trend for decreased tissue Doppler imaging velocities was seen in 25.0% of patients, while significant systolic and diastolic dysfunction was seen in 14.3% of patients, associated with a significant reduction in left ventricular mass and independent of disease duration.

Anorexia nervosa is a major eating disorder with a prevalence of 1–3% in adolescents and young adults and has the highest mortality rate (20%) among psychiatric disorders with an aggregate mortality rate of approximately 5.6% per decade shown by meta-analysis.^{1–5} Approximately one-third of deaths in patients with anorexia nervosa have been attributed to cardiovascular complications, second only to suicide.^{6,7}

Cardiac abnormalities are found in up to 80% of patients with anorexia nervosa.^{4,8,9} Significant electrocardiographic findings include sinus bradycardia, decreased voltages, and prolongation of the QT interval and QT dispersion. The latter two abnormalities have been implicated with arrhythmias and sudden death in patients with anorexia nervosa; however, a causal role has not yet been demonstrated.^{10–17} Structural abnormalities in anorexia nervosa reported by echocardiography include decreased cardiac mass, mitral valve prolapse, pericardial effusion, reduced left ventricular diastolic and systolic dimensions, and decreased cardiac output. Remarkably, these patients do not present with congestive heart failure observed by ejection fraction and fractional shortening remaining normal as measured by echocardiography in most patients with anorexia nervosa. This suggests an underlying cause to cardiac muscle dysfunction, despite it not being detected by standard echocardiographic indices such as ejection fraction and fractional shortening.^{8,18–26}

Tissue Doppler imaging has been shown to be a useful tool in the evaluation of systolic and diastolic dysfunction in other cardiomyopathies.^{26,27} Tissue Doppler imaging abnormalities in anorexia nervosa could indicate early myocardial compromise and could prove as a useful marker for aggressive nutritional intervention in these patients. The purpose of the present study was to describe cardiovascular anomalies, particularly myocardial dysfunction, using tissue Doppler imaging in young patients with anorexia nervosa.

Table 1. Demographic characteristics of anorexia nervosa cohort.

Characteristic	Value
Female sex	20 (71.4%)
Mean age	14.4 years
Mean duration of disease	10.3 months
Mean BMI (kg/m ²)	18.0 ± 2.69
Mean BMI (%)	28.0% ± 25.6

Materials and methods

Patients

We retrospectively reviewed 28 patients referred for initial cardiac evaluation with a diagnosis of anorexia nervosa. The diagnosis was made by the referring paediatrician and psychiatrist based on standard criteria made by the American Psychiatry Academy, DSM-IV (American Psychiatric Association, 2000). Evaluation included history of cardiac symptoms, physical examination, electrocardiogram, 24-hour heart rhythm Holter monitoring, and echocardiography. The chart review was performed with permission and according to the standards of the Hospital Clinical Research Committee.

Electrocardiogram

Twelve lead electrocardiograms were recorded on a Burdick Atria 3100 system at 25 mm/second paper speed and 1 mm/mv amplitude. The electrocardiograms were obtained in the resting stage in the supine position. Heart rate was calculated from the average of RR intervals. QT measurements were manually obtained by a single co-author electrophysiologist on lead II from the earliest onset of the QRS complex to the end of the T wave as it joined the baseline. QT intervals were corrected using the Bazett formula for heart rate: $QTc = QT/\sqrt{RR}$. QTc was considered borderline when longer than 440 ms and prolonged when longer than 460 ms.

Holter

24-hour heart rate and rhythm Holter monitoring was performed on an ambulatory basis using a Mortara Hscribe 5 system. The results were analysed and interpreted by a single co-author electrophysiologist.

Echocardiography

Patients underwent a complete echocardiogram by a single co-author paediatric cardiologist in the lateral decubitus position using a GE Vivid E9 ultrasound machine. Standard measurements of diastolic left ventricular dimensions, fractional shortening, ejection fraction, and left ventricular mass were performed according to the recommendations of the American Society of Echocardiography.^{28,29,30} Fractional shortening was measured by 2D guided M-mode at the level of the papillary muscles and calculated using the formula $[(LVEDD-LVESD)/LVEDD] \times 100$. Ejection fraction was calculated using the Simpson's method by planimetry of the left ventricular area in apical four and two chamber views.

Tissue Doppler imaging

Tissue Doppler imaging was obtained at the cardiac base in the apical four chamber view. The early diastolic (e'), late diastolic (a'),

and systolic (s') annular velocities were measured in the lateral left ventricular wall and the interventricular septum using standard techniques.³¹ The values were compared to published standards for children and adolescents.³² Systolic and diastolic time intervals measured from tissue Doppler imaging; normal values and z-score tables, and effects of age, heart rate, and body surface area.

Results

Electrocardiogram and Holter

The electrocardiogram was abnormal in 20 children, representing 71.4% of our patients. The most common abnormality was sinus bradycardia, observed in 16 patients (57.1%). A borderline prolonged QTc interval (between 440 and 459 ms) was seen in 14%, and a significantly prolonged QTc (>460 ms) was seen in an additional 14% of patients. Low QRS voltage was seen in 14% of patients. Isolated atrial and ventricular premature contractions were seen in 14% of patients.

The 24-hour heart rate and rhythm Holter monitor confirmed the presence of sinus bradycardia in all patients. Second degree AV block, Wenckebach, was observed in one patient. Supraventricular or ventricular tachycardia was not observed.

Echocardiography

All patients had anatomically normal hearts, without CHD. Decreased ventricular mass (<44 g/m²) was seen in three patients (10.7%). Pericardial effusion without sign of tamponade was seen in two patients (7.1%).

In regard to left ventricular function, fractional shortening was within normal limits with a mean of 38.4% and a range of 26–48.9%. Only one patient showed a decreased fractional shortening at 26%. The patient was a 16-year-old female weighing 44.9 kg with a BMI of 18.7, and a left ventricular mass of 106 g. She had a disease duration of 4 months, which was no different from the rest. Ejection fraction was normal in all patients with a mean of 73% and a range of 59–87%.

Tissue Doppler imaging

Tissue Doppler imaging indicated abnormalities in four patients, representing 14.3% of the group. These patients had at least one decreased velocity –2 SD below the mean in the lateral and septal basal segments, indicating systolic and diastolic dysfunction. One of these patients had both diastolic and systolic dysfunction with four velocities –2 SD below the mean. One other patient showed diastolic dysfunction with three velocities –2 SD below the mean. Each of these two patients was also found to have severely decreased left ventricular mass at 42 and 40 g/m² with a disease duration of 17 and 9 months, respectively, which are no different from the group average.

The two additional patients were only found to have one velocity decreased –2 SD below the mean, consistent with diastolic dysfunction in one and systolic dysfunction in the other. Neither patient had severe decrease in left ventricular mass. Disease duration for these patients was 18 and 5 months, respectively.

Additionally, tissue Doppler imaging showed a trend towards lower lateral and/or septal basal segment velocities in nine patients (32.1%) between –1 and –2 SD of published standards for their age group. Two of these patients also had at least one velocity more than –2 SD below the mean as discussed above.

Table 2. Means and z-scores for tissue Doppler imaging sites.³²

Tissue Doppler imaging site	Mean	z-score n (%)				
		< -2	-2, -1	-1, 1	1, 2	> 2
e' lateral	0.20 ± 0.031	1 (3.6)	3 (10.7)	21 (75)	3 (10.7)	0 (0)
a' lateral	0.067 ± 0.017	2 (7.1)	3 (10.7)	21 (75)	0 (0)	2 (7.1)
s' lateral	0.12 ± 0.026	1 (3.6)	2 (7.1)	21 (75)	3 (10.7)	1 (3.6)
e' septal	0.14 ± 0.032	2 (7.1)	4 (14.3)	19 (67.9)	2 (7.1)	1 (3.6)
a' septal	0.066 ± 0.020	1 (3.6)	0 (0)	22 (78.6)	3 (10.7)	2 (7.1)
s' septal	0.089 ± 0.017	2 (7.1)	1 (3.6)	21 (75)	2 (7.1)	2 (7.1)

Discussion

Anorexia nervosa is a major eating disorder with a prevalence of 1–3% in adolescents and young adults and has the highest mortality rate (20%) among psychiatric disorders. Approximately one-third of deaths in patients with anorexia nervosa have been attributed to cardiovascular complications, second only to suicide. Cardiac abnormalities are found in up to 80% of patients with anorexia nervosa.^{1–7}

The present study showed that sinus bradycardia was a common finding in adolescents with anorexia nervosa, which has been well documented in previous studies.^{10–11} Possible aetiological factors include increased vagal tone, decreased sympathetic tone, thyroid dysfunction, electrolyte abnormalities, drug side effects, decreased myocardium glycogen content, and muscle atrophy.^{4,12,26,31–35}

Prolongation of the QT and QTc interval was also relatively common, seen in 28% of our patients. Prolongation of the QT interval and increased QT dispersion have been previously reported as well. These abnormalities have been implicated in the onset of arrhythmias and sudden death; however, a causal role has not yet been demonstrated in patients with anorexia nervosa. QT abnormalities in anorexia nervosa are unlikely the result of a channelopathy of the type seen in patients with hereditary long QT syndrome. Proposed mechanisms for QT abnormalities in anorexia nervosa include limitations of the measurement associated with bradycardia, autonomic imbalances, electrolyte disorders, nutritional deficiencies, rapid weight loss, and cardiac atrophy. More interestingly, structural myocardial changes due to starvation such as fibrosis and adipose infiltration possibly leading to non-homogeneous myocardial depolarisation and repolarisation could be the substrate for arrhythmia in anorexia nervosa.^{10–17}

Structural abnormalities in anorexia nervosa reported by echocardiography include decreased cardiac mass, mitral valve prolapse, pericardial effusions, reduced left ventricular diastolic and systolic dimensions, and decreased cardiac output. Remarkably, these patients do not present congestive heart failure consistent with the observation that fractional shortening and ejection fraction as measured by echocardiography remain normal in most patients. Histological and MRI findings in patients with anorexia nervosa suggest an underlying cause to cardiac muscle dysfunction, despite it not being detected by standard echocardiographic indices such as fractional shortening and ejection fraction.^{8,18–26}

Tissue Doppler imaging has been shown to be a useful tool in the evaluation of systolic and diastolic dysfunction in other cardiomyopathies.²⁷ In our series, we found four patients (14.3%) with abnormal tissue Doppler imaging indicating systolic or diastolic dysfunction. Two cases also had severely decreased left ventricular mass, which represented two of three total patients with

decreased left ventricular mass in our study. This could be an indication of an association between left ventricular mass and severe diastolic dysfunction as measured by tissue Doppler imaging in anorexia nervosa patients. The patients' disease duration was not different from the group average. One of these patients also had tissue Doppler imaging abnormalities indicating both systolic and dysfunction. None of these patients presented with QT abnormalities.

In addition, 7 (25.0%) of the remaining patients showed a trend towards decreased systolic or diastolic dysfunction with either tissue Doppler imaging velocities decreased to between -1 and -2 SD, which could represent an early manifestation of myocardial systolic and diastolic dysfunction despite normal fractional shortening and ejection fraction by standard echocardiography techniques.

Other reports of tissue Doppler imaging evaluation in patients with anorexia nervosa have yielded contrasting results.³⁶ Similar to our findings, the series by Escudero³⁷ showed that despite normal contractility by fractional shortening and ejection fraction the patients have abnormal tissue Doppler imaging indices. This could indicate early myocardial compromise in patients with anorexia nervosa and could prove as a useful marker for aggressive nutritional intervention in these patients. Refeeding has been shown to be an effective treatment in reversing the adverse cardiac effects of anorexia nervosa.^{9,11}

Therefore, the finding that tissue Doppler imaging could serve as a tool for identifying myocardial dysfunction over the more standard findings of reduced fractional shortening and ejection fraction values is potentially clinically relevant in anorexia nervosa patients. Abnormal tissue Doppler imaging could indicate abnormal histologic findings as described above which could be the substrate for QT prolongation and other possibly malignant ventricular arrhythmias. Further studies are necessary to evaluate the correction of the observed cardiac abnormalities after aggressive nutritional intervention and to establish a standard threshold using tissue Doppler imaging for such an intervention.

In conclusion, abnormal tissue Doppler imaging findings may be an effective tool in detecting early myocardial compromise which could help to reduce the risk for cardiac complications including arrhythmias and sudden cardiac death in these patients by means of closer monitoring and aggressive and timely nutritional intervention.

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Conflicts of interest. None.

Ethical standards. This article is a retrospective chart review and contains no experimentation with human participants or animals performed by any of the authors.

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