Cardiac complications of malnutrition in adolescent patients: A narrative review of contemporary literature

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ABSTRACT

Eating disorders are common. Between 1% and 2% of adolescent females and 0.5% of males suffer from anorexia nervosa, bulimia nervosa, and binge eating disorder. Although suicide represents nearly half of the mortality in patients with eating disorders, a majority of the remainder is cardiac arrest, likely secondary to cardiovascular complications of eating disorders such as bradycardia, hypotension, QT interval changes, structural heart disease, and pericardial effusion. Bradycardia is suspected to be secondary to increased vagal tone and is a common finding in patients admitted with disordered eating. Similarly, hypotension and orthostatic abnormalities are common complications due to atrophy of peripheral muscles. Descriptive studies report prolongation of the corrected QT interval (QTc) in these patients relative to controls, albeit within the normal reference range. Structural heart disease is also common, with left ventricular mass reported as lower than predicted in several studies compared to healthy controls. Pericardial effusion is also commonly described, although it is possible that this is underestimated, as not all patients with eating disorders undergo echocardiograms. Further, refeeding syndrome as a result of treatment of eating disorders carries its own cardiac risks. Cardiac complications of malnutrition are common but reversible with appropriate management and recovery. It is imperative that providers are aware of the epidemiology of these complications, as it is only with a high clinical suspicion that proper evaluation including a thorough history and physical examination, electrocardiogram, and when necessary echocardiogram can be performed.

Keywords: Adolescent medicine, malnutrition, pediatric cardiology

INTRODUCTION

Eating disorders are relatively common psychological disorders affecting between 1% and 2% of adolescent females and 0.5% of males.[1] This spectrum of disease includes anorexia nervosa, bulimia nervosa, binge eating disorder, purging disorder, and other specified feeding and eating disorders.[2] During the last decade, there has been a significant increase in eating disorders among adolescent patients.[3] Risk factors for eating disorders include other psychiatric disorders and suicidality.[4] However, differences in these factors exist between subtypes of this heterogeneous class of conditions.[4]

There are numerous health consequences of eating disorders and subsequent malnutrition. The aggregate mortality for anorexia nervosa is 5.6% per decade of illness, with suicide accounting for half of the deaths and cardiac arrest accounting for a majority of the remainder.[1] Aside from mortality, additional concerns including growth retardation, pubertal delay, and reduction in peak bone mass are common complications.[1] Adolescents with eating disorders are more likely to have other negative health outcomes

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including mental health disorders, substance use, self-harm, and continued challenges with body weight.[2]

In addition, numerous cardiovascular complications have been reported including hemodynamic changes, structural changes, cardiomyopathy, and premature death.[5] Much of the mortality and morbidity of eating disorders can be attributed to cardiovascular complications such as QTc prolongation, electrolyte abnormalities, hypotension, and bradycardia.[6] Patients with eating disorders exhibit myocardial atrophy related to hypovolemia, low cardiac output, and increased peripheral resistance despite hypotension.[6]

Although these manifestations are well reported in the literature, an abundance of data has been reported over the last decade as the prevalence of eating disorders has increased. The aim of this study is to summarize and organize recent literature describing cardiac complications of malnutrition in adolescent patients.

METHODS

In the last decade, several single-center articles discussing the cardiac complications of malnutrition have been published. A review of the literature using PubMed and Google Scholar was undertaken, limited to articles published in the past 10 years. Hundreds of articles returned from this query. These papers were then reviewed by the authors to critically appraise the strength of the evidence presented and the relevance to the scope of this review.

CARDIAC COMPLICATIONS OF MALNUTRITION

Bradycardia

Bradycardia is the most common cardiovascular finding in pediatric patients admitted for malnutrition.[7] It is hypothesized that this may be a physiological adaptation to low caloric intake, resulting in an increased vagal tone and decreased metabolism.[8] Structural cardiac changes noted in these patients, including decreased left ventricular mass and bradycardia may be a compensatory mechanism to prevent heart failure.[9] In addition, decreased glycogen content and cellular atrophy may play a role.[10]

Numerous studies describe bradycardia in patients hospitalized with eating disorders. A study from the UK demonstrates greater risk of bradycardia in anorexia nervosa relative to other eating disorders.[11] Heart rate was significantly lower in patients with anorexia nervosa relative to normal controls in a series of 40 patients.[12] A separate study of 40 young women with anorexia nervosa demonstrated sinus bradycardia in 18 at baseline, but only 5 on follow-up after weight restoration.[13] A small

study of 11 patients with anorexia nervosa revealed lower heart rate than controls that recovered after refeeding.[14]

In a retrospective study, 16 of 20 patients admitted for anorexia nervosa demonstrated sinus bradycardia.[15] A different evaluation of 38 adolescent patients found a rate of bradycardia of 68% of subjects.[16] Interestingly, patients with a longer duration of illness were less likely to be bradycardic.[16] In this study, body mass index (BMI) was predictive of a lower heart rate.[16] Further, heart rate demonstrated to be a predictor of spinal bone mineral density (BMD) indicating a more profound degree of malnutrition.[16]

Another study of 171 adolescents with anorexia nervosa revealed that greater total and recent weight loss were associated with a lower heart rate nadir.[17] These same traits were associated with high incidence of bradycardia.[17] A study evaluating 33 adolescent males with eating disorders found that mean heart rate was 58.7 with mean orthostatic change in heart rate of 22 beats per minute (BPM).[18] This study was descriptive only of a male population and did not compare these findings to female patients or controls.

Interestingly, case reports have described referrals for cardiac pacing for patients later found to have symptomatic bradycardia due to malnutrition.[19,20] Pacemaker implantation is rarely indicated, given the recovery of heart rate with improvement of nutritional status.[20] Further, pacemaker implantation may further distort the patient perception of body image, increasing the risk of worsening symptoms of an underlying eating disorder.[20]

Hypotension and orthostasis

Patients with malnutrition have low cardiac output and increased peripheral resistance despite hypotension.[6] It has been proposed that, in eating disorders, atrophy of peripheral muscles results in decreased venous return, causing hypotension.[21] Usually, patients with eating disorders are not acutely volume depleted, so orthostasis reflects nutritional compromise rather than hypovolemia, though severe malnutrition and deconditioning may also play a role.[21] In patients with malnutrition, peripheral perfusion is often diminished to shunt blood centrally, so patients can have cool extremities and poor capillary refill.[21]

In a study of twenty adolescent females, the BMI Z-score correlated with low systolic blood pressure.[15] A series of 11 patients demonstrated lower blood pressure in anorexia nervosa than in controls which recovered to normal levels after refeeding.[14]

Repolarization abnormalities and QT changes

In a descriptive study of 38 patients with anorexia nervosa, 68% had sinus bradycardia, 8% of cases had

right axis deviation, and 5% had premature atrial contractions.[16] Admission BMI was predictive of a lower heart rate. These patients also had a longer mean QT interval than controls, though within the normal reference range.[16]

A study of 40 patients with anorexia nervosa demonstrated a longer QT interval in the sample relative to controls with improvement in QTc and QT dispersion from baseline to follow-up.[13] A separate study describes longer QT and QTc relative to controls and lower R wave amplitudes in V6.[14] Another article reports a widened QT dispersion among patients with malnutrition relative to healthy controls.[15] QT interval has also proven to be a predictor of spinal BMD.[16]

Aside from the QT interval, in a study of 40 patients with anorexia nervosa, 15 had premature atrial contractions and 3 had premature ventricular contractions on 24-h Holter monitoring.[13] After weight restoration, premature supraventricular contractions were noted in only four patients.[13]

Although bradycardia is common, it is typically without conduction impairment.[22] Fatal arrhythmias may be triggered by electrolyte abnormalities.[23] This is particularly worrisome in the setting of refeeding syndrome.[24] QT changes in malnutrition have been attributed to histologic changes in the myocardium and collagen which alters myocardial blood flow, causing direct effect on repolarization and subsequent degeneration of the conduction system.[6]

Structural heart disease

It is hypothesized that structural heart disease in patients with eating disorders is attributable to myocardial atrophy.[6] It is uncertain whether the decrease in left ventricular mass is secondary to malnutrition or simply a reduction in preload.[25] Left ventricular end diastolic dimension, mass, and cardiac output were lower in anorexia nervosa at diagnosis than after weight restoration in a series of forty patients.[13] Another study also demonstrated left ventricular mass and left ventricular mass index lower relative to healthy controls that improved after refeeding.[14]

Left ventricular mass was lower than predicted in 31% of patients in a series of 38 adolescents.[16] In this study, both posterior wall and septal thickness were lower than predicted in 9 and 12 patients, respectively.[16] However, fractional shortening and ejection fraction were normal.[14]

Left ventricular end-diastolic and end-systolic dimensions were lower than in controls in a study of 173 patients.[26] However, there were no differences in interventricular septal thickness, posterior wall thickness, or fractional shortening.[26] A strong correlation has also been demonstrated between left ventricular mass and QT dispersion.[14]

A study comparing 47 patients with malnutrition to 44 normal controls demonstrated decreased left ventricular mass but no difference in left ventricular mass index in the case sample.[24] Further, the left ventricular ejection fraction and fractional shortening were lower in those with malnutrition.[24] This study also revealed a higher myocardial performance index among controls.[24] It was also demonstrated that worse cardiac function was associated with the degree and duration of malnutrition.[24]

Another study of forty patients with anorexia nervosa revealed reduced left ventricular mass with normal systolic function.[9] Interestingly, patients with anorexia nervosa were more likely to have mitral valve prolapse, with a prevalence of 23% in the sample.[9] A separate study also describes mitral valve prolapse in 8 patients that persisted after recovery in 3 cases.[10] Further, myocardial fibrosis was seen in 23% of patients but no controls.[9]

Pericardial effusion

A study of 35 patients revealed pericardial effusion in three patients, described as small to moderate with BMIs ranging from 12.6 to 17.3.[16] In a retrospective study, a lower BMI Z-score was found to correlate with the presence of a pericardial effusion on admission.[16]

A study of 173 adolescents admitted with anorexia nervosa demonstrated pericardial effusion in 34.7% with no clinical correlates.[26] Patients with effusion were more likely to have a lower BMI, lower triiodothyronine, and longer duration of hospitalization.[26] Remission was noted in 88% of patients after weight restoration.[26]

The exact mechanism of pericardial effusion in eating disorders is poorly understood, though it is postulated that metabolic factors including carnitines or autoimmune mechanisms may be contributory factors.[27]

TREATMENT OF EATING DISORDERS AND ASSOCIATED COMPLICATIONS

Indications for hospitalization of adolescents with eating disorders

The Society for Adolescent Health and Medicine put forth recommendations in the Journal of Adolescent Health for hospitalization of adolescents and young adults with eating disorders in 2015. The medical provider's decision to admit a patient with an eating disorder is based on comprehensive clinical assessments that account for

the seriousness of the patient's health, the timing of weight loss, and failure of outpatient treatment. Eleven indications are listed as follows: <75% median BMI, dehydration, electrolyte abnormality, electrocardiogram (EKG) changes, severe bradycardia, hypotension, hypothermia, orthostatic hypotension, poor growth, failure of outpatient management, food refusal, refractory bingeing and purging, medical complications, and psychiatric or other medical conditions that prohibit or limit outpatient treatment.[28] If a patient demonstrates any one parameter listed above, it would be an indication for hospitalization. It is important to note that most of the worrisome complications of eating disorders are cardiac in nature, so providers taking care of these patients should monitor vital signs very closely during their care.[28]

Treatment of eating disorders

The most common goal for hospital-based stabilization is nutritional restoration.[29] Hospitalized patients with anorexia nervosa are monitored very closely due to the risk of refeeding syndrome. Their diets are strategically advanced slowly in order to prevent refeeding sequelae.[30] In the past, nutritional rehabilitation was based on conservative, consensus-based recommendations for lower calorie refeeding because of concerns about the refeeding syndrome; however, clinical practice is moving toward higher-calorie refeeding earlier in the course of hospitalization.[30] The "start low and go slow" maxim has been challenged since the risk of refeeding syndrome correlates with the severity of starvation; therefore, patients with less severe presentations of anorexia nervosa might be able to start at a higher calorie diet and advance more quickly.[31] Nasogastric tube feeding may be necessary for some patients, although some physicians find this method to be punitive or invasive. Others find it to be empathic since it is taking away the psychological and physical difficulties of eating for patients.[31] It is important to note that the majority of eating disorder treatment occurs in an outpatient setting. Over the past two decades, family-based therapy has become the mainstay treatment approach of eating disorders. It involves therapy where the entire family unit meets with a therapist.[31] Other treatment entities exist including day programs and residential treatment facilities. These types of treatment centers are for patients that need more structure than they would receive in their home setting.[31]

Cardiac complications of refeeding syndrome

Refeeding syndrome is associated with severe electrolyte disturbances, particularly low phosphate, magnesium, and potassium, after reintroducing nutrition to undernourished patients.[32] With long periods of nutritional deprivation, survival depends on the ability to efficiently use and preserve available energy reserves.[33] The depletion of electrolytes is further exacerbated by

conditions such as diarrhea or diuretic use, which can further exacerbate the depletion of electrolytes.[34] This can lead to hypoglycemia, metabolic acidosis or alkalosis, EKG abnormalities, hemodynamic instability, orthostasis, seizures, and pancreatitis, among others.[35]

Phosphorus is the principal ion discussed in many published reports related to refeeding syndrome.[35] Phosphate is essential to many metabolic pathways, specifically glycolysis, oxidative phosphorylation, and regulation of hemoglobin oxygen dissociation.[32] Phosphate depletion can therefore lead to respiratory muscle dysfunction, which can progress to acute respiratory failure in severe cases.[32] Low serum concentrations can also result in cardiac arrhythmias, particularly prolonged QT intervals.[32]

Serum concentrations of potassium decrease because of insulin stimulation of the sodium-potassium ATPase, a cell wall enzyme that is responsible for influx of potassium and efflux of sodium out of the cell. The Na-K-ATPase is essential in transmission of nerve impulses and contraction of muscles.[32] Hypokalemia may result in impaired transmission of electrical impulses, potentially leading to arrhythmias.[33] Hypokalemia can cause cardiac complications including prolongation of P-R interval, flattening of T waves, and prominent U waves on EKG.[32] Hypokalemia may also manifest as weakness, hyporeflexia, respiratory depression, and paralysis.[33] Hypomagnesemia has also been identified as a feature of refeeding syndrome. Hypomagnesemia can evoke potentially lethal cardiac arrhythmias including Torsades de Pointes.[32]

Finally, refeeding syndrome can also lead to thiamine deficiency. The demand for thiamine greatly increases during transition from starvation to feeding, since it is a cofactor for glucose-dependent metabolic pathways.[33] Thiamine deficiency can lead to the decreased production of adenosine triphosphate (ATP) in cardiac myocytes. This can eventually lead to congestive heart failure. Adenosine release into the plasma causes vasodilation, leading to increased cardiac output, decreased contractility of the heart muscle, and low diastolic blood pressure.[33]

DISCUSSION

Cardiac complications of malnutrition are common but reversible with recovery from eating disorders. A growing body of recent literature describing the frequency of bradycardia, hypotension, QT interval changes, structural heart disease, and pericardial effusion have improved the understanding of these processes. The pathogenesis and interplay of these factors are summarized in Figure 1. It is possible that these studies underestimate the true incidence of structural heart disease and pericardial effusion, as not all patients admitted with eating disorders
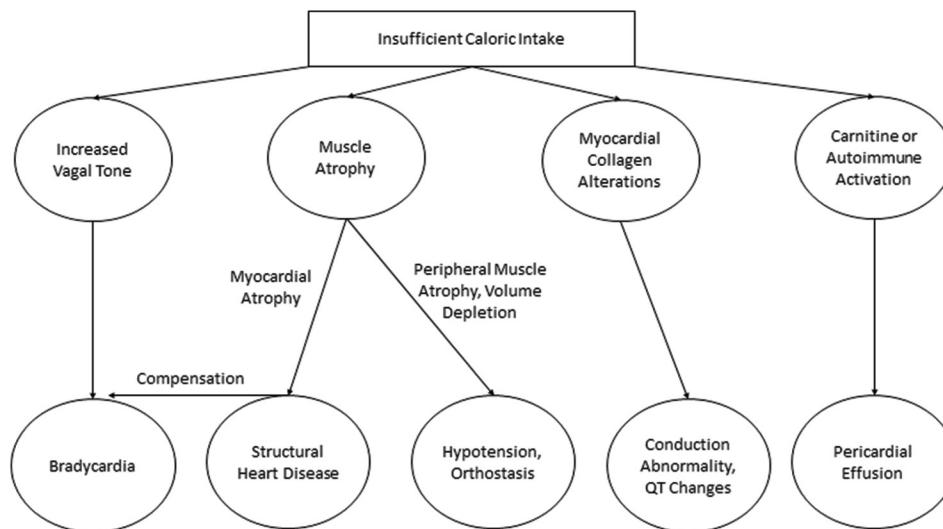
Figure 1: Visualization of pathogenesis and interplay of cardiac complications of malnutrition

receive an echocardiogram. Rather, these patients are far more likely to have frequent vital signs and EKG, accounting for the breadth of evidence reporting bradycardia, hypotension, and electrical abnormalities.

It is imperative that providers are aware of the epidemiology of these complications, as it is only with a high clinical suspicion that proper evaluation including a thorough history and physical examination, EKG, and when necessary echocardiogram can be performed.

Further research is warranted, not only in better describing the epidemiology and risk factors of eating disorders, but also of their associated cardiovascular complications. Multicenter studies may more accurately reflect the true incidence of this family of conditions. Further, an improved understanding of the mechanisms of these complications may empower clinicians to better prevent and treat their manifestations in pediatric patients.

Financial support and sponsorship

Conflicts of interest

There are no conflicts of interest.

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