

REVIEW PAPER

Cardiovascular complications in children and adolescents with anorexia

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ABSTRACT

Anorexia nervosa is a major public health problem that affects people of all ages, including children. Eating disorders can lead to many complications, one of the most serious of which are heart disorders. This article aimed to discuss the large scale of anorexia among children and adolescents, the most common cardiological complications, and presentation of a practical approach to the problem. For this purpose, a comprehensive review of the literature was conducted. The described cardiological complications in anorexics are as follows: arrhythmias, mitral valve prolapse, pericardial effusion, congestive heart failure, myocardial infarction, and Takotsubo cardiomyopathy. According to existing studies, it is essential to react quickly in the event of diagnosing an eating disorder among adolescents. Observation of the patient for cardiac complications is very important for saving the health of a child with anorexia nervosa. Children with eating disorders require long-term care, involving many people like doctors, psychologists, and parents.

KEY WORDS:

anorexia nervosa, cardiovascular diseases, eating disorders, children and adolescents, paediatric cardiology.

INTRODUCTION

Anorexia nervosa (AN) is an eating disorder that most commonly affects adolescents, especially girls. Anorexia is an eating disorder involving the deliberate loss of body weight caused and sustained by a sick person. It is characterized by a restriction of consumed eating, a strong fear of gaining weight, and an incorrect assessment of their own body. Anorexia most often affects young women (female-to-male ratio 10 : 1); nevertheless, AN may be underdiagnosed in men [1]. The aetiology and pathophysiology of AN are complex because they include genetic, neurobiological, psychodevelopmental, as well as social and cultural factors [2, 3]. It has been known since the 1980s that the cardiovascular system undergoes changes in AN and that cardiac complications significantly worsen the prognosis of patients [4, 5].

The main cardiovascular consequences of AN comprise a prolonged QT interval, sinus bradycardia, myocardial mass modification, hypotension, and arrhythmias [6].

Anorexia nervosa has a 5-fold higher mortality rate than in the general population [7, 8]. In the case of anorexia, cardiovascular complications are the leading cause of morbidity and mortality [5]. Eating disorders, such as anorexia nervosa, are linked to other mental disorders, such as depression, which is often the cause of suicide attempts in children [9].

Eating disorders are multi-system diseases. A proper diagnosis is the first step in treating an eating disorder. It is important to understand that patients with weight loss, despite the apparently short duration of their disease, may face serious medical complications requiring evaluation and treatment.

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TABLE 1. Cardiovascular complications in anorexia nervosa [5]

Type of disorder	Frequency	Diagnosis
Conduction disease		
Bradycardia	High	ECG
QT prolongation	High	ECG, electrolytic assessment, evaluation of psychotic drugs
Atrioventricular block (\geq type II Mobitz 2)	Very rare	ECG
Ventricular arrhythmia	Rare	ECG, consider if history of syncope
Structural heart disease		
Low left ventricular mass index, low cardiac output, reduced diameters	High	Echocardiography
Mitral prolapse	Moderate	Echocardiography
Pericardial effusion	Moderate	Echocardiography
Ischemic heart disease		
Dyslipidaemia	Moderate	Laboratory
Acute myocardial infarction	Very rare	ECG
Re-feeding syndrome		
QT prolongation	Moderate	ECG
Ventricular arrhythmia	Rare	ECG
Acute heart failure	Rare	Clinical evaluation. Consider echocardiogram before re-feeding

ECG – electrocardiography

The aim of the study was to review various studies on the effects of disfigurement on the cardiovascular system. Articles published in the period 1982–2021, relating to the discussed topic in the population of children and adolescents, included in the PubMed and Elsevier databases were analysed (Table 1).

The paper complies with the Helsinki Declaration, EU Directives, and harmonized requirements for biomedical journals.

EPIDEMIOLOGY AND RISK FACTORS FOR CARDIOVASCULAR COMPLICATIONS IN ANOREXIA NERVOSA

Cardiovascular complications occur in up to 80% of AN patients and can be a direct cause of up to 30% of deaths [10]. Complications such as sinus bradycardia, relatively low blood pressure (BP) (hypotension usually below 100/50 mm Hg), prolonged QT interval, and atherosclerosis are associated with AN even in children and adolescents [11].

Anorexia nervosa most often affects girls aged 15–19 years, and this group accounts for approximately 40% of all diagnosed cases [12]. The most common disorder among patients with AN is sinus bradycardia [6]. The exact epidemiology and risk factors for cardiac complications in AN are still unclear. Oflaz *et al.* found myocardial fibrosis in 23% of AN patients (detected as late enhancement with gadolinium in magnetic resonance imaging) [13]. This finding points to the possibility of scar

tissue formation and theoretically suggests a propensity for sudden cardiac death in patients with eating disorders.

MECHANISMS OF CARDIOVASCULAR COMPLICATIONS IN ANOREXIA NERVOSA

Although cardiovascular complications are the leading cause of fatality among patients with anorexia nervosa, their aetiology and pathogenesis are still uncertain. However, there are some theories. Malnutrition and following metabolism decrease seem to be responsible for changes in cardiac cells, leading to functional, structural, and electrocardiological complications. Myocardial impairment has been interpreted as a form of adaptation to starvation [14]. Undernutrition is also associated with significant dysregulation of the neuroendocrine system, including many hormonal axes (hypothalamic-pituitary-adrenal/-gonadal/-thyroid axis), as well as growth factor, insulin-like growth factor 1 (IGF-1), appetite-regulating hormones, and adipokines, which contribute to the disturbances of cardiovascular functioning [11]. The endocrine disorders and following menstrual cycle irregularity are responsible for hypoestrogenaemia, which is associated with a significant increase in the risk of cardiovascular diseases [15].

Anorexia nervosa is connected with increased levels of inflammatory markers like interleukin 6 (IL-6) and tumour necrosis factor α (TNF- α) [16]. Inflammation has a destructive impact on the cardiac tissue and therefore may be responsible for the accelerated cardiovascular risk [17].

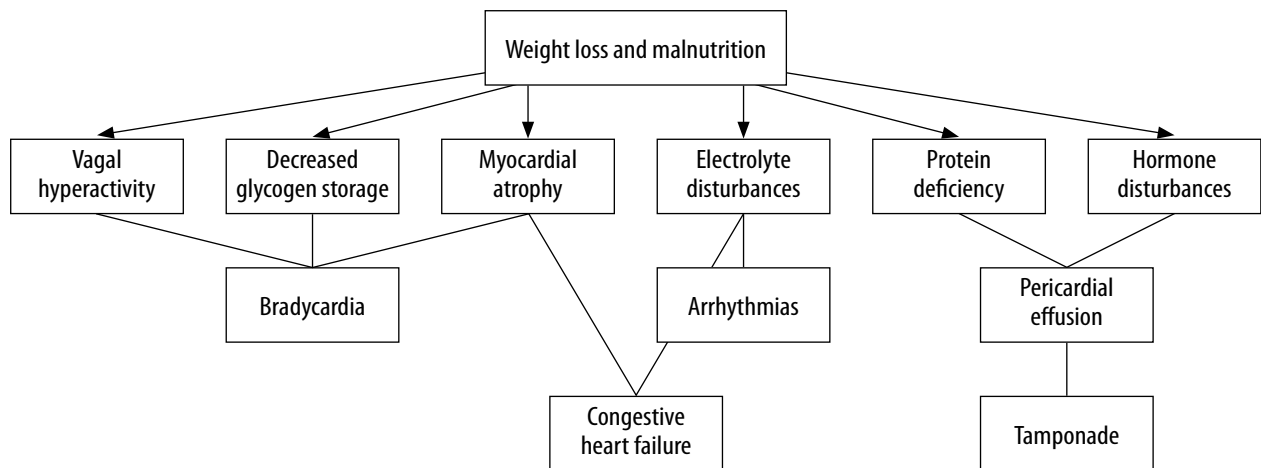


FIGURE 1. Presentation of the probable pathogenesis of cardiovascular complications of malnutrition

Autonomic nervous system dysfunction is believed to play a role in cardiovascular complications among patients with AN. The autonomic nervous system maintains the homeostasis of the body. It regulates the internal processes, like BP, heart rate (HR), respiration rate, etc., to adapt the body to external changes. The parasympathetic system is predominant among patients with AN; therefore, bradycardia, hypotension, and HR variability are widely observed. The consequences of the overactivity of parasympathetic division are still undetermined [18] (Fig. 1).

ARRHYTHMIAS

The most common disorder among patients with AN is sinus bradycardia [6]. Different mechanisms are postulated to explain this disorder: vagal hyperactivity, myocardial atrophy, and decreased glycogen storage [19]. Most of the patients are asymptomatic, while the rest of the patients present with presyncope, light-headedness, fatigue, and exercise intolerance [20]. A significant decrease in HR can be a serious condition, especially when coexisting with other electrocardiography (ECG) abnormalities. A study by Yahalom *et al.* showed that 16 of 23 analysed patients with anorexia have a heart rate (HR) lower than 50 beats per minute (bpm). The HR of patients ranges 26–68 bpm. No pacemaker therapy was needed [21]. Nutrition and weight restoration comprises a successful treatment of bradycardia in patients with AN, with normalization of HR while achieving 85–90% of ideal body weight [22]. However, in severe cases of anorexia, pacemaker implants are used temporarily [19, 23].

Some studies mention that a prolonged QT interval is a common finding in patients with AN [4], while other authors emphasize that the QT interval was not different among patients with AN relative to control subjects [14, 24]. In addition, QT correction is not standardized and is considered controversial in patients with AN, because of the low accuracy of Bazett's formula in bradycardia. However, QT prolongation is associated with ventricular arrhythmia and sudden death [25]. Clinicians should not

overlook that some conditions like severe hypokalaemia [14] or treatment with psychotropic drugs [26] can lead to QT prolongation among patients with AN.

Another arrhythmia that patients with anorexia experience is atrioventricular block. However, this condition is rare in AN [5, 27].

VALVE LESIONS – MITRAL VALVE PROLAPSE

Mitral valve prolapse (MVP) is common, but its clinical significance is uncertain [28]. It is important that MVP is always confirmed or ruled out by echocardiography because a physical examination does not always reveal clinical signs of this defect [21, 29]. According to studies published by Cheng, MVP is common, with rates ranging 0.6–2.4% in the general population and 33–62% in patients with AN [30–32]. Johnson *et al.* found MVP in 37% of people with eating disorders. For comparison, in the control group of healthy people, this defect was found only in 4% of people. From these results, they concluded that the frequency of MVP is increased in patients with eating disorders. In addition, the arrhythmogenic effects of MVP may be an additional risk factor in these patients [33].

PERICARDIAL EFFUSION

Little is known about the relationship between eating disorders and pericardial effusion, but information has recently started to appear in the literature. There are theories linking pericardial effusion with protein deficiency and decreased levels of thyroid hormones and insulin-like growth factor 1 [34]. The risk factors of pericardial effusion in AN include body mass index (BMI) < 13 kg/m², weight loss > 25%, low triiodothyronine (T3) syndrome, IGF-1 < 100 ng/ml, and elevated prohormone of brain natriuretic peptide (Pro-BNP) [35]. It is estimated that up to about 35% of patients with AN suffer from pericardial effusion. However, the majority of cases are mild and without haemodynamic significance [5]. Docx *et al.* studied 128 female adolescents with AN. In 29 cases, ECHO eval-

uation showed evidence of pericardial effusion, ranging 0.35–2.5 cm. All patients were asymptomatic. The effusion disappeared in 18 of 29 cases after 3 months of refeeding [36]. A life-threatening case of huge pericardial effusion and pneumocardium was observed in 14-year-old boy with massive weight loss – 60% of weight in 9 months (BMI: 10.9 kg/m²). The pericardial effusion regressed to 8 mm after 6 months of refeeding treatment [37]. In another case, 15-year-old girl with AN (BMI: 11.83 kg/m²) presented asymptomatic but with rapidly increasing pericardial effusion. Pericardiocentesis was required to prevent tamponade [38]. However, cases like these seem to be anecdotal.

CONGESTIVE HEART FAILURE

Congestive heart failure (CHF) is described as a clinical syndrome in which heart disease reduces cardiac output, increases venous pressure, and is accompanied by molecular abnormalities that cause progressive deterioration of the failing heart and premature myocardial cell death [39]. Heart failure has been reported in patients with anorexia [40, 41]. Congestive heart failure in AN can be caused by changes in the heart's structure, such as a decrease in cardiac mass and changes in the chamber's dimension [42]. Deficiencies of magnesium, phosphorus, selenium, and thiamine can also contribute to the weakening of cardiac muscle construction in AN [43–45]. Other reports suggest that hypoglycaemia [46] or elevated sympathetic activity [47] can cause cardiomyopathy in AN. Heart failure in AN can present with orthopnoea, shortness of breath on exertion, or oedema [41].

MYOCARDIAL INFARCTION

Only a few cases of myocardial infarction (MI) in AN have been reported in the literature [48, 49]; therefore, this complication seems to be rare in this eating disorder. In both cases the patients had a heart attack at the age of 39 years and had a long history of suffering from AN, since adolescence.

TAKOTSUBO CARDIOMYOPATHY

Takotsubo cardiomyopathy (TTC), also known as “stress-induced cardiomyopathy”, “broken heart syndrome”, or “apical ballooning syndrome” [50], is an acute, reversible cardiac condition characterized by symptoms and electrocardiographic changes mimicking acute MI without any angiographic signs of vessel occlusion. Takotsubo cardiomyopathy, due to its similarity to myocardial infarction, requires careful diagnosis and treatment [51]. Takotsubo cardiomyopathy was first described in 1990. Since then, more and more case reports have appeared in the literature that clearly show a correlation between patients with anorexia and their risk of TTC [50, 52].

The exact pathophysiology of TTC is unclear. However, an apical ballooning syndrome in AN may be triggered by hypoglycaemia [53] or refeeding syndrome [54]. Takotsubo cardiomyopathy is generally considered a benign disease with a good prognosis. However, during the acute phase, potentially life-threatening complications may occur [51]. Volman *et al.* described a young female with TTC, who presented with severe cardiogenic shock [50]. In the general population, patients with TTC and lower BMI (< 18.5 kg/m²) have a favourable early prognosis, but 5-year observation is associated with a very high fatality rate [55].

TREATMENT OF CARDIOVASCULAR COMPLICATIONS IN ANOREXIA NERVOSA

The management of AN is a complex and demanding challenge for health care professionals, especially when patients feel a lack of desire to be provided with the help. Therefore, AN should be treated by a multidisciplinary team, experienced in the treatment of eating disorders [56].

Hypotension can be corrected with intravenous fluids in hospitalized patients. It is also worth remembering that hypotension improves as body weight is restored. Hypotension may also accompany bradycardia, exacerbating postural symptoms [57]. Bradycardia is one of the most common cardiac complications of anorexia nervosa, but if high-degree atrioventricular block (AV block) is not present, it rarely requires consultation with a cardiologist. Occasionally, patients with severe AN may experience a sustained nodal rhythm leading to prolonged hospital treatment. In the presence of sustained nodal rhythm, provocative treadmill testing is recommended to demonstrate adequate conversion to sinus rhythm in these patients, as a means of assessing the electrical reserve of the heart. In the event of prolongation of the QTc interval, ECG, electrolyte replacement (potassium and magnesium), and treatment of drugs known to prolong the QTc interval (including antiemetics and antipsychotics) should be discontinued [58]. Some patients may develop pericardial effusion, which generally resolves spontaneously as weight is restored. Pericardiocentesis is reserved for patients who have had cardiac tamponade based on echocardiographic and/or clinical criteria [13]. Paediatric patients with TTC can be treated with supportive therapy, as in CHF, until the left ventricular function returns. Compared to adults, children can be safely treated with inotropes. Anticoagulation should be considered in severe cases. However, treatment of TTC should be personalized according to the patient's disease presentation [59]. Among patients with AN, in one case rest and oxygenation were sufficient for the return of cardiac function [53], while in another the patient required intra-aortic balloon pump treatment [50]. The first menstruation or resumption of menstruation is an important indicator of biological health in women [60].

Cardiological complications of AN, which are very important for diagnosis, are often reversible due to restoration of body weight.

CONCLUSIONS

Anorexia nervosa is an eating disorder, associated with many medical complications as a result of weight loss and malnutrition. AN may contribute to increased cardiovascular risk, especially in young adults and children during adolescence. The physician treating patients with AN must remember that this is not only a mental illness, but that AN is also a physical disease. A patient with AN should be looked after by an interdisciplinary team including, among others, a psychiatrist and cardiologist. Importantly, medical complications, including arrhythmias, mitral valve prolapse, loss of cardiac muscle, and a decrease in cardiac output are reversible with weight restoration and correction of the deficiencies.

DISCLOSURE

The authors declare no conflict of interest.

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