

Does anorexia nervosa with adolescent onset need long-term follow-up?

Czy jadłowstręt psychiczny z początkiem w okresie młodzieńczym wymaga długotrwałej obserwacji?

Małgorzata Wasniewska, Alessandra Li Pomi

¹Department of Human Pathology of Adulthood and Childhood, University of Messina, Italy

²Department of Human Pathology of Adulthood and Childhood, Pediatric Clinic, Italy

Słowa kluczowe:

anorexia nervosa, eating disorders, adolescent, complications, follow-up.

Anorexia nervosa (AN) is a disease mainly of the female sex (90-95% of cases). Almost exclusive, in the past, of the middle-upper classes, in more recent years it has spread to all social strata. The origin and course of eating disorders (ED) are determined, due to the multifactorial etiology, by a plurality of variables, none of which, alone, is capable of triggering the disease or influencing its course and outcome. Therefore, to understand them in full, it is necessary to take due consideration of biological, psychological and evolutionary factors. The role of some conditions present since birth or childhood, such as genetic vulnerability, family environment and traumatic experiences is not yet well understood in AN pathogenesis. In many cases, some individual characteristics such as perfectionism, low self-esteem, poor ability to regulate emotions, difficulty in conscious management of the body and body image in adolescence precede the onset of ED. Certainly, socio-cultural factors also favor the development of these disorders, in particular the association of thinness with beauty and personal success.

It has been observed that in patients suffering from AN there is a variable percentage of psychiatric comorbidities such as personality disorders (in about 40-45% of cases). An unbalanced relationship with food can also express an attempt to regulate mood and relieve a state of tension, which can sometimes result in feelings of guilt, anxiety, shame, depression, devaluation, difficulty in maintaining social and work relationships, without becoming a real mood disorder. Depression is a frequently encountered disorder in patients with ED. Obsessive personality traits are frequently found, such as perfectionism and the search for symmetry, which express aspects that favor the onset of AN. This comorbidity often persists even after many years from the onset of the disease.

The complications of anorexia nervosa (AN) are varied and complex, with a significant over-lap with pathophysiological mechanisms. Moreover, the devastating effects of malnutrition perpetuate the eating disorder causing physical and psycho-

logical discomfort during malnutrition and refeeding [1]. Implications of the disorder can involve the endocrine system, causing growth hormone (GH) resistance with low insulin-like growth factor-1 (IGF-1) levels, hypothalamic hypogonadism, hypercortisolemia and changes in appetite-regulating hormones such as leptin, ghrelin, peptide YY, and possibly adiponectin, affecting both anterior and posterior derived pituitary hormones [1].

The drop in serum levels of leptin and the decrease in gonadotropin-releasing hormone leads to decreased LH, FSH, and anovulation, resulting in amenorrhea, that occurs in up to 84% of females with AN. This has important consequences on fertility and pregnancy related complications such as preterm birth, cesarean section, microcephaly, small for gestational age, and perinatal mortality [1]. Moreover, males and females with AN are both at risk of bone disease with reduction of Bone Mineral Density (BMD) Z score. An earlier age of onset of AN (< 18 years) is associated with a greater decrease in BMD [1].

On the other hand, refeeding syndrome (RS) has been used to describe the adverse consequences that can occur in all malnourished patients during the early stages of nutrition repletion, where hypophosphatemia is the most common complication of nutritional restoration for patients with AN. Other consequences of RS include acute thiamine deficiency resulting in Wernicke's encephalopathy and Korsakoff syndrome, with the potential for permanent cognitive impairment, hypokalemia, hypomagnesemia, metabolic acidosis or alkalosis, and fluid overload resulting in cardiac failure [1]. Gastrointestinal implications could be constipation, nausea, abdominal pain, abdominal fullness, vomiting, heartburn, epigastric pain, decreased appetite, diarrhea and dysphagia [1]. Hematologic Complications are also very important, such as trilinear hypoplasia with leukemia, anemia and thrombocytopenia, caused by gelatinous marrow transformation [1]. The most common cardiovascular complications, which have long been implicated in sudden death of patients with AN, are bradycardia and decreased heart rate

variability (HRV). Bradycardia is reversed with weight restoration, hence permanent pacemaker placement is not recommended [1].

The factors for maintaining food pathology, on the other hand, are to be found in the persistence of predisposing factors and in the establishment of feedback circuits that generate pathological vicious circles. Recent studies of the literature on ED show that treated AN heals completely in about 40% of cases and evolves towards an incurable chronicity in 25%. Treatment for this eating disorder is not always successful. Around 70% of patients with a severe course do not overcome the disorder in the long-term and around 5% of patients die in long-term observation periods. Moreover, treatment discontinuation rates are about 30–40% [2]. International treatment guidelines for EDs concur that psychotherapy is the first-line treatment for patients with AN, preferably in outpatient settings [2]. Patients with a severe form of AN are often treated as inpatients. Many of them benefit from this acute treatment. Unfortunately, a significant number of patients experience relapse after discharge. Moreover, approximately one-fifth to one-third of patients with adolescent AN need intensive care over the course of their illness [3].

A study conducted by Wallin and Holmer shows that the Family treatment apartment (FTA) group seems to have a more favorable outcome than the group of patients treated in the regular psychiatric inpatient care. (full recovery in 51.2% of patients in FTA group compared to 36% of the other group) [4]. Unfortunately, only a limited number of randomized controlled trials (RCTs) investigating aftercare interventions for patients with AN is available. A specific issue is how to increase uptake of and reduce dropout from aftercare interventions [2].

Mortality from AN currently appears lower than in past years. Until the predictive factors of the clinical evolution of the disease are not definitively identified, what must be suggested today is to ensure an AN early diagnosis and an integrated medical-psychiatric approach as a therapeutic strategy.

Refeeding is a central part of the treatment for AN and should be coordinated by a multidisciplinary and collaborative enterprise, together with nutritional rehabilitation and psychological support. However, to date there are no clear guidelines on the management of refeeding in clinical practice and clinicians rely on clinical confidence [5]. There is evidence that early weight restoration has an impact on outcome, justifying an aggressive approach to refeeding in the early stages of the illness [5]. The importance of early weight gain for long-term recovery has been demonstrated by several studies, supporting a switch in current care practices for refeeding from a conservative approach to higher calorie refeeding. Refeeding aims to decrease the risk of death due to undernutrition, to improve nutritional status, to normalize somatic disorders secondary to undernutrition (such as growth failure, delayed or arrested puberty in prepubertal children and young adolescents and low bone mineral density and functional digestive symptoms in adolescents and adults), to combat acute somatic effects such as hypoglycemia, muscle weakness, bradycardia, severe hypotension, leucopenia and severe bradycardia and to improve

mental state (anxiety, depression) [5]. It may occur in various settings, including hospitals, outpatient settings, psychiatric units or somatic services [5]. Nevertheless, the impact of approaches to refeeding on long-term outcomes is unknown, and there is currently no evidence of an association between higher calorie refeeding and better long-term outcomes [5].

The evaluation and treatment of psychiatric comorbidities could be another possible path to a better long-term therapeutic outcome. Furthermore, it is difficult to predict how this ED could develop and which factors might affect the outcome of the condition. A higher initial rating of self-blame was found as the only predictor factor. So the treatment should focus on recognizing and reducing self-blame and increasing self-acceptance [6]. The symptom change during early treatment resulted the most robust predictor for outcome at end of treatment and follow-up. Other important variables included illness duration, weight and shape concern, general psychopathology, ED pathology, and self-esteem [6].

Nevertheless, our current knowledge of risk and protective factors for the course of EDs is still unsatisfying [7]. Only few studies have evaluated long-term follow-up in patients treated for AN. In the present issue of the *Pediatrics Endocrinology, Diabetes and Metabolism*, there are two articles on the longitudinal follow-up and treatment results of patients with adolescent onset of AN, coming from the Center of Pediatric Endocrinology in Zabrze, Poland, with significant experience in this pathology [8, 9].

It is generally known that, even in the case of only one episode of the disease in adolescence, the effects of the disease may persist into adulthood. The first of the two studies about the Assessment of long-term results in women suffering from AN in Adolescence analyzes the percentage of recoveries and relapses of the disease and to attempt the determination of predictive factors for such patients [8]. The severity of symptoms in these girls does not eliminate the chance of recovery and of achieving important life goals, such as completing education, finding a life partner and having children [8].

The study revealed that, in the group of women engaging in purging behaviors over time, the risk of a worse recovery prognosis was significantly higher. Moreover, the risk of persisting symptoms was 3.7 times higher in the group of women who do not maintain regular contacts with their mothers. Obsessive-compulsive disorder and/or obsessive-compulsive personality disorder or autism spectrum disorder accompanying AN also had a negative effect on the course of the disease [8].

In the second paper, the same authors have evaluated the incidence of disorders of the gonads hormonal function and of a decrease in the bone mineral density 7 years after hospitalisation in women treated for anorexia nervosa in adolescence, confirming that the treatment does not succeed in obtaining normal hormonal activity of gonads in all AN patients. Therefore, normal bone mineral density levels were confirmed only in 14.3% of women [9].

AN is a serious, dangerous, difficult to cure disease that tends to become chronic. ED are mental illnesses that most deeply affect and upset the body and its biology. The under-

lying disorder is not only psychopathological, therefore long-term care must be based on integrated medical-psychiatric therapy for a form of protein-energy malnutrition secondary to severe ED.

References

1. Puckett L, Grayeb D, Khatri V, et al. A Comprehensive Review of Complications and New Findings Associated with Anorexia Nervosa. *J Clin Med* 2021; 10: 2555. doi: 10.3390/jcm10122555.
2. Giel KE, Behrens SC, Schag K, et al. Efficacy of post-inpatient aftercare treatments for anorexia nervosa: a systematic review of randomized controlled trials. *J Eat Disord* 2021; 9: 129. doi: 10.1186/s40337-021-00487-5.
3. Herpertz-Dahlmann B. Intensive Treatments in Adolescent Anorexia Nervosa. *Nutrients* 2021; 13: 1265. doi: 10.3390/nu13041265.
4. Wallin U, Holmer R. Long-Term Outcome of Adolescent Anorexia Nervosa: Family Treatment Apartments Compared With Child Psychiatric Inpatient Treatment. *Front Psychiatry* 2021; 12: 640622. doi: 10.3389/fpsy.2021.640622.
5. Bargiacchi A, Clarke J, Paulsen A, et al. Refeeding in anorexia nervosa. *Eur J Pediatr* 2019; 178: 413-422. doi: 10.1007/s00431-018-3295-7.
6. Petersson S, Birgegård A, Brudin L, et al. Initial self-blame predicts eating disorder remission after 9 years. *J Eat Disord* 2021; 9: 81. doi: 10.1186/s40337-021-00435-3.
7. Fichter MM, Quadflieg N. How precisely can psychotherapists predict the long-term outcome of anorexia nervosa and bulimia nervosa at the end of inpatient treatment? *Int J Eat Disord* 2021; 54: 535-544. doi: 10.1002/eat.23443.
8. Wszolek M, Ziara-Jakutowicz K, Gorczyca P, et al. Assessment of long-term treatment results in women suffering from anorexia nervosa in adolescence. *Pediatr Endocrinol Metab* 2022; 28: 4-15. doi: <https://doi.org/10.5114/pedm.2021.109268>.
9. Wszolek M, Ziara-Jakutowicz K, Gorczyca P, et al. Assessment of the frequency of hormonal disorders of the gonads and bone mineral density among women treated for anorexia nervosa in adolescence. *Pediatr Endocrinol Metab* 2022; 28: 16-22. doi: <https://doi.org/10.5114/pedm.2022.112866>.

Acknowledgments

The authors wish to thank Dr. Alberta Ragno for proofreading of this manuscript.