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Somatic complications and nutritional management of anorexia nervosa

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SUMMARY

Anorexia nervosa (AN) in its two major types (restricting type and binge-eating/purging type) is one of the most frequent and serious eating disorder. Severe undernutrition due to intake restriction and pathological associated behaviors such as potomania and vomiting can cause serious somatic complications such as cardiac and/or hepatic disturbances. Nutritional rehabilitation of undernourished AN patients should be very causes to avoid refeeding syndrome. Managing AN need a multidisciplinary approach including psychiatric and nutritional care.

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1. Introduction

Anorexia Nervosa (AN) in its two major forms, the restricting (ANR) and binge-eating/purging type (ANBP), is one of the most serious eating disorder, often chronic and inducing serious somatic consequences. AN has been associated with one of the highest rates of mortality among all psychiatric disorders, with a rate of 5% [1]. Somatic complications are the first cause of death, before suicide. AN is characterized by an emotional and cognitive inability to maintain a normal weight and by an active fight against the feeling of hunger [2]. This behavioral symptomatology is often associated with severe protein-energetic malnutrition marasmus, the adaptive form of semi-prolonged fasting, is the predominant form of malnutrition associated with AN. However, the kwashiorkor type is present in some cases, and is characterized by a constellation of features including peripheral edema, hypoalbuminemia, fatty liver, skin, hair lesions, and a relative immuno-depression with high risk of infections. Some patients have a mixed picture of marasmic-kwashiorkor malnutrition.

Somatic complications could be presented on three axes (Fig. 1): 1) undernutrition complications with cardiac failure risk, hypertransaminasemia and hepatic failure, functional intestinal disorders, hematological disturbances, bone demineralization, hormonal disorders and others; 2) pathological behaviors consequences (vomiting, potomania, drug abuse): stomatological complications, hypokalemia and hypernatremia; 3) refeeding metabolic complications.

AN care should be based on a multi-disciplinary approach in addition to the initial nutritional care, along with a psychiatric and psychological specialized program [3].

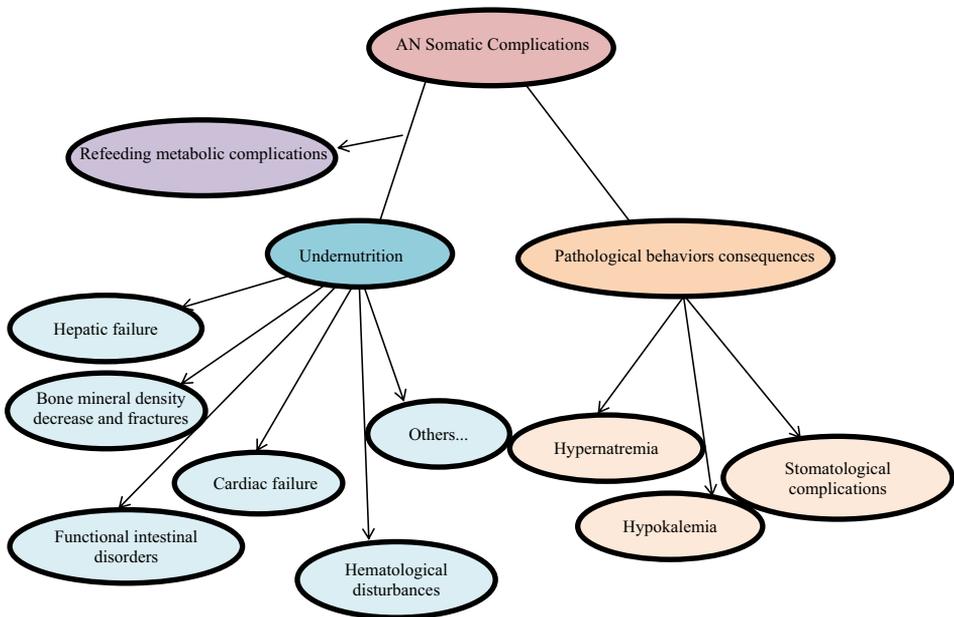


Fig. 1. AN somatic complications.

2. Somatic complications

2.1. Related to malnutrition

a) Cardiac disturbances

Among medical complications, cardiac features are frequent, reaching 60% [4,5]. These complications range from cardiac to electrical abnormalities with a potential risk of sudden death [6–9]. Cardiac abnormalities may involve the myocardium, the pericardium, the mitral valve and/or the heart related conduction system. Cardiac histological studies reported vacuolar degeneration, myocardium attenuation and moderate interstitial fibrosis, without inflammatory or necrosis features [10]. Clinical observations includes left ventricular dysfunction, cardiac hypotrophy, mitral valve prolapse, pericardial effusion [4,11] and QT long prolongation. In this context, electrocardiogram (ECG) and echocardiography-Doppler are routinely performed in patients with AN as recommended by French and UK guidelines [12,13].

Cardiac impairment should require in AN patients a systematic cardiac non invasive exploration. Echocardiography should be performed, particularly in patients with severe under-nutrition and during refeeding period, in order to assess left ventricular function, hemodynamic status and cardiac preload.

b) Bone mineral density (BMD) decrease and risk of fractures

Low bone mineral density in chronic malnutrition is frequent and well defined, in particular for patients before 50 years old, by a Z-score under -2 SD [14]. In anorexia nervosa, the BMD decrease is multifactorial and associating estrogen, vitamin D and calcium deficiencies with hypoproteinemia, hypercortisolism, IGF-1 and leptin low levels. Severity of malnutrition (low BMI and lean mass), early age of disease onset and amenorrhea duration are identified risk factors [15]. Risk of fractures is 7 times more important in patients with AN [16].

There are no strong recommendations for prevention and treatment of BMD decrease during anorexia nervosa. Weight gain is essential and only beneficial if leading to a spontaneous return of menstruations [17]. Physiologic estrogen replacement [18] and bisphosphonates increases BMD and may be prescribed in some cases [19]. Physical activity has a beneficial effect only after a return to normal weight. It is recommended to perform a bone densitometry in initial assessment and then every 2 years as part of the follow-up [12].

c) Hematologic abnormalities

Anemia, leukopenia and thrombocytopenia are the most frequent hematological complications of anorexia nervosa with a prevalence of 16.7, 7.9 and 8.9% respectively [20]. These abnormalities are the consequence of chronic malnutrition and could be secondary to some micronutrients deficiencies (folic acid, vitamin B12, copper ...) and/or to bone marrow gelatinous transformation. This central complication is characterized by hypocellularity and patchy or diffuse replacement of the bone marrow with hyaluronic acid-like mucopolysaccharide material. The only effective treatment remains renutrition with at least partial reversibility of the spinal cord lesions [21].

d) Intestinal disorders

Digestive disorders are common in anorexia nervosa and worsen with the deterioration of nutritional status. For High Functional Digestive Disorders according to the Rome III criteria [22], reported lesions are dysphagia and gastric burns, described respectively in 6 and 22% of patients respectively [23], with no obvious link to structural involvement of esophagus [24]. Some patients report the notion of early satiety, gastric distension and postprandial nausea, which may indicate a delay in gastric emptying [25,26]. This symptomatology can constitute a hurdle to weight restoration. The psychological accountability of these functional disorders remains poorly evaluated [26].

According to literature, 41–52% of patients with eating disorders have symptoms suggesting irritable bowel syndrome (IBS) [23,27], which is at much higher prevalence than in the general population. IBS is a clinical entity of multifactorial origin, whose pathophysiological mechanisms are still poorly explained (dysfunction of the gut–brain axis associating motor disorders, sensory afferent sensitization, low grade inflammation and abnormal intestinal permeability). The role of gut microbiota dysbiosis in functional intestinal disorders of malnourished AN patient has recently been explored [23].

Constipation is one of the most commonly reported symptoms in the literature in patients with eating disorders. This may or may not fit within the framework of IBS, depending on the presence or absence of other signs (abdominal pain, bloating and digestive discomfort). Its prevalence in anorexia nervosa varies, depending on the type of population studied and the diagnostic method used, between 67 and 100% of patients [28,29]. The impact on the quality of life of patients and on the psychological aspects of the disease is considerable.

Clinicians to these digestive symptoms should pay special attention. Symptomatic treatment of constipation and abdominal pain should be prescribed with caution.

e) Hepatic disturbances

Liver abnormalities are frequent and largely described in undernourished AN patients. Hypertransaminasemia can be observed in 40–50% of patients depending on the severity of malnutrition [30]. Two types of hypertransaminasemia can be distinguished: 1) hypertransaminasemia due to undernutrition observed during weight loss period. It can be moderate (AST and/or ALT <200 IU) with spontaneous favorable evolution or rarely (AST and ALT > 200 IU) acute and worsening following rapid renutrition. Starvation-induced autophagy and glycogen hepatocyte depletion may be involved in liver cell death leading to hypertransaminasemia and hepatocellular insufficiency [31]. 2) Renutrition hypertransaminasemia is most often moderate and in most cases not exceeding 10 times the higher normal values. In case of hypertransaminasemia higher or equal to 200 IU, the speed of renutrition must be reduced and food intakes must be proceeded exclusively by continuous enteral nutrition to prevent hypoglycemia as much as possible. Daily biological monitoring of transaminases, liver function (TP/FactV) and capillary glycaemia is indicated in such situation.

f) Infections complications

Protein-energy malnutrition is a common cause of immunodeficiency and increase susceptibility to infections. In AN patients acute infections are rare but potentially serious. Clinical and biological inflammatory markers may be moderately delayed or absent at the onset of infections. Chronic infections are associated to lymphopenia due to bone marrow gelatinous transformation and to the severity of malnutrition. Pulmonary atypical mycobacterium infections with slow and paucisymptomatic evolution are mostly frequent [32]. Thus special attention must be given to the possibility of opportunistic infections in AN patients.

g) Endocrine disturbances

Endocrine dysfunctions in anorexia nervosa result from disturbed regulation of hypothalamo-pituitary-gonadal axis along with the hypothalamo-pituitary-adrenal, hypothalamo-pituitary- thyroid and hypothalamo-pituitary-GH-IGF1 axes. These disturbances are associated with altered peripheral endocrine metabolism. Hypogonadotrophic hypogonadism induces amenorrhea, infertility and contribute to BMD decrease. This infertility is the consequence of undernutrition and is reversible when patients regain a normal weight (BMI > 18.5) for 12 to 18 consecutive months. A resistance to Growth Hormone, (GH) and high level of IGF1 helps to maintain glycaemia in a normal level. Hypercorticism, in response of stress due to undernutrition, is observed and can induce muscular atrophy and cutaneous fragility. If the renutrition is too fast, we may observe an increase of subcutaneous fat; the return to normal corticotrophin functions being slower than weight gains. A low Triiodothyronine

(T3) syndrome, with low level of T3 but normal TSH and T4 level, limits consumed energy and concentrate the rest for vital organs. These thyroid hormone disturbances don't need to be subject to treatment as it's usually returning to normal rates after refeeding [33].

Leptin level, an anorexigen adipocyte-derived hormone is low and can be involved in BMD decrease and in high physical activity often described in AN patients [34]. Ghrelin, an orexigenic peptide hormone, has a high secretion level compared with healthy people. It shows that anorexia nervosa patients fight against hunger. Post-pituitary secretion can also be disturbed with a Syndrome of inappropriate antidiuretic hormone secretion (SiADH) inducing moderate hyponatremia.

No exploration or treatments are necessary for these adaptive physiological mechanisms as all these hormonal disorders should disappear after nutritional rehabilitation.

h) Micronutrients Deficiency

Several micronutrients (including vitamins, minerals and trace elements) deficiencies are described in patients with eating disorders. These deficiencies are the consequence of restrictive food and low micronutrients intakes largely described in eating disorders patients. In malnourished patients, initial asymptomatic electrolytes, vitamins and trace elements deficiencies can worsen with renutrition. The cause is the increased of body needs that could lead to occurrence to refeeding syndrome (RS). A prophylactic electrolytes and micronutrients supplementation is recommended for eating disorders patients with high risk of RS by the French and American guidelines of eating disorders [3,12]. This supplementation includes, in addition to unspecific vitamins and trace elements supplementation, phosphorous (0.5–0.8 mmol/kg/d) and thiamin (200–300 mg/d) [35].

Zinc deficiency is frequent in eating disorders patients. A link between zinc and eating behavior regulation was found [36]. Zinc is reported to be an appetite stimulator and to play a role in limiting the progression of cachexia and sarcopenia [36]. Thus, zinc supplementation should be considered in malnourished eating disorders patients [37].

Depending on series, 23–58% of eating disorders patients had vitamin D deficiency. A relationship between vitamin D deficiency and BMD decrease, the most frequent chronic complication of AN disease, was found [38]. In addition, hypovitaminosis D3 may be responsible of the lack of inflammatory response and depressive symptoms in patients with long-term eating disorders [39]. Despite severe malnutrition, bioavailability of oral ergocalciferol in young AN patients was similar to that of healthy controls. Oral supplementation of vitamin D should be provided to all malnourished eating disorder patients [17]. Other rare micronutrient deficiencies are reported; such as cases of sensory neuropathy due to vitamin B12 deficiency [40] and cases of cardiac involvement due to selenium deficiency [41]. Though are no recommendations on specific supplementation on vitamin B12 or selenium, it is necessary to perform plasma concentration monitoring in order to supplement if any clinical or biological specific symptoms are observed.

2.2. Complications related to the associated pathological behaviors

a) Hypokalemia and hyponatremia

Hypokalemia is frequent complication during AN purge bingeing type. It is the consequence of vomiting or laxative abuse. More rarely it can be the consequence of a diuretic abuse [42], hypokalemia is then often moderate (3–3.5 mmol/l) and chronic. In cases of severe purging behaviors, hypokalemia can be acute and lead to electrical abnormalities and sudden death [43]. Oral and/or intravenous potassium supplementation is recommended depending on the severity of hypokalemia and oral preventive potassium supplementation should be prescribed to AN patients with severe purging behaviors.

In cases of potomania, severe water intoxication leading to hyponatremia can be observed sudden convulsion and coma may occur [44]. The treatment consists on a progressive water restriction, in order to avoid complications due to fast natremia correction like centropontine myelinolysis.

b) Stomatological disorders

Patients presenting purging behaviors, especially vomiting, can have dental injuries. Loss of tooth enamel, cavities, gingivitis and stomatitis, which can lead to loss of teeth by loosening, are the most frequent. Treating these dental injuries is important because they can constitute a functional brake to the renutrition and perpetuate pathological alimentary behavior. The psychological and social impact of dental injuries can be significant. Proton pump inhibitors could be prescribed to prevent and lower these dental injuries along with the psychiatric treatment.

2.3. Refeeding complications

AN malnourished patients are at high risk of refeeding syndrome (RS) [13], defined by all potential metabolic and hormonal disturbances that can occur in malnourished patients after rapid change from a catabolic to an anabolic phase at the beginning of refeeding [45]. Nonspecific symptoms and metabolic disorders, with hypophosphatemia as a hallmark feature, may follow initial phase of nutritional care (3–7 days) [46]. To prevent RS, it is therefore necessary to start a progressive and continuous enteral renutrition, preceded by an intravenous supplementation with phosphorus, vitamins and trace elements. Indeed, renutrition induces a re-entry of phosphorus inside cells, an hypophosphoremia is consequently observed and can induce muscular and diaphragmatic weakness by lowering ATP, which is responsible of dyspnea and rhabdomyolysis. Clinical and biological monitoring during the first weeks of nutritional rehabilitation in the most severely undernourished patients (BMI <12) is essential [47].

3. Nutritional management

3.1. Renutrition: modalities and goals

Weight restoration is an important first step in treating patients with AN, because it is essential for medical stabilization before starting specific psychiatric care [48]. Enteral nutrition (EN) is the most appropriate therapeutic tool for malnutrition management of AN patients [49]. It is indicated if undernutrition is severe and/or associated with metabolic disorders (BMI <13) and/or if prolonged weight stagnation despite adequate nutritional and psychiatric management [12]. EN is considered safe and well tolerated [50], and effectively enhanced caloric intake and rate of weight gain in patients with AN [51]. Although only few studies focused on the long-term effect of EN, outcomes appeared favorable [52].

Enteral nutrition must always be performed by a small nasogastric tube. Even if few studies experienced percutaneous endoscopic gastrostomy [53], this pathway isn't recommended in the nutritional management of anorexia nervosa, as it can aggravate the disturbance of body shape perception of patients. An isocaloric and isotonic solute must be used (1 ml = 1 Kcal) continuously the first days, in case of severe undernutrition in order to avoid post-stimulatory hypoglycemia [54]; a nocturnal refeeding can be performed. Caloric scale up should be cautious in the first days, beginning by 10–15 Kcal/kg/day, then slowly increasing up to 30 to 40 kcal/kg/day at the end of the first week in order to prevent refeeding syndrome [55]. EN should be maintained only as needed to keep patients in normal eating behavior. A pre-progressive oral feeding should always be encouraged and accompanied by an experienced dietician [56]. Enteral nutrition should be done only in hospitalization in medical or psychiatric services trained in the use of this technique [12].

Oral nutritional supplementation has a limited indication in eating disorders. It can be prescribed in patients waiting for hospitalization to limit weight loss, its efficiency though remains modest [12].

Parenteral nutrition is contraindicated in anorexia nervosa for the major risk metabolic and infectious complications [47,57].

3.2. Special case of enteral nutrition in bulimic withdrawal

Bulimia crisis situations are known to be improved by enteral nutrition. A study conducted by Rigaud et al. showed the results of home enteral nutrition associated with 2-month psychotherapy versus a dietary and behavioral approach in patients with severe bulimia. Enteral nutrition allowed: disappearance of bulimic attacks in 78% of the NEAD group vs 13% of the control group at one week; at 8 weeks the results are 65% (NEAD) vs 26% (T). At 5 months, there was a clearer improvement in nutritional status, depression and anxiety in the NEAD group, with 55% of patients remaining free of bulimia.

Often, it is initially necessary to stop oral nutrition. The goal should be the weaning and deconditioning of bulimia attacks with a gradual reintroduction of food and a return to a normal diet. NE should not be a substitute for long-term oral feeding.

4. Conclusion

The management of anorexia nervosa is multidisciplinary based, involving a common intervention between psychiatrists, somatic physicians, psychologists and dieticians. The temporality of their intervention depends on the somatic or psychiatric priorities of the moment. Somatic complications may be at the forefront when undernutrition is severe and chronic, imposing specialized care and in some cases using enteral nutrition assistance which modalities are specific.

Conflicts of interest

Authors have no conflict of interest related with this article.

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