

Experience of Management of Anorexia Nervosa Patients With Extremely Severe Malnutrition In A Transdisciplinary Eating Disorders Inpatient Unit

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Abstract

Background: The question of where to hospitalize extremely malnourished patients with anorexia nervosa (AN) is a real dilemma. On one hand, psychiatrists have to deal with severe medical complications that are not within their competences and that justify hospitalization in an internal medicine ward. On the other hand, medical doctors have to face psychic decompensations that would justify admission to a psychiatric ward. In this context, we share our experience of management of severely malnourished AN adult patients in a transdisciplinary specialized eating disorders (ED) unit, referral center for AN associated with somatic severity.

Method: First, we described the modalities of care proposed to patients with AN hospitalized in the medical unit. Intensive medical care, both somatic and psychiatric, are provided thanks to a transdisciplinary therapeutic program, where objectives are to: medically stabilize the patient, initiate progressive refeeding and start supportive psychotherapy before being transferred to a psychiatric ED unit. Secondly, we conducted a retrospective descriptive study that included all adult patients with AN admitted for the first time to the unit, between November 1997 and January 2014, for severe malnutrition and/or complications of the ED. Objective was to specify patients characteristics: demographic, nutritional status, history of ED, care pathway.

Results: Among a cohort of 386 adult patients with AN (21 males and 365 females) admitted for the first time in the unit, mean age was 29.4 (± 11.5) years, mean BMI was 12.7 (± 2.2) kg/m². Before being supported in the unit, 78.2% of patients had already been hospitalized in other hospitals. Mean length of stay was 35.2 days. Patients were clinically serious and unstable because of life-threatening somatic complications due to a low BMI. During hospital stay, a temporary transfer to medical intensive care unit was necessary for 25.6% of patients. Average patient weight gain was 0.777 kg per week and 81.9% of patients benefited from enteral nutrition.

Conclusion: This specialized transdisciplinary unit where physician nutritionists and psychiatrists coordinate medical care together, allow a better understanding and management of extreme malnutrition associated with AN. Thanks to their expertise, care teams are less critical and less rejecting towards patients. Thus, therapeutic alliance could be optimized.

Plain English Summary

The question of where to hospitalize extremely malnourished patients with anorexia nervosa (AN) is a real dilemma. On one hand, psychiatrists have to deal with severe medical complications that are not within their competences and that justify hospitalization in an internal medicine ward. On the other hand, medical doctors have to face psychic decompensations that would justify admission to a psychiatric ward.

In this context we would like to share our experience of management of severely malnourished adult patients with AN, in a transdisciplinary specialized eating disorders (ED) unit. Intensive medical care, both somatic and psychiatric, are provided thanks to a transdisciplinary therapeutic program, whose objectives are to optimize care and enable a therapeutic alliance between patient and caregiver.

The goals of treatment are to medically stabilize the patient, to initiate progressive refeeding and to start supportive psychotherapy before being transferred to a psychiatric ED unit.

This specialized transdisciplinary unit where physician nutritionists and psychiatrists coordinate medical care together, allow a better understanding and management of extreme malnutrition associated with AN. Thanks to their expertise, care teams are less critical and less rejecting towards patients. Thus, therapeutic alliance could be optimized.

1. Introduction

With a Standardized Mortality Ratio (SMR) estimated at 5.86 (1), anorexia nervosa (AN) is a serious psychiatric disease whose mortality rate is one of the highest of all psychiatric pathologies (2). This mortality is especially high in tertiary care centers that treat the most severe forms of the disease (SMR at 10.6) (3). Indeed, AN can cause severe undernutrition, which can lead to medical complications and expose the patient to life-threatening risks. Thus, more than half of the deaths (54%) of patients with AN are attributable to the medical complications of AN, including undernutrition (4). Moreover, psychiatric comorbidity often accompanies the undernutrition, which makes the patient's treatment more difficult to manage. Therefore, AN requires specific care. Most treatment programs provide medical and psychiatric components in the same milieu to optimize treatment to the extent possible.

But when a patient's nutritional status is too altered, (extremely severe undernutrition with BMI 8 kg/m² to 13 kg/m²) careful weight restoration with refeeding must be conducted in an inpatient medical facility to limit the risk of refeeding syndrome (RS). Nutritional rehabilitation often corresponds to "nutritional resuscitation" in extreme forms of AN. In addition, somatic complications associated with psychiatric comorbidities are often worse and difficult to manage in a non-medical unit (5).

Our team has developed since 1997 a clinical nutrition unit specialized in the management of extremely severe undernutrition and its somatic complications resulting from different illnesses (peculiarly patients with HIV, chronic illnesses and eating-disorders (ED)) in adult patients. It was localized in Raymond Poincaré (RP) University-Hospital (Garches, 92380, France)[1]. It has been progressively oriented towards the exclusive care of patients with ED with life-threatening medical complications. Since 2004, the clinical nutrition unit was only dedicated to the management of extremely severe undernutrition and its complications associated with ED.

Thanks to its expertise, the unit is now considered, in France, a regional and national "referral center" by the administrative authorities for the treatment of patients with AN whose clinical condition can be serious and complicated. The unit is a partner of both the regional ED professional network, "Réseau TCA Francilien", and the national ED professional network, the "French Federation Anorexia Bulimia" (FFAB), associating all ED professionals in a collaborative network.

Our unit is a 15-bed unit in a conventional inpatient hospital setting.

In order to prevent runaways and suicide attempts, (which is high risk in compulsory hospitalisations), the unit is equipped with secure equipment and controlled access. It is only possible to enter or leave the unit by using a specific code (password). In addition, videophones allow caregivers to open the unit's entrance briefly, as necessary. To further enforce the security, all windows are locked and lined with an anti-burglary glass, measures designed to protect the patients.

The medical team is composed of two physicians, an assistant physician, two psychiatrists and two **internal medicine** residents **who are interested in nutritional care**. The paramedical team consists of a pool of 10 nurses, 8 nursing assistants, a nursing supervisor, a clinical psychologist, a social worker, a dietician and a physiotherapist.

Ambulatory care is also provided in the department to assess patients before their hospitalization in the unit and to follow them after discharge. It is represented by two weekly outpatient consultations and by day-activities. The mission of the outpatient clinic is to provide comprehensive clinical assessments: complete nutritional and psychiatric assessment **as well as** screening for complications related to under-nutrition. It is a transdisciplinary outpatient clinic; a nurse, a dietician, a physician nutritionist, a psychiatrist and/or a psychologist, evaluate patients successively (or jointly).

Our clinical nutritional rehabilitation team has developed expertise in treating extreme malnutrition due to severe AN. In order to deliver tailored care for the most severe cases of AN, we developed a transdisciplinary medical and psychiatric unit including both medical and psychiatric care in RP Hospital.

The goal of this paper is to describe this transdisciplinary program of management of emaciated patients with severe forms of AN and the characteristics of patients hospitalized in the unit. We will explain the modalities of somatic and psychiatric care proposed, and we will describe patient characteristics and patient care pathways. We will then discuss the potential benefits that the development of such a unit could bring.

[1] : The clinical nutrition unit at Raymond Poincaré university hospital was transferred to Paul Brousse university hospital in September 2019

2. Materials And Methods

II.1. Study Design and Aims

The primary objective was to describe the modalities of somatic and psychiatric care proposed to patients with AN hospitalized in the clinical nutrition unit.

The secondary objective was to specify characteristics of patients with AN hospitalized in the clinical nutrition unit: demographic, nutritional status, history of ED, care pathway. In order to do so, we conducted a monocentric retrospective observational descriptive study in the cohort of adult AN patients admitted to the clinical nutrition unit in RP hospital for severe malnutrition and/or complications of the ED.

II.2. Description of inpatient treatment and management

II.2.1. Objectives of treatment in a full-time hospitalization

Inpatient treatment has the following objectives:

- Begin a careful and gradual refeeding to stabilize critically ill patients suffering from severe malnutrition before they are transferred to a psychiatric inpatient unit specialized in ED. Psychiatric units are not usually sufficiently equipped and do not have the medical competence to handle the first stage of intensive care in case of severe malnutrition (6) (7)
- Diagnose and treat any medical complications.
- Initiate, continue or resume psychiatric care. The objectives of psychiatric intervention at this stage of undernutrition are limited to: detecting and preventing any suicidal behaviour, taking security measures to protect the patient if necessary, providing supportive therapy and creating specific a short-term and long-term treatment plan.
- Decrease invasive binging and purging behaviors, (self-induced vomiting, laxative or diuretic abuse), potomania, and problematic exercising, as necessary.
- Effort to preserve and improve the socio-professional integration of the patient (if deficient) in anticipation of his discharge from the hospital.

To achieve these goals, medical care should be multifocal and therefore transdisciplinary including meetings to coordinate planning. Two different transdisciplinary staff meetings are organized regularly to optimize and coordinate patient care.

In addition, the therapeutic alliance between the patient and the healthcare team is essential to the efficacy of the treatment program. Ideally, (except in cases of emergency hospitalization), the conditions of hospitalization are discussed in advance with the patient and his family during a pre-admission consultation.

II.2.2. The individualized therapeutic program

The therapeutic program is adapted to each patient specifically. A written care contract is agreed between the patient and his caregivers. It sets out weighted objectives and the steps needed to combat anorexic cognitions. The conditions of hospitalization are also explained and detailed. Discharge planning for the continuation of medical care (specifying the medical team and treatment facility) is determined progressively based on discussions with the patient and his family as clinical improvement of the patient progresses.

II.2.3. Enteral nutrition

When a patient's BMI is below 13 kg/m^2 , artificial nutrition support is usually indicated to initiate the refeeding of the patient (7), taking into consideration his clinical condition (presence of edema, physical exhaustion), his calorie intake and his blood test results[1] (8) (9). The existence of medical complications weighs in favor of instituting nutritional support therapy². When a patient's BMI is less than 12 kg/m^2 , artificial nutrition is systematically proposed from the start (10) (8) (9).

Assuming the patient has an accessible and intact digestive tract (which is true in most cases) (11), the choice of nutritional support is typically enteral nutrition (EN) administered via a small-caliber nasogastric tube as recommended (6,12). Parenteral nutrition is not used in AN (10) (13,14) (15). Vomiting is not a contraindication to EN.

The good tolerance of EN (16), its effectiveness on both weight gain (a weight gain between 500 g and 1 kg per week is recommended (6)) and on the reduction of the duration of hospitalizations, have been demonstrated (17) in malnourished patients with AN.

EN is prescribed in the following manner:

- A standard polymeric product, isocaloric (providing 1kcal / ml) (10,18), normoprotidic (18), without fiber² is most often prescribed
- As excessive protein intake is hazardous in cases of impaired renal function (18) or particularly in very low weight patients, a paediatric product less rich in protein is preferred².

To improve its performance and clinical and metabolic tolerance, EN is administered in a continuous flow over 24 hours (18) (12) using a flow control pump. When undernutrition is severe ($BMI < 12 \text{ kg/m}^2$), refeeding is exclusively enteral in the first days². An oral diet is gradually introduced later² (see dietary management).

Calorie intake is started at 10 kcal / kg body weight / 24 hours during the first 48 hours as recommended with severely malnourished patients (18). Then it is increased gradually (18), in increments of 250 kcal, according to the patient's clinical and biological tolerance, to reach 45 kcal / kg body weight/ 24 hours.

II.2.4. Hydration, vitamins and trace elements

During the first 48 hours of hospitalization, intravenous supplementation with vitamins, trace elements and phosphorus is carried out to correct potential micronutrient deficiencies and to prevent RS as recommended (10) (18) (19). Intravenous rehydration with a 5% glucose polyionic solution is also administered, limited to 30 ml / kg body weight / 24h. Patients are put on a low sodium diet (sodium intake $< 1 \text{ mmol} / \text{kg body weight} / 24\text{h}$) to prevent water inflation. Daily intake of phosphorus, vitamins and trace elements is continued orally (10,18).

Additional intravenous contributions of potassium, magnesium and phosphorus are added in case of hypokalemia, hypomagnesemia or hypophosphatemia (10,18).

II.2.5. Oral nutrition

Dietary management is an integral part of overall care and it becomes more and more important with the progression of the patient's hospitalization, in parallel with the decrease in EN (10,18). The reintroduction of oral feeding is done gradually, once refeeding has begun and in the absence of critical metabolic

abnormalities, at a rate adapted to the physiological and psychological capacities of the patients. The reintroduction of food must be progressive, as under-nutrition is severe (10,18).

Protein foods are re-introduced last (after vegetables and carbohydrates)², in order to limit protein intake at a level under 2.5 g/kg of body weight per day. Oral feeding is carried out with 3 meals per day and, if necessary, a snack at 4 pm. The meal duration must not exceed 30 minutes for lunch and 45 minutes for dinner².

A food-monitoring sheet is displayed in the patient's room which notes the current oral intakes of the patient. Once established, the composition of the meal can only be changed after the dietitian has interviewed the patient. As oral nutrition and weight gain are acquired, enteral caloric intakes are progressively reduced (18). It is recommended to interrupt EN if the oral intake is satisfactory when the BMI is around 14 kg/m² (18).

II.2.6. Prevention of refeeding syndrome

The severe and chronic undernutrition of the patient with AN (BMI <16 kg/m²) exposes the patient to an increased risk of RS at the initial phase of refeeding (6,20). The metabolism of the patient, which was idling in a state of adaptation to prolonged fasting, faces a new situation: the reintroduction of nutrients and its resulting increase in insulin levels (21). This metabolic change puts the patient at risk, especially if the increased calorie intake is not introduced gradually with movement of water and electrolytes from the extracellular sector to the intracellular sector. RS can manifest with ionic disorders, (mainly hypophosphatemia, hypokalemia and/or hypomagnesemia), fluid retention and one or more organ dysfunction(s) (acute heart failure, renal failure, respiratory failure, liver failure, convulsion or even coma) (22) (18).

To prevent RS, various measures are implemented:

- Refeeding is started with a minimum calorie intake, then increased very gradually, following the rule "start slow, advance slow." (10,18) (21)
- Adjustment of calorie intake is individualized to the patient's metabolic tolerance and weight gain. Ideally, the weight gain should be 0.5 to 1 kg / week (6,21) (18)
- Supplementation with multivitamins, trace elements, potassium, phosphorus, and magnesium is started empirically from the first day of admission, and then adapted, based on the biological results (10) (18)

- Comprehensive clinical monitoring with special attention to heart rate, edema and hydration status (10) (18)
- Regular biological monitoring (initially **daily during the first week of hospitalization**) of blood glucose, creatinine, liver enzymes, plasma electrolytes, and phosphorus (6, 10, 18,21). **Later, blood tests are repeated once a week if there is no acute abnormality** (10, 18).

II.2.7. Psychotropic treatment

There is no specific psychotropic treatment for AN (6,23) and those medications can have severe side effects in case of malnutrition. This is the reason why psychotropic medications are not systematically ordered in the unit. However, as recommended in all international guidelines (23), antidepressant medications are **occasionally** used when the patient still presents anxious depressive symptoms leading to an anxious or depressive disorder diagnosis despite **a significant improvement in his nutritional status** (25). **Antidepressant prescription is ordered by psychiatrists only with strict monitoring of potential adverse effects (in particular cardiac). It only concerns a small subgroup of patients whose nutritional status allows.** When the patient's anxiety symptoms are so severe that it is a barrier to his refeeding process, a small dose of anxiolytics can also be prescribed.

II.2.8.Prevention of decubitus ulcers and deep vein thrombosis

Strict bed rest is ordered in the beginning of hospitalization. It can be extended for some patients. Daily nursing care provided by nurses and nursing aids, and the use of air mattresses are the main measures to prevent bedsores in the unit. In addition, a prophylactic dose of anticoagulant treatment is ordered to prevent deep vein thrombosis.

II.2.9. Blood analysis and imaging

Some analyses are carried out during the early phase of the hospital stay, as recommended (10,18):

- Blood analysis (CBC, platelets count, electrolytes, urea, creatinine, calcium, phosphorus, magnesium, albumin, transthyretin, glycemia, liver enzymes, PT, PTT, CRP, Thyroid Function Tests, folate, vitamin B12, vitamins A, D and E, zinc, copper, selenium)

- ECG

A bone densitometry is done to assess the patient's bone mineralization status and to detect potential osteoporosis. It may be the first time a patient has had a bone densitometry in his medical history. If the patient had already a bone densitometry done in the past, a waiting period of two years is needed before repeating it (6).

An echocardiogram is also provided in the presence of clinical signs of cardiac insufficiency and/or ECG abnormality. "

II.2.10. Clinical and bio-clinical monitoring

An internal medicine doctor and a psychiatrist perform daily ward rounds together. All the patients present in the ward are seen every day by the team of doctors who provide physical examinations, discussions about hospitalization conditions, adjustment and revaluation of treatment, management of acute medical issues. Thus, each medical complication is managed adequately.

II.2.11. Psychiatrist's role

All hospitalized patients are assessed by psychiatrists through structured interviews with particular attention to the search for psychiatric comorbidities. Psychiatrists manage acute psychiatric symptoms. They are responsible for prescription of psychotropic medications when needed, according to the patient's biological and clinical tolerance. In cases of compulsory hospitalization, they write medical certificates in collaboration with the medial doctor.

In cooperation with psychologists, psychiatrists provide supportive psychotherapy. Structured therapy is difficult and may be impossible in case of extremely severe malnutrition. In fact, some psychiatric symptoms can be caused by malnutrition. Moreover, in the early phase of hospital, cognitive functions are altered by undernutrition itself (21).

II.2.12. Psychologist's role

The psychologist is responsible for individual psychotherapy support for each patient at least once a week. The frequency of these interviews is adjusted taking into account both the patient's preferences and the medical and psychiatric teams' evaluation. The psychologist also coordinates group activities or occupational therapy (3 times per week) to enable the patient to build alliances with the team and develop social relationships based on mediational activities. Different themes are explored through these activities. The different workshops include: group therapy focused on life and treatment in the unit, a newspaper workshop, cultural mediation, creative arts, and writing. Patients are invited to participate as soon as their physical conditions allow it.

II.2.13. Discharge from the unit and continuation of care

When a patient leaves the zone of critical danger, and his clinical condition is stable, he can be discharged. The refeeding process should achieve a minimum BMI of 13 kg/m². From then on, usually patients are transferred to an ED psychiatric unit to continue the refeeding process and initiate ED specialized therapies. This transfer is organized when the patient agrees. But some patients are unwilling to accept the transfer. When this occurs, there are two possibilities: if their clinical state is still critical, a compulsory treatment is implemented in the ED psychiatric unit; if not, they are discharged to ambulatory treatment. When the transfer takes place, it is preceded by a pre-admission consultation in the designated specialized ED psychiatric unit. Follow-up care can also be provided in a conventional psychiatric unit.

II.3. Patients

II.3.1. Inclusion criteria

We selected all patients hospitalized for the first time in the CNU in RP Hospital between November 1997 and January 2014, aged 15 years or older, diagnosed with AN according to the DSM IV criteria. The patient selection was provided by the hospital's department of statistics and medical information.

II.3.2. Exclusion criteria

We excluded from the study any patients who did not allow the use of their data for the study.

II.3.3. Parameters studied

For each patient, we performed a retrospective chart review and we recorded demographic and anamnesic data. Type of AN (restrictive, “AN-R” or purging/binging, “AN-BP”), duration of disease, purging behaviours, history of hospitalization for AN were detailed. Anthropometric data on admission and on discharge were noted as were patient psychiatric comorbidities, referral, length of stay and any intercurrent events which occurred during hospital stay.

II.4. Procedures and ethical approval

This study was conducted in accordance with the relevant French guidelines and regulations. It is part of a mortality study for which protocol was approved by the French data protection authority (CNIL, *Commission Nationale de l’Informatique et des Libertés*) and by two independent review boards (CCTIRS, *Comité Consultatif sur le Traitement de l’Information en matière de Recherche dans le domaine de la Santé* and CPP, *Comité de Protection des Personnes*). An information letter was sent to all patients selected for the study. Patient non-opposition was a prerequisite for the use of their data. Written informed consent for publication was obtained.

II.5. Statistical analysis

Analyses were performed with R software (version 3.5.3. 2019-03-11, R Foundation for Statistical Computing Platform: x86_64-w64-mingw32/x64 (64-bit)). Univariate statistics were used to describe the sample. Data were expressed as frequencies and percentages for nominal variables, and as means \pm standard deviations (SDs) for continuous variables.

[1] : Specific practice in the unit based on expert opinions (and not on standard feeding protocols)

3. Result

III.1. Patient characteristics

Initially, 395 patients were selected but 9 of these were excluded because they declined use of their data in the study. Finally, we included a total number of 386 patients: 365 (94.6%) were female and 21 (5.4%) were male. Mean age at admission was 29.4 (\pm 11.5) years old. Duration of AN at admission was 9.9 (\pm 9.3) years. BMI at admission was 12.7 (\pm 2.2) kg/m².

To achieve this weight gain, EN was widely prescribed in our cohort: 316 (81.9%) patients benefited from EN during their hospital stay. We observed that more than one-third of patients were still on EN on

discharge: 137 (35.5%) patients were still receiving EN when they left the unit. Hence, EN was ongoing in their transfer unit to continue the refeeding process

Patient characteristics are presented in Table 1.

Characteristics	Mean ± SD or (Percentage)	N
Female /Male	365 (94.6 %)/ 21 (5.4 %)	
Age at admission (years)	29.4 (± 11.5)	
Subtype of anorexia nervosa:		
Restrictive	180 (46.6 %)	
Binge purging	186 (48.2 %)	
Atypical AN	20 (5.2 %)	
Age at AN onset (years)	19 (± 7.6)	
Duration of AN at admission (years)	9.9 (± 9.3)	
History of hospitalization for AN in other hospitals (before admission in the unit)	302 (78.2 %)	
Number of hospitalizations for AN (before admission in the unit)	2.9 (± 3.4)	
Patient's regular behavior:		
Self induced vomiting	162 (42 %)	
Laxative misuse	81 (21 %)	
Potomania	54 (14 %)	
Diuretic use	15 (3.9 %)	
Problematic exercice	175 (45.3 %)	
BMI (kg/m²):		
Admission	12.7 (± 2.2)	
Discharge	14.2 (± 1.9)	
Weight gain during hospitalization (kg)	3.8 (± 4)	
Psychiatric comorbidities:		
Personality disorders	84 (21.8 %)	
Obsessive-compulsive disorders	32 (8.3 %)	
Mood disorders and/or Anxiety disorders	181 (46.9 %)	
History of suicide attempt	81 (21 %)	

Self-mutilations (nonsuicidal self-injury disorder)	28 (7.3 %)
Attention Deficit Hyperactivity Disorder	5 (1.3 %)
Kleptomania	3 (0.8 %)
Addictions:	
Alcohol use disorder	34 (8.8 %)
Substance use disorder	24 (6.2 %)
Tobacco use disorder	127 (33 %)

Table 1. Patient characteristics (N=386).

III.2. Patient's referral to the unit

Among the patient cohort, the most frequent reason for admission was extremely severe undernutrition. **It concerned 295 (76.4%) patients. Fifty-four (14%)** patients were hospitalized for other reasons such as the treatment of one or more medical complications related to undernutrition or to the process of refeeding itself initiated outpatient or inpatient in other hospitals. Short admissions were also organized for nutritional evaluation and development of a treatment regime **in 19 (4.9%) patients.** Finally, **18 (4.7%) patients were admitted** in order to wean purging behaviours (self-induced vomiting, laxative or diuretic abuse).

The protocol for the treatment of patients in the unit was individualised following an initial consultation or evaluation in psychiatric or general medicine day hospital. In case of emergency, the patient could be also admitted after a transfer from an inpatient unit in another hospital (e.g., an emergency room, medical ward, medical intensive care unit (MICU), or psychiatric ward), (refer to Table 2).

Medical unit that referred the patients to the unit	N (Percentage)
Psychiatric inpatient unit	54 (14.8 %)
Emergency department	25 (6.8 %)
Medical Intensive Care Unit	65 (17.8 %)
Medicine outpatient clinic	100 (27.3 %)
Psychiatric outpatient clinic	59 (16.1 %)
Medical ward	51 (13.9 %)
Student medical and psychiatric clinic	2 (0.5 %)
Adolescent care inpatient unit	3 (0.8 %)
Surgical ward	1 (0.3 %)
Obstetrics and gynecology inpatient unit	2 (0.5 %)
General pediatrics inpatient unit	4 (1.1 %)

Table 2. Distribution of medical units that referred the patients to the unit (n=366).

III.3. Length of stay, Number of admission

Our unit has 180 to 200 admissions per year with an average length of stay of 35.2 (\pm 30.2) days. Patients can be hospitalized multiple times in the unit if necessary. Among the cohort, 127 (32.9%) patients were re-hospitalized one or more times in the unit after their first admission because of **a somatic complication and/or** a relapse of the disease resulting in a life-threatening clinical condition, **within 1.7 (\pm 1.5) years, over the study period from November 1997 to January 2014.**

III.4. Medical management difficulties

Because of the extreme severity of the patients' medical conditions and despite all the precautions taken during the refeeding process, some acute medical complications could appeared. It was rarely a refeeding syndrome (23 cases in our cohort-5.9% of patients); most often, these complications corresponded to: hemodynamic instability, electrolyte imbalance, anemia, severe neutropenia, acute organ dysfunction (cardiac, hepatic, renal) or sepsis linked to the relative immunosuppression induced by the malnutrition. Consultations to other sub-specialties such as infectious diseases or hepatology could also be required to optimize the management of patients at times.

All these situations were managed individually. In cases of critical or unstable clinical parameters or vital organ dysfunction, a transfer to the MICU was organized. Among our cohort, 99 (25.6%) patients were temporarily transferred to the MICU during their hospitalization in the unit. Reasons for these MICU transfers are presented in Table 3.

Reason for medical intensive care unit (MICU) transfer during hospitalization in the unit	Number of patients	Percentage of the total number of MICU transfers (N=99)
Hypokalemia complicated by ECG changes	21	21,2%
Hypophosphatemia complicated by ECG changes	11	11,1%
Severe hyponatremia ¹	9	9,1%
Severe hypertransaminasemia ² and hepatic failure	20	20,2%
Acute cardiac failure	6	6,1%
Hemodynamic instability and / or cardiac arrhythmias	24	24,2%
Hypothermia	5	5%
Acute renal failure	10	10,1%
Suicide attempt	8	8,2%
Acute pancreatitis	1	1%
Severe sepsis ³	14	14,1%
Anasarca	3	3%
Neurological disorders	5	5%
Severe symptomatic hypoglycemia ⁴	6	6,1%
Gastric distension	1	1%
Parenteral nutrition use	1	1%

Table 3. Reasons for MICU transfer during the hospitalization in the unit.

¹: Hyponatremia < 120 mmol/l; ²: Elevated Liver Function Tests with aspartate transaminase and alanine transaminase ≥ 10 times the normal upper limit; ³: Sepsis associated with organ dysfunction, hypoperfusion or hypotension; ⁴: Hypoglycemia < 2.8 mmol/L associated with neurological symptoms

III.5. Psychiatric care difficulties

Main difficulties encountered in psychiatric care were: the presence of psychiatric comorbidities (refer to table 1), cases of runaways (9 cases in our cohort - 2.3% of patients) and case of discharges against medical advice before the end of the care protocol (46 cases among our cohort – 11.9% of patients without immediate life-threatening conditions). However, in cases of vital risk, (when the patient's condition is compromised and the continuation of refeeding is urgently required), if the patient does not agree to the continuation of care, a legal procedure for compulsory treatment under French Law can be implemented in the unit. This procedure is developed in collaboration with the regional reference psychiatric center and implemented in our medical unit until the clinical state of the patient allows other modalities of treatment. In our cohort, 24 (6.2%) patients were affected by this procedure.

III.4. Discharge from the unit

The different facilities receiving the patients after hospitalization in the unit are presented in table 4. In our cohort, 44.1% of patients benefited from a transfer to a psychiatric ward (general psychiatry, psychiatric unit specialized in ED, psychiatric rehabilitation center) and 43.8% were discharged at home after hospitalization in the unit (refer to table 4). Among the patients discharged at home, 11.9% were discharged against medical advice and 31.9% were allowed to leave the unit under medical team permission.

Facility receiving the patient after discharge from the unit	N (Percentage)
Home	169 (43.8 %)
General psychiatry	45 (11.7 %)
Psychiatric unit specialized in eating disorders	116 (30.1 %)
Medicine rehabilitation center	6 (1.5 %)
Nutrition rehabilitation center	8 (2.1 %)
Psychiatry Day Hospital	14 (3.6 %)
Endocrinology department	1 (0.3 %)
Surgical ward	4 (1%)
Psychiatric rehabilitation center	9 (2.3 %)
Internal medicine ward	3 (0.8 %)
Clinical nutrition unit	1 (0.3 %)
Home hospitalization	1 (0.3 %)
Obstetrics and gynecology department	2 (0.5 %)
Medical Intensive Care Unit	1 (0.3 %)
Death during the hospital stay	6 (1.5 %)

Table 4. Distribution of facilities receiving patients after discharge from the unit (N=386).

4. Discussion

The question of where to hospitalize extremely malnourished patients with AN is a real concern raised in the literature by psychiatric teams specialized in the management of AN (26) (27). It may seem like a dilemma. On one hand, in case of extreme malnutrition related to AN, psychiatrists have to deal with severe medical complications that are not within their competences and that justify hospitalization in an internal medicine ward. On the other hand, medical doctors have to face the resistance to treatment inherent to patients with AN (denial, treatment refusal, ambivalence about treatment) » and psychic decompensations that would justify admission to a psychiatric ward (26). This problem is mentioned in the MARSIPAN report which specifies that specialist- ED- units are not suitable for treating severe medical complications (27). Thus, a survey in specialist- ED- units published by the MARSIPAN working group showed that services could not offer intravenous infusion, parenteral nutrition and treatment of serious medical complications in these units. Patients with electrolyte or renal abnormalities or comorbidity increasing the risk of refeeding syndrome should not be managed in a specialist- ED- unit. MARSIPAN

guidelines recommend to transfer these patients to a medical ward. Then there are the issues of liaison and transfer between the two settings (specialist- ED- unit and medical ward) (27).

Our unit responds to this problem by providing both somatic and psychiatric care, in the same place, to make the management of severely malnourished patients with AN more safe and effective.

The development of a team specialized in the management of severe malnutrition and the regular admission of patients with AN in the unit has allowed us to develop expertise in the most extreme clinical situations. As explained by E. S. Chu (28), the management of patients with complex illnesses, is better when it is provided by a medical team with specific expertise. In this context, transdisciplinary management involving psychiatrists and medical doctors appears essential. Indeed, the goal of having a transdisciplinary team is to respect the patient's individuality by proposing both a global and a personalized approach. The team-work of the different professionals who exchange ideas and mutually enrich each other makes it possible to offer optimal care for the patient.

The other specific benefits of transdisciplinarity are the possibility of: initiating early psychiatric follow-up, ensuring continuity of care by preparing for subsequent care in specialized ED psychiatric unit, initiating compulsory treatment if necessary. Thanks to the centralization of treatment for difficult medical situations, the unit has become an important referral center for effective treatment of serious ED.

The development of the therapeutic alliance is favored by the involvement of the close entourage of patients in the care program. The involvement of the families is an important factor in patient adherence to care (29).

To the best of our knowledge, we did not identify either in France or elsewhere in Europe, a similar unit providing **simultaneously** medical and psychiatric transdisciplinary **combined** care to patients with severe forms of AN: **with psychiatrists and internal medicine doctors working full time in the same unit with daily cooperation and interactions**. However, we did find an acute medical unit in Denver accepting patients with ED and severe medical complications (28). This unit does not have an onsite psychiatrist but psychologists can support the patients during their hospitalization. In Munich, there is also a psychiatric intensive care unit accepting severely malnourished patients with AN for refeeding since 2000 (30). **There is no internal medicine doctor working full time in this unit but if necessary, opinions for the somatic management of patients are requested by psychiatrists from internal medicine doctors working in the internal medicine department of the hospital.**

Providing in parallel, in the same venue, both medical and psychiatric care in a transdisciplinary way to patients with severe forms of AN appears essential for patients and care givers as we discussed previously. That is why our transdisciplinary model of treatment could be adapted in other treatment programs (medical or psychiatric) for severe AN. Hence, medical units who are receiving malnourished patients with AN could integrate a psychiatrist specialized in ED, into their teams, to complement medical care with psychiatric support. And, psychiatric units specialized in ED could integrate a physician-nutritionist, into their teams, in order to manage EN prescription, refeeding process and medical complication in case of extreme malnutrition.

This transdisciplinary program which provide both somatic and psychiatric treatment could allow a more complete and global care of patients suffering from AN. It could also facilitate management of patients with extreme malnutrition and/or medical complications. Indeed, such patients cannot be admitted directly to psychiatric Specialist-Eating-Disorders- Unit due to the severity of their somatic condition. With a transdisciplinary model of treatment, Specialist-Eating-Disorders- Unit could be able to admit such patients.

We formulate the hypothesis that a transdisciplinary model of treatment could optimize and improve the quality and effectiveness of care for patients with AN. However, the positive impact of this model needs and remains to be proven, particularly in terms of clinical or public health benefits. Does this model of care could participate to reduce chronicization of disease, frequency of relapse, number of admission, length of stay or patient mortality? It would be interesting to study all these parameters.

We share the opinion of E.S.Chu (28) that this rare, medically unstable and complex population of patients with severe malnutrition secondary to AN requires a specific medical management by a highly specialized multidisciplinary team within a referral center. The team also has a mission, through clinical research perspectives, to provide a better understanding of the somatic complications associated with extreme malnutrition and thus participate in the elaboration of protocols and management guidelines (6,31).

5. Conclusion

The transdisciplinary model of management and treatment of adult patients suffering from AN in the clinical nutrition-ED-unit in Raymond Poincaré-University Hospital could, if it were available more widely,

benefit the most distressed patients and potentially decrease complications and mortality related to severe AN and promote patient care compliance. Thanks to their expertise, specialized care teams are very competent, less critical and less rejecting towards patients (32).

Abbreviations

AN = anorexia nervosa

AN-R=anorexia nervosa restrictive subtype

AN-BP=anorexia nervosa binge purging subtype

BMI = body mass index

ED= eating disorders

EN= enteral nutrition

MARSIPAN=management of really sick patients with anorexia nervosa

MICU = medical intensive care unit

RP= Raymond Poincaré

RS=refeeding syndrome

Declarations

Ethical approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

Consent for publication: Written informed consent for publication was obtained (please refer to paragraph: II.3. Procedures and ethical approval).

Availability of data and materials: The datasets generated and analysed during the current study are not publicly available due to other works being under progress but are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: MG collected and analysed the patients' data and wrote the initial manuscript. JCM, NG and MH analysed the patients' data and contributed in writing the manuscript. All authors read and approved the final manuscript.

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