Table 1. An example of behavioral limitation (For target bodyweight 45kg)

BW (kg)	Behavior	Communication	Bathing	Others
32	Restricted to the room		Wiping with towel	
33				Permission to do handicrafts
34	Restricted to the ward		Showering once per week	
35		Permission to send letters		Permission to read books
36	Permission to go to the terrace			
37		Permission to receive letters	Showering twice per week	
38	Permission to go to the rooftop			Permission to listen to music
38		Permission to make tele -phone calls		
40	Free movement within the hospital		Showering three times per week	
41		Permission to receive tele -phone calls		
42	free movement within the hospital grounds			Permission to use seasoning
43			Bathing	
44		Unlimited visits		
45	Permission to go outside the hospital grounds			

Table.2. Clinical data of patients followed-up and not followed-up

	Followed-up patients (N=67)		Not followed-up patients (N=21)		t value	df	p
Age at onset (years)	21.6	(8.1)	22.0	(9.0)	0.149	86	0.882[a]
Age at admission (years)	22.3	(8.4)	22.9	(9.0)	0.292	86	0.771[a]
Duration from onset to admission (months)	36.4	(62.8)	33.9	(32.7)	-0.176	86	0.861[a]
Subtype							0.210[b]
AN-R	29	(43.3%)	13	(61.9%)			
AN-BP	38	(56.7%)	8	(38.1%)			
BW at admission (kg)	22.3	(8.4)	22.9	(9.0)	-0.127	86	0.899[a]
BMI at admission	13.4	(1.9)	13.4	(1.9)	0.001	86	0.999[a]
SDS at admission[c]	51.0	(10.9)	51.5	(11.9)	0.146	80	0.885[a]
GCS at admission							0.198[b]
symptomatic	14	(20.9%)	4	(19.0%)			
poor	53	(79.1%)	17	(81.0%)			
BW at discharge (kg)	41.4	(6.1)	39.5	(5.6)	-1.271	86	0.207[a]
BMI at discharge	17.1	(2.2)	16.3	(2.0)	-1.331	86	0.187[a]
Increase in BW during inpatient treatment (kg)	8.8	(5.7)	7.1	(3.9)	-1.296	86	0.199[a]
Increase in BMI during inpatient treatment	3.7	(2.5)	2.9	(1.6)	-1.230	86	0.222[a]
Duration of hospital stay (days)	153.2	(94.9)	146.3	(64.5)	-0.374	86	0.710[a]
Timing of discharge							0.207[b]
Before achieving target body weight	24	(35.8%)	11	(52.4%)			
After achieving target body weight	43	(64.2%)	10	(47.6%)			

Values are expressed as mean (SD) or number of patients (%) a : Unpaired student's t test. b : Fisher's exact test. c : N=65/17 (Followed-up/Not followed-up)

Table 3. Clinical features of patients at admission, discharge and follow-up (N=63)

	At admission		At discharge		At follow-up	
Age at onset (years)	19.0	(5.9)	-		-	
Age (years)	21.2	(6.9)	21.6	(6.9)	28.0	(6.8)
Duration after onset (months)	25.9	(38.6)	31.1	(37.7)	106.9	(41.6)
Subtype						
AN-R	29	(46.0%)	-		2	(3.2%)
AN-BP	34	(54.0%)	-		6	(9.5%)
BN	-		-		4	(6.3%)
EDnos	-		-		7	(11.1%)
Bodyweight (kg)	32.9	(5.9)	42.1	(5.5)	44.8	(5.8)
BMI	13.5	(2.0)	17.3	(2.0)	18.3	(2.2)
Increase in bodyweight (kg) during inpatient treatment	-		9.2	(5.6)	-	
Increase in BMI during inpatient treatment	-		3.8	(2.4)	-	
GCS						
excellent	-		-		36	(57.1%)
much improved	-		-		9	(14.3%)
Symptomatic	14	(22.2%)	-		9	(14.3%)
Poor	49	(77.8%)	-		9	(14.3%)
Duration of hospital stay (days)	-		157.8	(95.0)	-	
Duration after discharge (years)	-		-		6.3	(1.8)
Duration of treatment after discharge (months)	-		-		43.0	(29.1)
Number of rehospitalized patients	-		-		18	(28.6%)
EDI	-		-		45.4[c]	(29.9)
SDS	50.3[a]	(10.7)	40.5[b]	(9.0)	43.9[c]	(11.0)

Values are expressed as mean (SD) or number of patients (%).

a : N=66, b : N=44, c : N=47.

Table 4. Multiple regression analysis for predicting GCS at follow-up

Variables	β	Standardized β	t	p
Age at admission	.290	.365	3.162	.002
BMI at discharge	-.668	-.244	-2.115	.039

Backward elimination method (probability of t to remove > 0.05).

R=.464, R^2=.216, adjusted R^2=.189, F-statistic=8.243, df=2, p=0.001

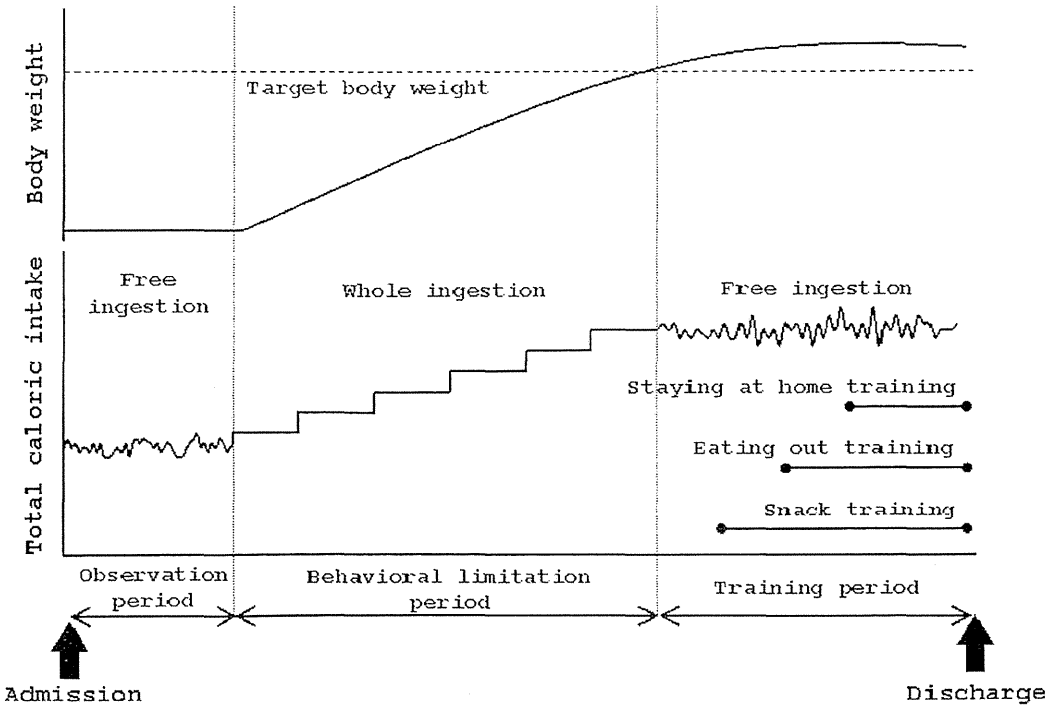
β: partial regression coefficient

Table 5. Comparison of clinical features and prognosis by achievement of target body weight

	Achieving (N=42)			Not Achieving (N=21)			t value	df	p
Age at admission (years)	20.9	(7.0)		21.7	(6.8)		0.399	61	0.692[a]
Duration from onset to admission (months)	21.5	(29.5)		34.7	(52.1)		1.077	61	0.291[a]
Subtype									0.063[b]
AN-R	23	(54.8%)		6	(28.6%)				
AN-BP	19	(45.2%)		15	(71.4%)				
BW at admission (kg)	33.1	(6.2)		32.5	(5.3)		-0.345	61	0.731[a]
BMI at admission	13.6	(2.1)		13.2	(1.6)		-0.856	61	0.396[a]
BW at discharge (kg)	44.2	(4.1)		37.8	(5.6)		-5.161	61	<0.001[a]
BMI at discharge	18.3	(1.3)		15.3	(1.7)		-7.834	61	<0.001[a]
Increase in BW during inpatient treatment (kg)	11.2	(5.3)		5.3	(3.8)		-4.488	61	<0.001[a]
Increase in BMI during inpatient treatment	4.7	(2.4)		2.2	(1.6)		-4.396	61	<0.001[a]
Duration of hospital stay (days)	197.0	(79.0)		79.5	(74.4)		-5.669	61	<0.001[a]
Age at follow-up (years)	28.1	(6.8)		27.6	(6.9)		-0.286	61	0.776[a]
Duration after discharge (years)	78.1	(21.1)		69.5	(22.2)		-1.501	61	0.138[a]
Duration of treatment after discharge (months)	41.3	(28.2)		46.5	(31.4)		0.666	61	0.508[a]
Number of rehospitalized patients	9	(21.4%)		9	(42.9%)				0.087[b]
BW at follow-up (kg)	44.7	(5.5)		45.0	(6.6)		0.191	61	0.849[a]
BMI at follow-up	18.4	(2.1)		18.3	(2.6)		-0.175	61	0.861[a]
Increase in BW after discharge (kg)	0.6	(5.0)		7.2	(6.5)		-4.512	61	<0.001[a]
Increase in BMI after discharge	0.1	(2.0)		2.9	(2.7)		-4.356	61	<0.001[a]
GCS at follow-up									
excellent	26	(61.9%)	[1.1][d]	10	(47.6%)				0.058[c]
much improved	5	(11.9%)	[-0.8][d]	4	(19.0%)	[-1.1][d]			
Symptomatic	8	(19.0%)	[1.5][d]	1	(4.8%)	[0.8][d]			
Poor	3	(7.1%)	[-2.3][d]	6	(28.6%)	[-1.5][d]			
Total score of GCS	4.1	(4.7)		6.6	(6.6)	[2.3][d]			

Values are expressed as mean (SD) or number of patients (%) a : Unpaired student's t test, b : Fisher's exact test, c : Chi-square test, d : residual analysis

Figure 1 Treatment protocols



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BIOPSYCHOSOCIAL MEDICINE

RESEARCH Open Access

The longitudinal BMI pattern and body composition of patients with anorexia nervosa who require urgent hospitalization: A case control study

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Abstract

Background: The prevention of serious physical complications in anorexia nervosa (AN) patients is important. The purpose of this study is to clarify which physical and social factors are related to the necessity for urgent hospitalization of anorexia nervosa (AN) patients in a long-term starvation state. We hypothesized that the change of longitudinal BMI, body composition and social background would be useful as an index of the necessity for urgent hospitalization.

Methods: AN patients were classified into; urgent hospitalization, due to disturbance of consciousness or difficulty walking(n = 17); planned admission (n = 96); and outpatient treatment only groups (n = 136). The longitudinal BMI pattern and the clinical features of these groups were examined. In the hospitalization groups, comparison was done of body composition variation and the social background, including the educational level and advice from family members.

Results: After adjusting for age and duration of illness, the BMI of the urgent hospitalization group was lower than that of the other groups at one year before hospitalization ($P < 0.01$) and decreased more rapidly ($P < 0.01$). Urgent hospitalization was associated with the fat free mass (FFM) ($P < 0.01$). Between the groups, no considerable difference in social factors was found.

Conclusions: The longitudinal pattern of BMI and FFM may be useful for understanding the severity in AN from the viewpoint of failure of the homeostasis system.

Introduction

Anorexia nervosa (AN) is a severe mental health disorder that is thought to be of psychogenic origins and that often results in an extreme starvation state. Serious medical complications have been reported, including electrolyte disorders, severe bone loss, and cardiac dysfunction [1,2]. Most pathophysiological complications of AN are reversible with improved nutritional status, however some physical consequences can be life-threatening [3-5].

In AN, various factors have been suggested to be responsible for the development of severe physical complications; for example, low nutritional status, drug and alcohol use, bulimia, depressed body temperature, hypotension, and electrolyte abnormality [3,5-9].

The prevention of serious physical complications by AN is important. Many practice guidelines indicate how to assess medical risk [7-10]. Judgment is not difficult on the need for urgent admission on the day of consultation using these criteria. However, the decision on whether or not urgent hospitalization will be necessary in the near future has been left to the experience of the clinician.

A longitudinal study that addresses all the pertinent criteria for outpatient and untreated patients is clinically difficult to perform. Therefore, we focused on BMI as a longitudinal factor and variables in the social background that could be objectively investigated. In addition, we

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assessed the body composition of AN patients who required urgent hospitalization or who had a planned hospitalization to further clarify the factors associated with urgent hospitalization. Both the physical severity and socio-demographic variables, including educational level and the advice of family members seem to be associated with a decision for hospitalization. In this paper, for the purpose of making the clinical condition apparent, we compared the pre-hospital social background and the body composition of the patients at admission.

We hypothesized that changes in the longitudinal BMI, body composition and social background would be useful as an index of this phenomenon.

Methods

The present study was based on the principles of the Declaration of Helsinki and was approved by the Kyushu University Research and Ethics Committee. All participants provided written informed consent.

Design

The study group was composed of 291 consecutive new outpatients with AN at the Department of Psychosomatic Medicine of Kyushu University Hospital from 2002-2008. All were diagnosed with AN according to the criteria of the Diagnostic Statistical Manual of Mental Disorders IV (DSM-IV)[11].

Study 1

We investigated the longitudinal Body Mass Index (BMI) and clinical factors related to the necessity for urgent hospitalization of AN patients.

A study investigator interviewed all participants to determine illness duration, medical history, menstrual history, purging history, and exercise history. We calculated BMI on the first consultation day, one month before, three months before, six months before, and one year before consultation at this hospital, (5 points in total). The past BMI was determined through a letter of introduction from the previous medical institution, direct telephone inquiry to any medical institution that performed medical examinations in the past, and statements of patients and their families. BMI (kg/m^2) was calculated as the ratio of body weight (kg) to height (m) squared. All BMI calculations were done with at least a two week interval. Patients were excluded from study if data was not available for at least three of the five BMI measurement points.

Patients were classified into the following three groups by differences in physical condition (Figure 1).

Urgent group

The urgent group consisted of patients hospitalized with disturbances of consciousness and/or difficulty walking on the day of consultation.

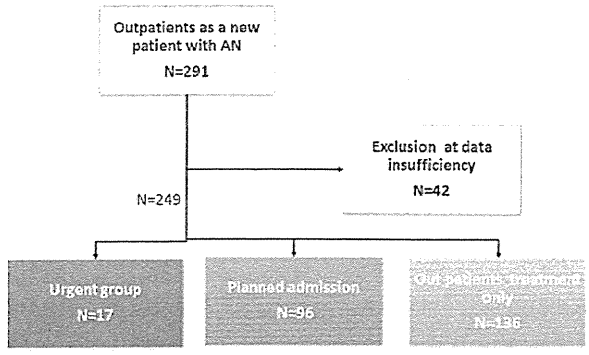

Figure 1 Algorithm for classification into three groups. Urgent group: This group consisted of patients hospitalized with disturbance of consciousness and/or difficulty walking on the day of consultation. Planned admission group: This group consisted of AN patients hospitalized for therapeutic purposes up to one year after the day of consultation. Outpatient treatment only group: Patients not admitted in the year after the initial consultation.

These symptoms are absolute indicators of hospitalization[7-9]. For patients referred from other hospitals and patients with a history of urgent hospitalization, we defined a hospital day due to disturbance of consciousness or difficulty walking as the hospitalization day of this study. All causes of difficulty walking, including muscle weakness, heart failure, and infection, were included.

Planned admission group

This group consisted of patients hospitalized for AN up to one year after the day of consultation. For patients whose BMI was not expected to increase and/or eating behavior abnormality was not expected to improve even with treatment for two months on an outpatient basis, we proposed inpatient treatment with our cognitive behavior therapy (CBT) program for eating disorders. We defined a planned admission day as the hospitalization day. In addition, urgent admission due to low weight, bradycardia, liver damage, or other physical causes was included in the planned admission group in order to eliminate the possibility of vagueness of the research data of this study. This is because the decision on the physical state of these patients on admission involves subjective factors related to the judgment of the chief physician, in contrast to disturbance of consciousness or difficulty walking as was used for the urgent group.

Outpatient treatment only group

This group of patients was not admitted within the year after their initial consultation. Included in this group are patients who were recommended to the outpatient clinic, patients who had interrupted treatment at the

outpatient clinic, patients who did not agree to proposed inpatient treatment, and patients hospitalized for a short period of several days for self- mutilation or suicide attempts, such as by wrist cutting or drug overdose.

All control group

Planned admission group and outpatient treatment only group.

Matched control group

A group with age and duration of disease matching the urgent hospitalization group was extracted from the all control group.

Because many factors had a serious influence on the decision for urgent hospitalization, this study was done as a case control study.

BMI change of each group was followed over one year (12, 6, 3, 1,and 0 months before). In addition, we investigated the association between BMI at the initial consultation and the necessity of urgent hospitalization.

Study 2

Differences in the body composition and socio-demographic variables of the urgent and planned admission groups were examined. Body composition was measured after two weeks of hospitalization. Weight, fat mass (FM), lean body mass, and bone mineral content were determined for the whole body using dual-energy X-ray absorptiometry (DXA) with a HOLOGIC QDR-4500 densitometer (Hologic, Waltham, MA). All measurements were performed by an experienced technician. Fat free mass (FFM) was defined as lean body mass and bone mineral content. We investigated the association between FM and FFM and the necessity of urgent hospitalization.

Socio-demographic variables consisted of age, marital status, divorce of the parents, educational level, and employment status. Lifestyle-related factors considered were smoking and alcohol consumption. These factors were included in between group comparisons.

Statistical Analysis

SPSS Ver. 14.0 J was used for all statistical tests. Results were presented as means ± standard deviation (SD). *P* values <0.05 were considered statistically significant. Significance at baseline was determined by the appropriate test, either chi-square test or paired f-test. We examined the change of BMI at five time-points. Comparison of between group longitudinal changes of the BMI were analyzed by repeated measures analysis of variance (ANOVA) for matched pairs. We evaluated the association between the necessity of urgent hospitalization and BMI, FM and FFM at admission using the Cochran-Armitage test of trends.

Results

Of 291consecutive patients, 42 were excluded for lack of BMI data, leaving the data of 249 available for analysis. The treatment of 17 patients was interrupted after one consultation. The urgent group consisted of 17(7%) of the studied patients, the planned admission group 96 (39%), and the group treated as outpatients only 136 (55%) (Figure 1).

Study 1

Group Characteristics

Urgent group(n = 17) 13 of the 17 patients showed disturbance of consciousness. For 9 of the 13 patients with disturbed consciousness, hypoglycemia (<50 mg/dl) was confirmed in the emergency room. Of these, severe hypoglycemia (<30 mg/dl) was confirmed in six. 10 of the 17 patients showed difficulty in walking. Five patients without disturbance of consciousness were urgently hospitalized only because of difficulty in walking, one had infective endocarditis, and another dehydration due to acute enteritis. Four patients had low body temperature (<35 degrees). In addition, one patient had a severe infection.

Planned admission group(n = 96) 80 of the 96 patients were admitted for therapeutic purposes. 16 patients were urgently hospitalized on a consultation day or the following day with associated physical factors such as bradycardia, severe liver damage, electrolyte abnormality, or low body weight. These patients had set a date to be hospitalized on the initial diagnosis day and were hospitalized within a few days after consultation.

Outpatient treatment only group (n = 136) 17 patients from this group interrupted treatment after one consultation.

The changes in BMI over the previous year of the urgent (n = 17), planned admission (n = 96) and outpatient groups (n = 136) are shown in Figure 2. The BMI's over the past year (12,6,3,1,and 0 months before) of the urgent hospitalization group were 13.9 ± 2.5, 13.4 ± 1.9, 12.1 ± 1.2,11.3 ± 1.3, and 10.8 ± 1.4 kg/m^2(mean ± SD), respectively. Those of the planned admission group were 15.9 ± 3.1, 15.1 ± 2.6, 14.3 ± 2.0,13.9 ± 1.7, and 13.7 ± 1.7 kg/m^2 respectively. Those of the outpatient treatment only group were 16.2 ± 2.8 15.3 ± 2.4, 14.7 ± 2.1,14.3 ± 1.9, and 14.2 ± 1.8 kg/m^2, respectively. In the planned admission and outpatient groups, BMI followed a similar course along the temporal axis and values. Subsequently, we treated these groups as one (all control group) in study 1 with regard to physical severity.

Comparison of the urgent and all control groups found no difference in age (25.6 ± 9.7 vs., 22.5 ± 8.6 yr), type of AN, or sex (Table 1). The urgent group had a significantly longer duration of illness than the all

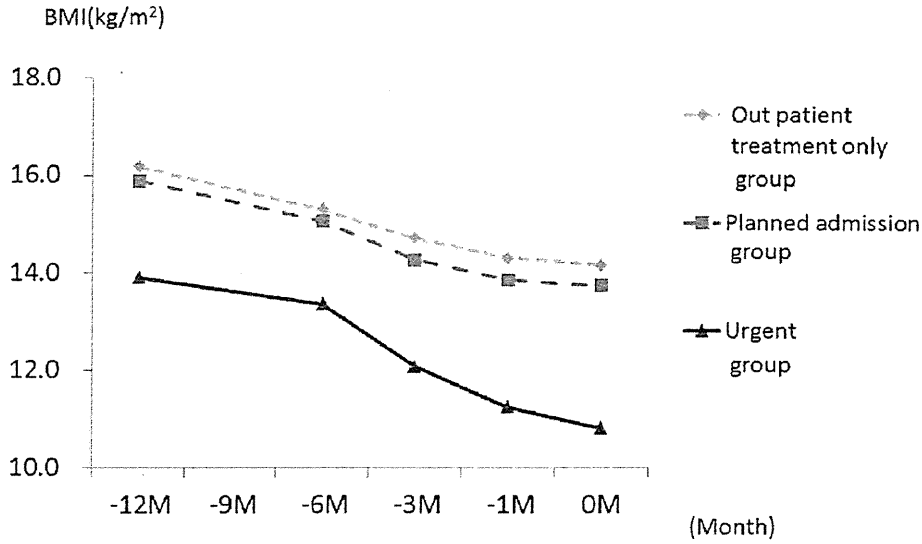

Figure 2 Longitudinal pattern of BMI over the year before the first consultation.

control group (P < 0.05), and the BMI at first visit was significantly low (P < 0.01).

Differences in longitudinal BMI patterns of the urgent and matched control groups are shown in Figure 3.The BMI course of the urgent group was significantly different from that of the matched control group (P < 0.001). The BMI of the urgent group was already lower than that of the matched controls 12 months before, even when adjusted for the disease period and age (Table 2). Furthermore, the urgent group had rapidly decreasing weight as the patients got closer to admission, significantly decreased in comparison with the matched controls. In other words, a high interaction was found in the pattern of the time course towards admission and the BMI of both groups, even when adjusted for the disease period and age.

The rates of urgent hospitalization for each BMI level on consultation day are shown in Figure 4. The rate of urgent hospitalization significantly rose with a decrease in BMI (P < 0.001). All of the patients required urgent hospitalization when BMI became less than 10 kg/m^2.

Table 1 Clinical characteristics of the urgent hospitalization and all control groups.

	Urgent group (n = 17)	All control (n = 232)	p
Age (y)	25.6 ± 9.7	22.5 ± 8.6	.13
Sex (male/female)	1/18	7/224	.52
Duration (y)	7.3 ± 7.4	4.5 ± 5.4*	.04
Subtype(AN-R/AN-BP)	9/8	119/112	.92
BMI at first visit (kg/m^2)	10.8 ± 1.4	14.0 ± 1.8*	.00

All control: Outpatient treatment only group + planned admission group.
AN-R: Anorexia nervosa restricting type AN-BP: Anorexia nervosa binge eating and purging type * P < 0.05

Study 2

Ten of the 17 patients of the urgent group and 75 of the 96 patients of the planned admission group were the subjects of this study.

The fat mass (FM) and fat free mass (FFM) of the urgent group were significantly lower than for the planned admission group (FM; 2.79 ± 0.48 vs. 4.76 ± 2.3 kg, P = 0.008, FFM; 25.2 ± 4.6 vs. 31.4 ± 4.4 kg, P = 0.00). Urgent hospitalization was required when FM was less than 3.6 kg and FFM less than 31.1 kg. The rate of urgent hospitalization rose with significantly decreased FFM and FM (P = 0.004 and P = 0.004, respectively Figures 5a, 5b). Urgent hospitalization gradually increased when FFM decreased to less than 35 kg. However, it remained at the same level when FM decreased to less than 4.0 kg.

In the comparison of the socio-demographic variables, significantly more in the urgent group were married than in the planned admission group (41.2% vs. 15.5%: P = 0.095). No other significant between group differences were found in other social support factors (Data not shown).

Discussion

The BMI course and body composition of AN patients who developed disturbance of consciousness and/or difficulty walking were clearly different from those of the control group patients. Quantitative analysis showed that the urgent hospitalization group had a lower BMI one year before admission and that weight loss was significantly more rapid than that of the control group. The rate of urgent hospitalization increased with a reduction in BMI, FFM and FM. No considerable

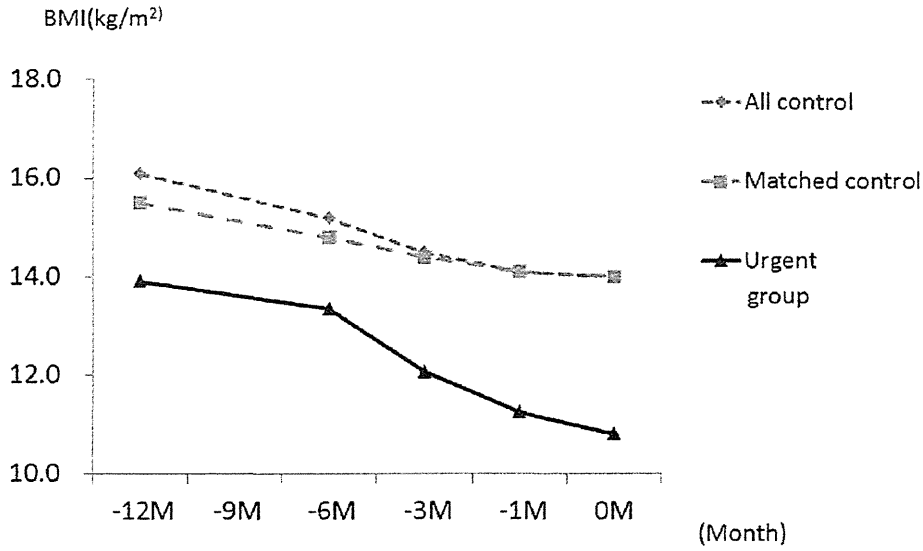

Figure 3 Differences in longitudinal BMI pattern between the urgent hospitalization and the other AN groups. All control: Planned admission group+ outpatient treatment only group Matched control: the duration of disease and age of the urgent group were matched with the all control group.

difference in social factors was found between the urgent and planned admission groups. It is not surprising clinically that patients at very low BMI require urgent hospitalization more often than those at higher BMI. We felt that it was important to empirically demonstrate this relationship and hope that our proof using the statistical procedure is useful for primary physicians in their efforts to better care for their AN patients.

For patients with AN, low BMI at referral indicates a substantial risk for chronic AN and death related to emaciation [12]. A BMI of less than 13 kg/m^2 has been proposed as a cutoff point for a poor prognosis [12]. Another paper showed that the relative risk of infection is 11.6 times greater for patients with BMI<12 kg/m^2 [13]. Recently, we reported BMI of 13-14 kg/m^2 to be the boundary at which body composition changes significantly and that BMI and FFM and FM had a curvilinear relation at the time of hospitalization[14]. In this study, FFM was more closely associated than FM with urgent hospitalization. It is interesting that FFM, which represents muscle and internal organ tissue, is more closely related to urgent hospitalization than FM, which represents energy storage. In addition, there were no cases of FM decreasing to 2.0 kg or less, even if the weight was extremely decreased. FM may play some kind of role as a life support.

Table 2 Association between BMI and urgent hospitalization by Repeated measures ANOVA for matched pairs.

Drive	df	F value	Pr>F
Urgent hospitalization	1	17.87	<0.0001
Time	2	31.46	<0.0001
Urgent hospitalization X time	2	11.36	<0.0001

BMI: body mass index ANOVA: analysis of variance df: degree of freedom

When BMI is 13-14 m/kg^2 or more, the body uses fat as energy under conditions of starvation. When BMI is lower than 13-14 m/kg^2, the supply of energy is converted from fat mass to protein. 1 g of fat mass (9 kcal/g) has about twice the calories of protein (4 kcal/g). It is speculated that the speed of BMI reduction increases with the same caloric output if BMI becomes low (<13-14 kg/m^2). For the causes of disturbance of consciousness, hypoglycemia and abnormality of the cardiovascular and peripheral vascular systems are suggested[15]. For gait disturbance, reduction of muscle mass, abnormality of metabolic systems, including electrolyte imbalance and dehydration, are suggested[16]. The hypoglycemia of AN patients is generally mild, and it rarely reaches hypoglycemic coma [17]. It is suggested that it is counteracted by the secretion of counter hormones such as adrenocorticotropic hormone(ACTH) or growth hormone(GH)[17]. In a state of starvation, the muscle tissue becomes an important resource for glycogenesis. From these facts, the following are suggested. Values for BMI of 13 m/kg^2, FFM of 30 kg, and FM of 3.0 kg may indicate the turning point of the failure of the homeostasis mechanism in the starvation state and be the stage before the development of a serious physical crisis.

BMI alone on the first consultation day is not sufficient to adequately determine the physical situation of

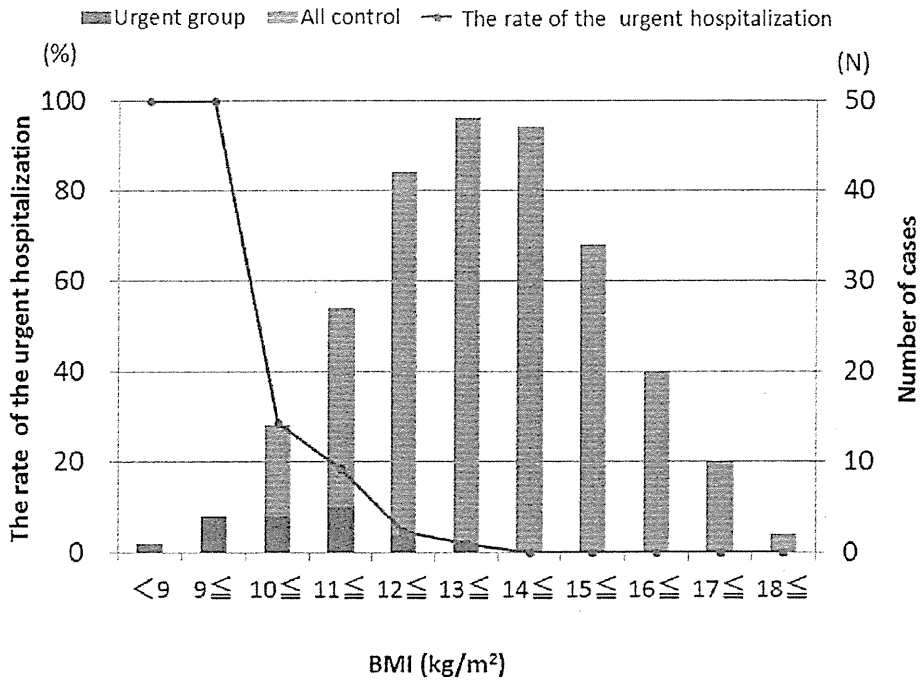

Figure 4 The rate of urgent hospitalization, by BMI. The bar graph shows the number of patients of each group. The line graph indicates the number of urgent hospitalizations by BMI. BMI: Body mass index.

AN patients. However, temperature or blood pressure used as guidelines for the necessity of urgent hospitalization fluctuate intensely along with changes in the physical state, making them difficult to use as a predictors. We suggest that the pattern of BMI (Figure 4) and FFM (Figure 5b) are more predictive and easy to use than the above mentioned factors, and their use will contribute not only to the welfare of patients but also to medical economy by preventing physically severe onset at the primary care stage. The definition of the urgent group

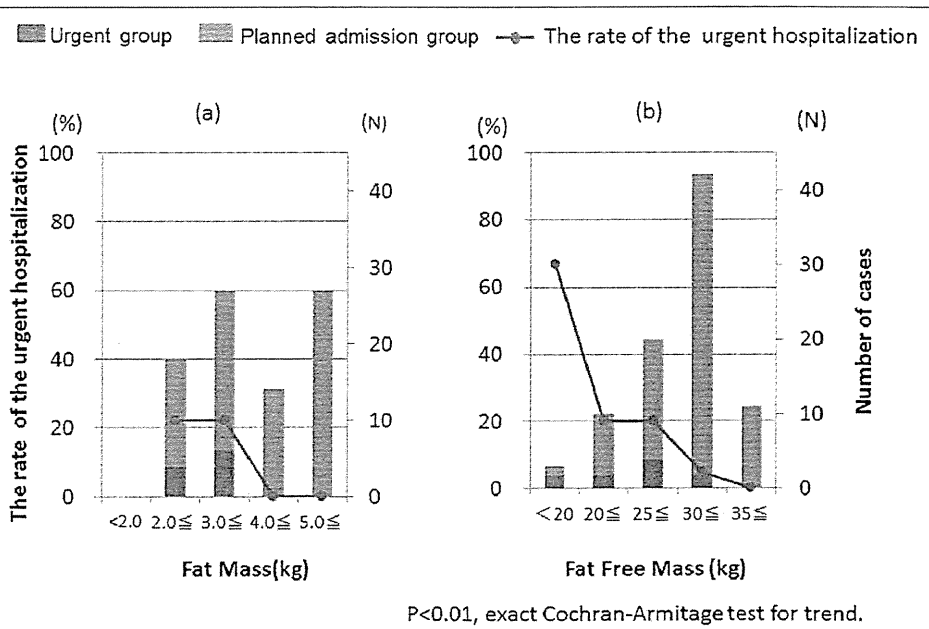

Figure 5 The rate of urgent hospitalization, by FM and FFM. The bar graph shows the number of patients of each group: FM (a) and FFM (b). The line graph indicates the number of urgent hospitalizations: FM(a) and FFM (b). FM; fat mass FFM: fat free mass.

was done strictly, as described in methods. It is possible that the data in study 2 would have been more accurate if the data of 16 hospitalized participants who were placed in the planned admission group were instead added to the urgent group.

Most social background factors showed no between group differences. Although age was not different, the percentage who were married was high in the urgent hospitalization group. The above suggests that the decision as to the need for urgent hospitalization was made mainly by physical factors, with very little contribution of factors related to social background.

From the aspects of psychosocial and genetic background, we cannot determine the factors responsible for the differences between the urgent admission and control groups in this study. There is undoubtedly a genetic predisposition and a range of environmental risk factors in the pathogenesis of eating disorders [1,18]. Numerous factors related to the serious physical state of AN patients are included in their psychological evaluation, and the patient's psychological status tends to fluctuate in the early period of treatment. These factors are too complex to evaluate in this paper, so we have left them for future study. Virtually nothing is known about the individual causal processes involved or about how they interact and vary across the development and maintenance of the disorders[18]. It is known that starvation shrinks the brain and is associated with many psychological disturbances, such as rigidity, emotional deregulation, and social difficulties [1]. This vicious cycle might develop gradually into a weight decrease.

Limitations: This study applies data on patients who visited a hospital; thus, data on AN sufferers who did not visit a hospital are not included. Only hospitalized patients were included in the study of body composition. There was no change in the BMI before hospitalization between the outpatient and hospitalized groups. Therefore we substituted perspective by an evaluation of the hospitalized group in this assessment. There is a risk when using the data from a single institution. Comorbidity is the rule rather than the exception for patients with eating disorders[1]. The social background factors that were evaluated may not be complete. It will be necessary to consider the income of the family and the convenience of the access to the hospital in future study. It is important that we evaluate certain personality traits such as perfectionism, obsessive-compulsive tendencies, social withdrawal, and depression. An evaluation of comorbidites and the psychological severity are future themes.

In conclusion, the pattern of BMI change and FFM may be useful for understanding the physical severity in AN. More research is needed on the accurate prediction of a need for urgent hospitalization. However, this combination of BMI and FFM might be useful for clinicians to monitor to help them avoid urgent hospitalization of their AN patients.

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Authors' contributions

KK designed the study, collected the data, analysed the data, interpreted the results, and drafted the manuscript. SY participated in the design of the study, interpret the results and reviewed the manuscript. TY participated in the design of the study and performed the statistical analysis. MG, CM, TN, ST, TH,YY and MT helped the collection of data and interpret the results. SM, CK and NS participated in the coordination of the study and reviewed the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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神経性食欲不振症の栄養管理の注意点

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Keyward
神経性食欲不振症，入院治療，
栄養療法，低栄養状態

概念

神経性食欲不振症（以下，ANと略）の患者は心身両面から治療を行う必要がある．治療の過程で体重減少や電解質異常といった重篤な身体的異常も合併する疾患であるため，身体管理は重要な治療的因子である．また身体の状態が心理療法の効果に与える影響も大きい[1,2]．

イギリスのNational Institute for Clinical Excellenceの『NICE guideline』[3]，わが国では『神経性食欲不振症のプライマリケアのためのガイドライン2007』[4]，『摂食障害緊急患者治療マニュアル第2版　改訂版2010』[5]など，摂食障害の身体管理に対して活用できるガイドラインが近年，出版されている．

本稿では以下に神経性食欲不振症の病態，入院患者における急性期と急性期以降に分けた栄養管理について述べる．

神経性食欲不振症の栄養障害の病態

AN患者の入院時のBMI値と脂肪量および除脂肪量（筋肉・骨格・内臓・血液量など）を検討したわれわれの研究では，入院時BMI値と脂肪，除脂肪量の関連を検討してみると，それは非線形の関係にあり，その曲線はBMI 13～14 kg/m^{2}あたりを境に変化する傾向にあった（**図1**）[6]．入院時BMIが13～14 kg/m^{2}以下になると除脂肪量の減少が中心になる．言い換えればBMIが13～14 kg/m^{2}以下になると，貯蔵エネルギーとして蓄えられた脂肪が枯渇し，筋肉等の異化によって主にエネルギーが産生されると考えられる．実際にBMIが13～14 kg/m^{2}以下になると身体的要因での緊急入院の比率は，通常入院に比べて上昇した（**図2**）[4]．

神経性食欲不振症で認められる主な身体症状と検査所見

主要症状として，やせはもとより，その二次的な反応として，下肢の浮腫，便秘，徐脈，低体温，低血圧，肝機能障害，骨粗鬆症など種々の身体異常をきたす．

低栄養状態の評価は血液所見のみで評価せず，総合所見で判断することが大事である．

入院時に必要な検査項目を以下に示す[2]．

- 身長・体重の正確な測定
- 皮膚や粘膜の状況，う歯の確認

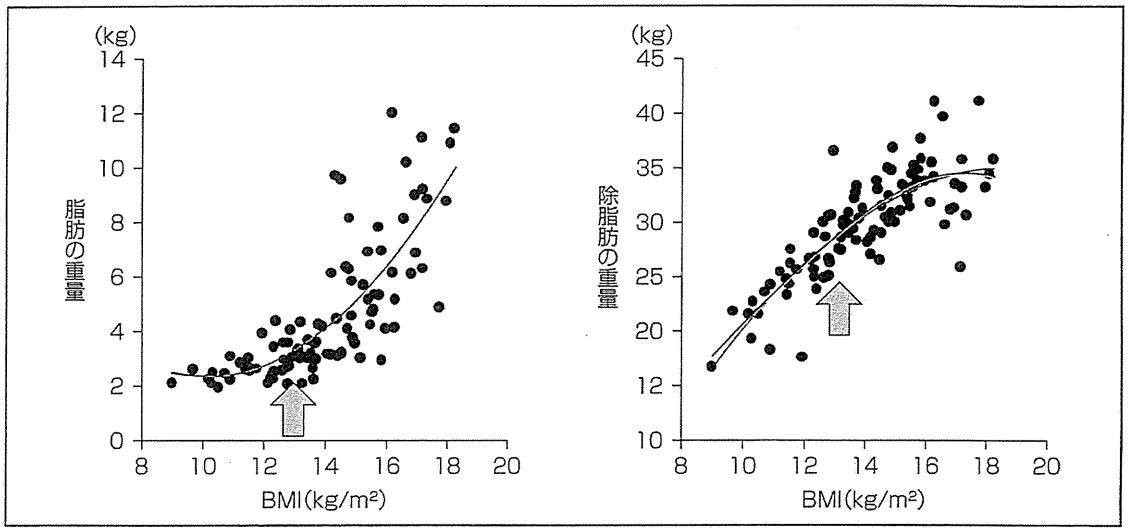

図1　入院時 BMI と脂肪，除脂肪の関係（n＝97）（文献[6]）

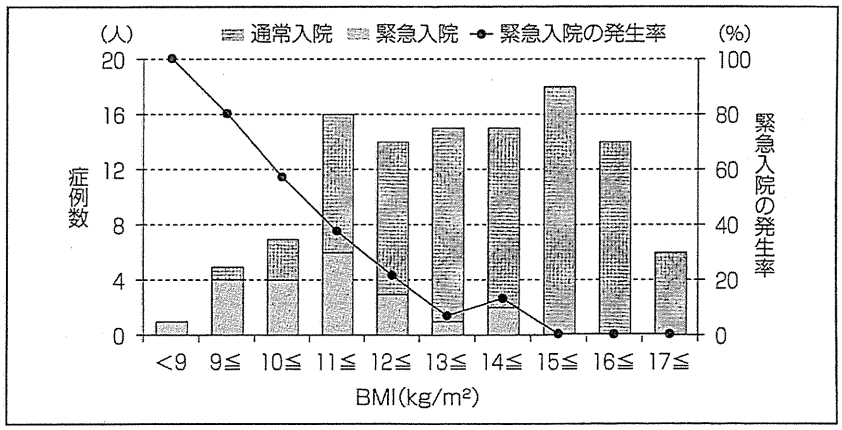

図2　BMI 別の緊急入院の発生率

2003～2006 年までに九州大学心療内科に入院した AN 患者のデータ（文献[4]）．
棒グラフは，症例数，折れ線グラフは発生率を示す．

- 起立性低血圧の有無，筋力の測定（蹲踞からの立ち上がり）
- 尿量測定を含む尿検査，便潜血
- 血算，一般生化学（カルシウム，マグネシウム，リンを含める）甲状腺機能検査
- 胸腹部単純 X 線，心電図検査，心エコー検査・頭部 CT 検査，骨密度測定

筋力低下の簡便な検査として当科では蹲踞からの立ち上がりの可否を導入し，不可の場合は入院の指標の一つにしている．重症度の評価ポイントとその注意点を**表**に示す．

治療

低体重で緊急入院した神経性食欲不振症患者の急性期の栄養管理

- **1 号液・乳酸リンゲル液**から開始．尿量や

表　神経性食欲不振症の低栄養の評価ポイントと注意点

- 重症度の判断：ただちに対処すべきものとして，意識障害・歩行困難，血圧の低下・不整脈をともなう心機能低下・電解質異常・低血糖・白血球減少・貧血・血小板減少などがある．
- 脱水のため，血中ヘモグロビン値，総蛋白値，アルブミン値がみかけ上，高値を呈することが多い．
- 体重や皮膚所見の重症度に比べて，こられの数値がよくみえる場合は脱水の関与を疑う．

電解質をチェックしながら3号液に切り替える．

- 低栄養状態にあった患者の摂取熱量が急激に増加する際には，refeeding症候群（別項目参照）に注意する．毎日，モニタリング（入院3日間は毎日採血，その後徐々に採血期間を延ばす）する．
- 治療初期より**微量元素の補充**を忘れない．ただし注射薬（ミネラリン®）は中心静脈栄養法でのみ保険適応のため，注意を要する．入院治療で，嘔吐と下剤乱用が止まれば，電解質異常（ナトリウム，カリウムなど）は改善するため，電解質の補正は最低限度でよい．
- かくれた下剤の使用や嘔吐を止めるための**心的同盟**を患者と結ぶことが大事である．

■低体重で緊急入院した神経性食欲不振症患者の急性期の栄養管理の実際（例）

- **入院時**，ラクテックG®など500 m*l*/6時間＋ビタメジン®（ビタミンB_1，B_6，B_{12}など）1バイアルを混注．低血糖がある場合は，側管から50%Glu 40 m*l*を投与．入院1日目，糖質は，1日100 g＝400 kcalを目安とする．
- **入院後24時間**に投与する総エネルギーは24時間で400～500 kcal，水分は，約1,000 m*l*，尿量400 m*l*を確保することが目安．最初の末梢輸液（500 m*l*/6時間）のあと維持輸

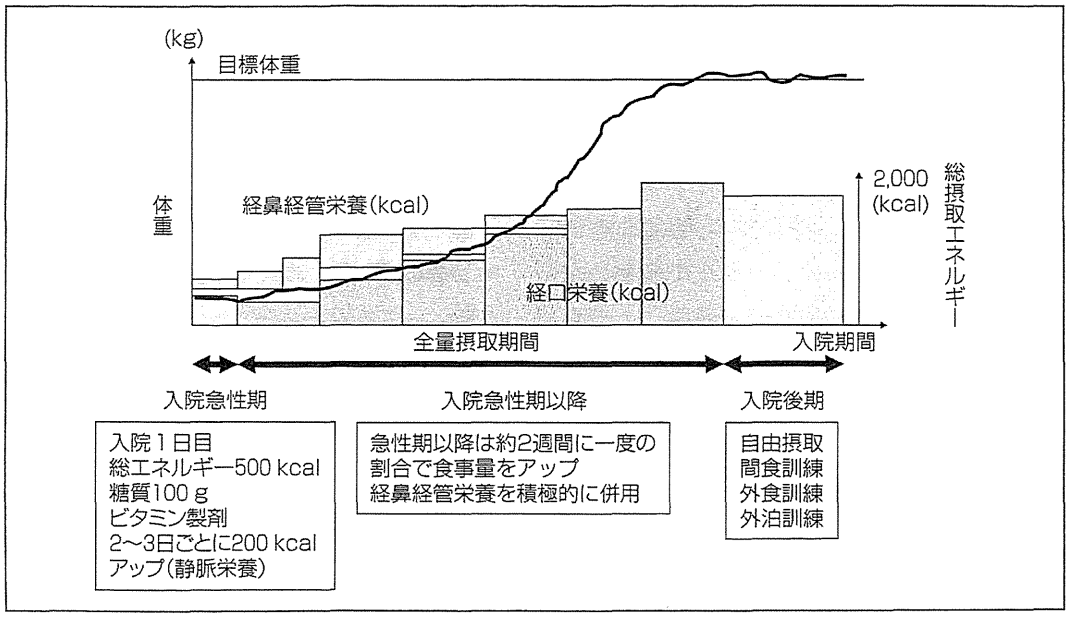

図3　神経性食欲不振症の栄養管理プログラム（九州大学心療内科）

液を500～1,000 m*l*/18時間.

- **その後，2～3日**ごとに総エネルギーを200 kcalずつアップする．急性期を乗り切るまで，総水分量は1日1,500 m*l*/日程度に留める．また，患者の不安（肥満恐怖）を増強しないよう慎重に増量する．
- ビーフリード®には糖質，アミノ酸，ビタミンB_1が含有されているため，3号液と併用することがある．
- 経口あるいは経鼻経管栄養によるビタミンの補給にはブイクレス®，さらにセレン，亜鉛などの微量元素とリンの補給には，アイソカル・アルジネード®の投与が簡便である．さらに，われわれは後述の微量元素が入った経腸栄養剤や栄養補助食品を入院初期より用いている．

■急性期以降の入院治療における栄養療法

症例により個体差があるが脱水，浮腫，電解質異常が改善するのに4日～1週間ほど必要なことが多い．これ以降は経口食や経鼻経管栄養を中心に行う．

経口摂取以外に経鼻経管栄養や経中心静脈高カロリー輸液（TPN）がある．当科では経口摂取に加え，積極的に経鼻経管栄養を併用している（**図3**）[2]．経口食の量は段階的に増量する．目標体重に達するまで食事の全量摂取を基本とした治療契約を結ぶことが多い[7]．経鼻経管栄養のメリットとして，他疾患での適応と同様に，TPNと比して，合併症が極めて少ないこと，患者が抜去してもすぐ挿入できること，腸管の細胞外液貯留の機能を利用できることなどがあげられる．患者によっては，当初，経鼻経管栄養に拒否感を示すことも多いが，治療者が，家族や患者に治療の必要性をねばり強く説明することが大事である[7]．また，認知行動療法の視点からは，経鼻経管栄養が嫌悪刺激となり経口摂取量を促す効果をもたせることも可能である．TPNの適応として，急性膵炎，DIC，refeeding症候群の合併や強い嘔吐反射（恐怖）の患者などがある．やせの程度が強くなると脂肪のみならず，筋肉量も減少，さらに消化吸収能力にも変化があるため，健常人とは体重増加に必要なエネルギーは異なると考えられる．当院のデータでは入院開始から4カ月間における食行動違反が明らかではなかった症例の平均体重増加量は1週間で約500 gであり，その平均エネルギー摂取量は体重1 kgあたり約50 kcalであった[6]．

■当院における急性期以降の入院治療における栄養療法の実際（例）

- **体重増加**の速度は0.5～1 kg/週が目安．
- 微量元素を含んだ，経腸栄養剤としては，エンシュアH®（1.5 kcal/1 m*l*），経鼻経管栄養食品としては，テルミール2.0 α®（2 kcal/1 m*l*），リカバリーミニ®（1.6 kcal/1 m*l*）などがある．これらは1 m*l*あたりの熱量が高く使用しやすい．1日2回食後に投与することが多い．
- **下痢の予防**には，投与速度の確認（60 m*l*/時），グルタミン，ファイバー，オリゴ糖を含有するGFO®の投与，等張圧の経鼻経管栄養食品であるアイソカル®の使用，脂肪を含まないエレンタール®の使用を考慮する．
- セレン，亜鉛などの**微量元素**と**リン**の補給には，アイソカル・アルジネード®（100 kcal/125 m*l*）による補充が簡便である．

おわりに

神経性食欲不振症の治療では，心理的な治療に加えて日々の身体管理が重要である．致死的な身体異常もあるため，栄養学的な知識が必要である．

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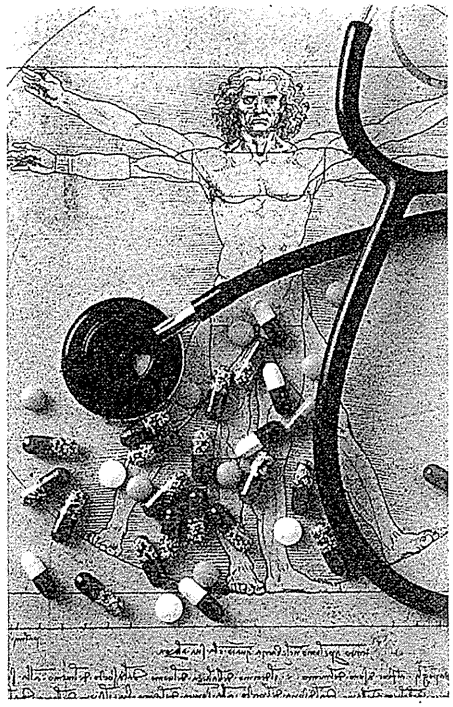
病気と薬 パーフェクトBOOK 2011

Perfect Book of Disease & Medicine



神経性食欲不振症 anorexia nervosa；AN

摂食障害は，持続する意図的な少食や下剤乱用，過食後の嘔吐などの行動異常によって特徴づけられる障害で，大きく神経性食欲不振症（anorexia nervosa；AN）と神経性大食症（bulimia nervosa；BN）に分類される．ANは，正常体重の最低限を維持することを拒否し，BNは基本的に標準体重の範疇にある．ここでは摂食障害の基本的病態であるANについて述べる．

ANの病型には制限型（小食）とむちゃ食い/排出型（やせを維持するための過食後の自己誘発性嘔吐や下剤・利尿薬の乱用）がある．病院を受診した摂食障害の患者数はこの5年間で3倍に増加し，女子大生を対象とした調査ではANの推定頻度は0.4%であった[1]．主に10～20歳代の女性に発症する．多くはその年代に特有の心理的ストレスに対処できないことを契機に発症する．やせ願望や体重増加に対する恐怖，自分の存在価値が体型および体重の影響を過剰に受けるなどの臨床像を認める[2]．

治療方針の要点

[精神症状や病的行動への薬物療法[2,3]]

- AN患者は，2次的にあるいは併存疾患による症状として，不安症，抑うつ，強迫性，衝動性などを伴っていることが多い．
- 不安症状には抗不安薬や抗うつ薬，抑うつや強迫症状には抗うつ薬，衝動性には非定型精神病薬などが用いられる．
- 非定型精神病薬のオランザピンは体重増加時の不安感や食行動異常の改善に効果があると報告されているが，日本では保険適応外である．

[無月経と骨粗鬆症の薬物治療指針]

GL 神経性食欲不振症のプライマリケアのためのガイドライン（2007年）[4]

- 無月経であっても，低栄養状態の悪化を防ぐために，低体重時には原則として女性ホルモン療法は行わない．しかし，標準体重の70%以上の無月経の場合は子宮の萎縮を予防するために，数ヵ月に1回程度月経を誘発してもよい．
- 骨密度の低下は低体重の程度と期間に依存するので，低栄養状態からの回復そのものが予防や治療となるが，低栄養が遷延する場合はカルシウムと活性型ビタミンD_3，あるいはビタミンK_2投与すれば，さらなる骨密度の低下を防ぐことができる．

治療計画を立てるまでに必要な情報と手順

症状・検査

1．成因[2]

やせを推奨する社会因子が背景にあり，完全主義・過剰適応などの性格や核家族・過保護などの家族因子が関与するといわれている．発症前はよい子でストレスに対する適切な対処が苦手なタイプが多い．患者は，「太っている」といわれ傷ついたり集団からの孤立などの挫折体験を直視することから回避してANとなる．その後，周囲からの賞賛や周囲を振り回すという代償・万能感に加え，低栄養状態も関与した認知のゆがみが絡み合い症状が持続する．

2. 予後[3]

長期予後の死亡率は5%前後で，それらは飢餓による身体的合併症（心血管性が多い）か自殺が多い．

3. 症状・検査

①症状：やせや低栄養が原因の無月経はもちろんであるが，徐脈，低血圧，骨粗鬆症，うぶ毛の増加，便秘症，下肢の浮腫などが認められる[4]．

初診時に必要な検査は，身長・体重の正確な測定，皮膚や粘膜の状況，起立性低血圧の有無，筋力の測定（蹲踞からの立ち上がり），う歯の確認，尿量測定を含む尿検査，便潜血，血算，一般生化学（Ca，Mg，Pを含む），甲状腺機能検査，胸腹部単純X線，心電図検査，心エコー検査，頭部CT検査，骨密度測定などである．

②検査：検査値では，低栄養・食行動異常による肝機能障害，脱水，代謝性アルカローシス，血清K値低下．無月経（FSHは低下か正常範囲・LHは低下）や甲状腺ホルモン値低下（トリヨードチロニン：T_3が低下しreverseT_3が上昇）などが認められる．これらの異常で内科や婦人科を受診することも多い．

診断

表1に米国精神医学会の診断基準（DSM-Ⅳ-TR）を示す．

・鑑別診断：機能性ディスペプシア，吸収不良症候群，腸管狭窄症，炎症性腸疾患などの胃腸管疾患，慢性膵炎，脳腫瘍，各種悪性腫瘍，結核，糖尿病，膠原病，統合失調症，甲状腺機能亢進症など．

治療

1. 治療における薬物療法の位置づけ

AN治療は心身両面から治療を行う必要がある．治療方針を決めるにあたって重要なのは，栄養状態や精神状態の評価である．とくに，体重を指標とした栄養状態の評価は重要である．標準体重の65%未満は，重症と判断する．心理面の治療は，身体的療法と併行して行う．低栄養の是正は心理療法を有効に進めるうえでも不可欠である．AN患者における薬物療法の有効性は乏しい．安易に薬物を使用することは，むしろ危険である．対症療法的な薬物の使用と2次的に発生する身体疾患の薬

表1　神経性食欲不振症　（米国精神医学会　DSM-Ⅳ-TRによる診断基準）

A. 年齢と身長に対する正常体重の最低限，またはそれ以上を維持することの拒否（例：期待される体重の85%以下の体重が続くような体重減少／または成長期間中に期待される体重増加がなく，期待される体重の85%以下になる）．	
B. 体重が不足している場合でも，体重が増えること，または肥満することに対する強い恐怖．	
C. 自分の体の重さまたは体型を感じる感じ方の障害：自己評価に対する体重や体型の過剰な影響，または現在の低体重の重大さの否認．	
D. 初潮後の女性の場合は，無月経，つまり，月経周期が連続して少なくとも3回欠如（エストロゲンなどのホルモン投与後にのみ月経が起きている場合，その女性は無月経とみなされる）．	
病型を特定せよ	
制限型	現在の神経性食欲不振症のエピソード期間中，患者は規則的にむちゃ喰い，または排出行動（つまり，自己誘発性嘔吐，または下剤，利尿薬または浣腸の誤った使用）を行ったことがない．
むちゃ喰い／排泄型	現在の神経性食欲不振症のエピソード期間中，患者は規則的にむちゃ喰いまたは排出行動（つまり，自己誘発性嘔吐，または下剤，利尿薬または浣腸の誤った使用）を行ったことがある．

物治療が推奨されている．

①身体的治療（栄養療法[2]を含む）：低栄養で緊急入院した場合は，脱水の改善とエネルギー補充のために輸液をすることが多い．1日の液量は1,000mL程度，糖質は100gが適切で，ビタミンB_1も併用する．体重増加が不良の場合には経管栄養法や経静脈栄養法を併用する．

急速な栄養補給は，低リン血症・低カリウム血症・肝機能障害など（refeeding症候群）が起こり得るので危険である．入院では，通常1日1,000kcalぐらいの少量からはじめる．

急性期を乗り切れば，患者が肥満恐怖を乗り越えられるようサポートしながら，急がず焦らず対応していく．

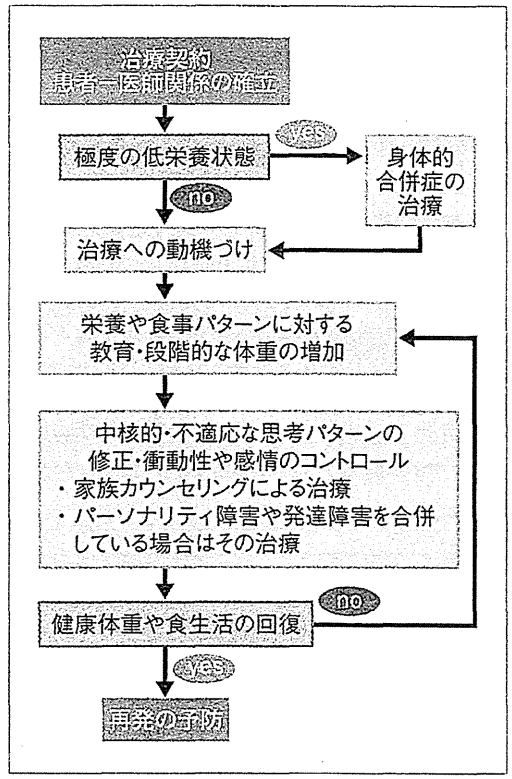


図1　治療のアルゴリズム

②心理的治療[2]：一般的な対応として，①治療同盟の形成と維持が大事である「体がきついのは治したいが，体重が増加するのは嫌」という一見相反する心理機制に理解を示す，②やせた状態が身体に及ぼす悪影響についての教育，③家族と情報交換，④ストレスを適切に処理する能力を身につけるよう指導，⑤食行動や体型の話題だけではなく，本人が本来抱えている問題「対人関係がうまくいかない」，「自信がない」などが面接の場に出てくるようにすることが大事である．

中～重症例は，専門施設で治療が行われることが多く，看護師，臨床心理士などのコメディカルスタッフとの協力体制を組みながら，認知行動療法，家族療法，精神分析的精神療法などが，患者の病態や治療者・治療施設の特性にあわせて行われている．図1に認知行動療法を基本にした治療のアルゴリズムを示す．

③薬物療法：ANは，生物学的異常に加え，病状の発症や持続に心理的因子や環境因子の関与が大きく，特異的に有効な薬物はない．薬物については，摂食障害に精通している精神科・心療内科医が処方するべきである．長年の食行動異常や低栄養による2次的な身体合併症への治療や，気分不安定に対す対症療法が中心である．食欲不振に対して，消化管運動改善薬は一般的に無効である．刺激性下剤は，乱用する危険がある．心機能に影響がある三環系抗うつ薬や抗精神病薬は使用を控えるべきである．

2．薬物療法のエビデンス

ANは精神症状に加え，重篤な身体症状をきたすため，無作為二重盲検法を用いた治療研究が進んでいない．抗うつ薬の一種であるセロトニン再取り込み阻害薬（selective serotonin reuptake inhibitors；SSRI）のプロザック®（わが国では未認可）は，体重の回復したANの再発率を減少させるという報告がある．しかし，大規模研究でその可能性は減じられた．ANの再発率の減少について，ほかのSSRIの有効性は乏しい．