An Investigation of Factors Influencing Late-onset Anorexia Nervosa:
Comparison with Early onset and Peak onset

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Summary  Anorexia nervosa (AN) easily becomes a chronic disease. Many studies pointed out the relationship between patients with late onset and their poor prognosis. The objective of our study was to discuss the clinical features of late onset AN and its comorbidity with physical and mental disorders.
Subjects consisted of 130 AN patients who were admitted to the Department of psychosomatic medicine of Toho University Hospital as outpatients. Based on the medical records, ten items were examined: age; age at onset; duration from onset until the first visit; type of disorder; body mass index (BMI) at the first visit; BMI max-min; depression level at the first visit; and percentage and details of comorbid physical and mental disorders. These 10 factors were compared among the three groups: early onset group (below 15 years old), peak onset group (15 to 24 years old), and late onset group (25 years old and above). The late onset group had the lowest mean BMI at first visit, which was significantly lower than the peak onset group. Moreover, the late onset group had a significantly higher prevalence of comorbid physical and mental diseases compared with the peak onset group. These results suggested that the BMI and comorbidities were important factors in late onset anorexia nervosa.

Keywords: Anorexia Nervosa, Eating Disorder, Late Onset, Body Mass Index, Comorbidity

Introduction
Eating disorder is often found among young women in developed countries. It is sometimes called a culture-bound syndrome because a culture admiring beauty of thinness is said to be influenced young women. A report on Western countries found that the prevalence of anorexia nervosa (AN) is 0.3% and 0.8% for bulimia nervosa for school girls (12-21 years old). In recent years, there has been an increase in the prevalence of eating disorders in Asia and Africa as well.

AN becomes chronic easily. For example, according to reviews on its prognosis in Western countries, 10-year follow-up surveys showed that 73.2% of all the patients recovered, 8.5% recovered partially, 13.7% poorly recovered and 9.4% died. Surveys of 8.3 years on average in Japan showed that 51% of the patients recovered, 13% recovered partially, 15% poorly recovered,
11% died, which was similar to the findings of Western countries\textsuperscript{5}. These studies suggested that late onset for eating disorders was one of factors for the poor prognoses. Many studies have reported the relationship between late onset and poor prognosis\textsuperscript{6-8}. Thus, late onset AN may differ from peak onset AN in pathology\textsuperscript{9-10}. Joughin et al.\textsuperscript{11} compared late onset AN with peak onset AN and reported similarities in the age at menarche, duration from onset until the first visit for medical examination, and present weight and past minimum weight. On the other hand, Boast et al.\textsuperscript{12} compared peak onset AN with late onset AN and found that patients of late onset AN weighed significantly lower. Similarly, Matsumoto et al.\textsuperscript{13} compared early onset AN with late onset AN and showed that there were much more patients among late onset AN whose weight was extremely low and those who had purging behavior than early onset AN. However, there was no significant difference in present weight between the two AN groups. In addition, Kimura et al.\textsuperscript{14} compared peak onset AN with late onset AN and showed that the body mass index (BMI) of late onset AN patients was lower at first clinical visit and a negative correlation between age at onset and BMI at first visit. On the contrary, Abbate-Daga et al.\textsuperscript{15} reported there was no significant difference in weight and purging behavior between the late onset AN group and other groups and that the late onset AN group included more patients with disturbed personalities and higher body dissatisfaction. In this way, having a lower weight at the first visit and comorbid purging behavior are often considered as features of late onset AN, although findings regarding these factors have been inconsistent.

These inconsistencies may be due to differences between preceding studies in terms of the questionnaires used and survey methods. The most important problem, however, is that there are no clear definitions of early onset AN, late onset AN and peak onset AN, and the ages sampled differed between studies. For example, late onset AN could refer to an age at onset of 14 years old and above, 15 years old and above, 20 years old and above, 25 years old and above, or 30 years old and above. In fact, the control groups in Boast’s study\textsuperscript{12} consisted of 15 to 20 year olds with AN while that in Kimura’s study\textsuperscript{14} consisted of 15 to 24 year olds with AN. It is interesting that both studies had similar definitions of late onset AN (at least 25 years old) and found that late onset AN patients had lower weights.

AN has been associated with depression\textsuperscript{8}, although such findings were criticized for the lack of comparison regarding the mental conditions of AN patients\textsuperscript{16}. In addition, it has been indicated\textsuperscript{15} that elderly AN was often comorbid with physical diseases, but preceding studies have not adequately evaluated these aspects of AN.

The objective of our study is to discuss the clinical features of late onset AN and its comorbidity with physical and mental disorders. Following preceding studies, we had two control groups: early onset AN and peak onset AN.

**Method**

Subjects consisted of 130 AN patients who were admitted to the Department of psychosomatic medicine Toho University Hospital as outpatients from April 2004 to October 2010. All five male patients were excluded due to their small number, resulting in all subjects being women. Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV)\textsuperscript{17} criteria were used for diagnosis. Based on the medical records of appropriate 130 patients, ten items were examined: age; age at onset; duration from onset until the first visit; type of disorder; BMI at the
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Results

There were 189 patients with eating disorders in this study. Of them, 41 patients (21.7%) had bulimia nervosa, 18 (9.5%) had eating disorder not otherwise specified, and the remaining 130 patients (68.8%) had AN. Of the AN patients, 21 were early onset, 86 were peak onset, and 23 were late onset.

(1) Clinical characteristics by group

Clinical characteristics of the early onset, peak onset, and late onset groups are shown in Table 1. Late onset group had the oldest patients and early onset group had the youngest. There were significant differences in clinical characteristics between peak onset and late onset and between early onset and late onset.

The mean age at onset for the early onset group was 13.2 years and that for the late onset group was 31.4. There were significant differences among all groups for age at onset.

The mean duration from onset until first visit was 2.6 years for the early onset group, 3.3 years for the peak onset group and 3.2 years for the late onset group. There was no significant difference between groups for this factor although the early onset group had the shortest duration.

We found that 85.7% of the early onset group was diagnosed as the restricting type and that 71.0% of the peak onset group was diagnosed as the restricting type and that 74.0% of the late onset group was diagnosed as the restricting type. The late onset group had the lowest mean BMI at first visit, and this value was significantly lower than that of the peak onset group (p=0.032). There was no significant difference among the groups in terms of BMI (max-min) (p=0.80) and in terms of present BMI (p=0.07).

The late onset group had a mean SRQ-D-II score of 47.2, which was significantly higher compared with the other two groups (p=0.006).

first visit which was actually measured by a doctor or nurse, not the patient's declaration; the difference of the maximum BMI in the past and the minimum BMI after onset (BMI max-min); BMI at present which was actually measured by a doctor or a nurse; depression level at the first visit; and percentage and details of comorbid physical and mental disorders.

These 10 factors were compared among the three groups: early-onset group (below 15 years old), peak-onset group (15 to 24 years old) and late-onset group (25 years old and above). The criteria for age in this study were derived from those of Kimura et al.9 and Boast et al.10.

The Self-rating Questionnaire for Depression II (SRQ-D II) was used to evaluate depression. The SRQ-D II is a self-rated questionnaire made by Kuraoka et al. to screen for depression; its reliability and validity have been verified9. Higher scores on the SRQ-D II indicate severer depression tendencies. Physical and mental disorders at the first visit were thought as comorbidities. Past histories, illness associated with thinness, diseases which directly influenced the appetite were excluded.

Patients were given a written notification at the first visit informing them about the study, and written consent was obtained from participants. This study was approved by the Ethics Committee of Omori Hospital of Toho University Medical Center.

Statistics

A one-way analysis of variance was performed to determine differences between groups and significant differences were followed up with Bonferroni test. Chi-square test and Fisher's exact test were conducted to ascertain differences between groups in terms of comorbid diseases. SPSS version 19.0J (SPSS Japan, Tokyo, Japan) was used to perform all statistical analyses.
(2) Percentage and details of comorbidities

Physical and mental comorbidities were found in 19.2% (25/130) of the participants. In the early onset group, 23.8% had comorbidities: two cases of depression, a case of pervasive developmental disorder (PDD), a case of obsessive-compulsive disorder (OCD) and a case of chronic hepatitis. In the peak onset group, 10.5% had comorbidities: two cases of panic disorder, two cases of borderline personality disorder (BPD), two cases of schizophrenia, a case of depression, a case of chronic renal failure (CRF), and a case of type 1 diabetes. In the late onset group, 47.8% had comorbidities (significantly higher than the peak onset group, p=0.016): a case of alcoholism, three cases of depression, a case of OCD, two cases of PDD, two cases of CRF, a case of Crohn’s disease, and a case of malignancy (Table 2).

The late onset group had a significantly higher prevalence of comorbid physical and mental diseases compared with the peak onset group (p=0.019, p=0.016).

Table 1 Comparison of the clinical features and depression among the 3 groups of anorexia nervosa

<table>
<thead>
<tr>
<th></th>
<th>Early onset (n = 21)</th>
<th>Peak onset (n = 86)</th>
<th>Late onset (n = 23)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.3 ± 6.0</td>
<td>26.8 ± 7.1</td>
<td>39.5 ± 8.1</td>
<td>0.001†</td>
</tr>
<tr>
<td>Age at onset (years)</td>
<td>13.2 ± 1.6</td>
<td>18.4 ± 2.7</td>
<td>31.4 ± 6.0</td>
<td>0.001†</td>
</tr>
<tr>
<td>Duration from onset</td>
<td>2.6 ± 4.1</td>
<td>3.3 ± 4.7</td>
<td>3.2 ± 5.1</td>
<td>0.86†</td>
</tr>
<tr>
<td>until first visit (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtype</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restricting</td>
<td>18 (85.7%)</td>
<td>61 (71.0%)</td>
<td>17 (74.0%)</td>
<td>NS‡</td>
</tr>
<tr>
<td>Binge-eating/purging</td>
<td>3 (14.3%)</td>
<td>25 (30.1%)</td>
<td>6 (26.1%)</td>
<td></td>
</tr>
<tr>
<td>BMI at first visit</td>
<td>16.5 ± 5.1</td>
<td>16.1 ± 3.9</td>
<td>13.5 ± 2.7*</td>
<td>0.032†</td>
</tr>
<tr>
<td>BMI (max-min)</td>
<td>6.9 ± 3.5</td>
<td>7.1 ± 4.0</td>
<td>6.2 ± 2.4</td>
<td>0.80†</td>
</tr>
<tr>
<td>BMI at present</td>
<td>17.2 ± 3.0</td>
<td>16.7 ± 3.8</td>
<td>14.8 ± 2.9</td>
<td>0.07†</td>
</tr>
<tr>
<td>SRQD-II</td>
<td>33.3 ± 12.1</td>
<td>37.7 ± 11.7</td>
<td>47.2 ± 8.9</td>
<td>0.006†</td>
</tr>
</tbody>
</table>

NS, non-significant; BMI, body mass index; BMI (max-min), BMI (maximum-minimum); SRQD, self rating of questionnaire for depression
†: a one-way variance analysis, ‡: chi-square test
**p < 0.01 vs. peak onset (Bonferroni test); **p < 0.01 vs. early onset (Bonferroni test)
***p < 0.01 vs. peak onset (Bonferroni test); *, p < 0.05 vs. peak onset (Bonferroni test)

Discussion

The objective of this study is to clarify the relationship between clinical features and comorbidities related to physical and mental conditions of the late onset AN by comparing early onset and peak onset AN. According to our survey, there was no difference among the three groups regarding duration from onset until first visit, BMI (max-min) and BMI at present. The BMI at the first visit was significantly lower in the late onset group compared with the peak onset group. Our results correspond with those of Matsumoto et al.13 and Kimura et al.9. However, Matsumoto et al. compared AN in patients below 14 years old (early onset group in our study) with that in patients aged 14 and above (peak onset and late onset combined), which differed from the age brackets in our study. Similarly, Kimura et al. compared between only onset at 15 to 24 years old and onset at 25 years old and above, excluding onset at 14 years old and below, which is also different from our age brackets.

There were few reports of AN divided into
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Table 2  Comorbid diseases among the 3 groups of anorexia nervosa

<table>
<thead>
<tr>
<th></th>
<th>Early onset (n = 21)</th>
<th>Peak onset (n = 86)</th>
<th>Late onset (n = 23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of comorbidities; n (%)</td>
<td>5 (23.8)</td>
<td>9 (10.5)</td>
<td>11 (47.8)</td>
<td>0.016 † peak vs late</td>
</tr>
<tr>
<td>Physical diseases; n (%)</td>
<td>1 (4.8)</td>
<td>2 (2.3)</td>
<td>4 (17.4)</td>
<td>0.019 ‡ peak vs late</td>
</tr>
<tr>
<td>Chronic hepatitis 1</td>
<td>CRF 1</td>
<td>DM 1</td>
<td>Crohn’s disease 1</td>
<td>Malignancy 1</td>
</tr>
<tr>
<td>Psychological diseases; n (%)</td>
<td>4 (19.1)</td>
<td>7 (8.1)</td>
<td>7 (30.4)</td>
<td>0.016 ‡ peak vs late</td>
</tr>
<tr>
<td>MD 2</td>
<td>PD 2</td>
<td>MD 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDD 1</td>
<td>MD 1</td>
<td>OCD 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OCD 1</td>
<td>BPD 2</td>
<td>PDD 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia 2</td>
<td>Alcoholism 1</td>
<td></td>
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</tr>
</tbody>
</table>

MD: Major Depression, PDD: Pervasive developmental disorders, OCD: Obsessive-Compulsive Disorder, CRF: Chronic renal failure, DM: Diabetes mellitus, PD: Panic disorder, BPD: Borderline personality disorder  
† χ² test, ‡ Fisher’s exact test

three groups according to age at onset. Our survey, together with the study of Daga et al.14, is one of the first to examine AN patients dividing three groups according to age at onset. On the other hand, the results of Daga et al. differed from ours; the authors found no difference in BMI among the three groups at first visit. This might be because the authors defined late onset AN as onset at the age of 20 years old and above. In many studies, late onset AN was defined as onset at the age of 25 years old and above.10,13,15. Therefore, considering that the higher the age, the lower the BMI at first visit, the results of Daga et al. might have been similar to ours if they had used the latter definition of late onset AN.

Possible explanations for the lower BMI of the late onset group at first visit were as follows. Matsumoto et al.11 suggest that psychopathology such as anxiety and a desire for thinness repressed in adolescence could lead to drastic and rapid build-up of anxiety and rapidly promote the desire for thinness, which could explain the lower BMI of the late onset group at first visit. Substance abuse could also have played a role in the lower BMI of the late onset group at first visit. Though Matsumoto et al.11 demonstrated a high prevalence of substance abuse and self-induced vomiting in late-onset AN, our results showed that, although the late onset group had a higher prevalence of binge eating/purging (29.1%) compared to the other groups, the difference was not significant. Nevertheless, such purging behavior could have affected weight loss. In late onset group, the level of using substance abuse may have been higher than the other groups. We did not examine substance abuse; future studies should examine this factor.

Finally, comorbidities might have contributed to the BMI at first visit. In our study, the late onset group had a higher level of depression and a higher level of having comorbid physical and mental disorders at first visit. Although there are only a few reports on comorbid physical disorders associated with AN, Patton et al.19 reported that 63% of AN patients had some physical disorders and suggested that such physical disorders
would be a risk factor of AN. Boast et al.\textsuperscript{10} also indicated that physical disorders were more likely to precede AN, especially for late onset patients, of whom 44% had comorbidities; this was significantly higher than that of peak onset patients. Our survey also showed that the prevalence of comorbidities related to physical disorders was higher in the late onset group compared to the peak onset group. It was difficult to compare our result with previous studies because previous studies did not examine the details of the physical disorders. That the longer time had passed before the onset was thought to be one of the incidental reasons for many comorbidities among late onset AN. On the other hand, Boast and Patton suggested that preceding physical disorders were the risk factors for late onset AN. Being different from peak onset AN, late onset AN may be associated in some way with preceding physical disorders. Our results showed that only 17% of the late onset AN had physical complications. We thought that the lower percentage of comorbidities in our survey might have been affected by the exclusion of past history in early childhood, such as infantile asthma, and diseases or physical complications associated with thinness.

Previous studies found there were many cases of mental comorbidities in late onset AN patients\textsuperscript{6,10,20,21}. Similarly, our survey found that 39% of the late onset group had mental comorbidities, which was higher than that of the peak onset group. Boast et al.\textsuperscript{10} found that 44% of their late onset patients had mental comorbidities, which was similar to our results. The authors also found that, of all comorbid mental disorders, depression was the most common, which was similar to our result as well (the late onset group scored significantly higher on depression). Some physical and mental illness can lead to AN and weight loss. For example, patients who are predisposed to AN, such as a desire for thinness or phobia of obesity, may succumb to AN more easily and lose weight more drastically and easily.

Late onset\textsuperscript{6,8} and low weight\textsuperscript{22} were associated with a poorer prognosis. In late onset AN, all of the physical and/or mental comorbidities must be identified, and intensive treatment of the comorbidities was important, along with psychotherapy and cognitive behavioral therapy for AN. These interventions could improve the poor prognosis of late onset AN. This, together with our results, suggested that it was necessary to consider age at onset in clinical AN.

Limitations of this study

This study contains some limitations. First, there were only a few cases in each group because the participants were divided into three groups. Second, this survey is retrospective and medical history was obtained through interviews with patients. Therefore, the possibility of bias through the patients’ recall cannot be eliminated. Finally, a survey about the severity of eating disorder was not conducted and the relationship between age at onset and severity of eating disorder could not be examined. Thus, a prospective study on age at onset, comorbidities, and prognosis, are needed.

Conclusion

To clarify the features of late onset AN, we compared three groups: early onset, peak onset and late onset. We found that the BMI at first visit was lower in the late onset group compared to the peak onset group and that the prevalence of physical and mental comorbidities were higher in the late onset group than the peak onset group.

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

Authors' contributions: YA participated in the design of
the study and carried out the statistic analysis. MO participated in the design of the study. MM carried out the revising the manuscript. YH and KT participated in the design of the study. All authors read and approved the final manuscript.

References

遅発発症神経性食欲不振症の特徴について：
早期発症，ピーク発症との比較

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概要 神経性食欲不振症は慢性的に経過しやすい、多くの研究が予後の悪さと遅発発症との関係を指摘している。本研究の目的は比較的高齢で発症した神経性食欲不振症の臨床的な特徴と身体的または精神的な随伴疾患を明らかにすることである。対象は東邦大学心療内科外来に受診した神経性食欲不振症130名である。診療録の情報により、年齢、発症年齢、発症から初診までの期間、病型、初診時のbody mass index（BMI）、最大BMI-最低BMI、初診時のうつ状態、身体疾患および精神疾患の随伴率を調べた。これらの要因を早期発症群（15歳未満発症）、ピーク発症群（15歳以上24以下発症群）、遅発群（25歳以上発症）の3つの群で比較した。遅発群では、3つの群の中で初診時のBMIが最も低く、ピーク発症群と遅発群との間で有意差を認めた。さらに遅発群では、ピーク発症群よりも身体疾患および精神疾患の随伴率が有意に高かった。これらの結果より、遅発の神経性食欲不振症においてBMIと随伴疾患は重要な要素であることが示唆された。