Retrospective study of anorexia nervosa, reduced mortality and stable recovery rates

Summary

Objectives Anorexia nervosa is an eating disorder that combines malnutrition, amenorrhea, and distorted body image. To learn more about the course of this disease we undertook a retrospective study of girls diagnosed with anorexia nervosa in the Saint Etienne Endocrinology Department between 1979 and 2004.

Methods Patients were diagnosed according to DSMIV criteria. Data collected to complete the Morgan-Russell outcome assessment schedule included chronology of illness, patients' morphological features, anorexia type, treatment choice, patient's gynecological history, and social status.

Results The study included 206 cases. The average follow-up period was 8.3 ± 5.3 years. Defining recovery as stable BMI > 17.5 kg/m² for at least one year and resumption of normal menstruation, full recovery was observed in 55.8% and partial recovery in 25.7%, while 18.5% remained chronically ill. Early onset (i.e., during adolescence) was associated with good prognosis, and advanced emaciation and delayed or insufficient medical care with poor prognosis.

Conclusions The seriousness of this disease is due more to the incidence of cases that become chronic than to the mortality rate. Prediction of severity would be improved by taking into account underlying personality traits, such as addictive tendencies and depression.

A

orexia nervosa (AN) is defined as a trio of symptoms combining serious malnutrition, hormonal abnormalities with amenorrhea, and eating disorder. Management is often multidisciplinary, with medical exploration and treatment of malnutrition and psychiatric treatment. AN is fatal in a substantial percentage of young patients, mainly young women.

This retrospective follow-up study of a population of girls with AN had a twofold aim: to determine the percentage of girls who had full recovery, resumed normal menstruation, and became socially well adjusted (e.g., job, relationship), and to characterize factors that predict severity of AN. We considered only somatic characteristics.

Methods This retrospective study examined the population of girls and women hospitalized with AN between 1979 and 2002 in the endocrinology department at Saint-Etienne University Hospital and followed up through 2004. All patients met the DSM-IV criteria for anorexia nervosa. We used two criteria to define recovery: body mass index (BMI) > 17.5 kg/m² for at least one year, and resumption of spontaneous normal menstruation. The BMI cut-off point of 17.5 kg/m² was selected to fit within the WHO classification of (grade I) malnutrition and to meet DSM-IV criteria. A one-year period of stability defi-
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ORIGINAL ARTICLE

We classified patients into 3 outcome categories, following Morgan and Russell5: total recovery (R), combining a BMI above the threshold of malnutrition (that is, >17.5 kg/m²) and resumption of normal menstruation; improvement (I) as defined by satisfying one of the two criteria, and chronic disease (C), as fulfilling none. Based on these criteria, we separated the population into 2 groups: those who recovered fully, and the rest (that is, improved or chronically ill). Relapse was defined by a BMI < 17.5 kg/m² for at least 3 months, after recovery4.

QUESTIONNAIRE

Our diverse assessment instruments6,7 included a simplified version of Morgan and Russell’s inventory. The six components we used excluded educational level:
- disease chronology (dates of onset and recovery, progress or relapse, and date of management, which was used to assess time until treatment);
- patients’ morphologic characteristics (age, height, initial BMI before illness, lowest BMI during disease and during recovery);
- type of anorexia (restricting or bulimic);
- type of management (standard treatment involved an outpatient contract to regain 1 kg per month, followed by hospitalization in case of failure) considered the following criteria: date and type of first specialist appointment, duration of hospitalization, number of consultations, psychiatric follow-up, and any associated psychotropic treatment;
- gynecologic history: menstruation before disease (spontaneous periods, primary amenorrhea, periods while on combination estrogen-progestin birth control pills), date and type of resumption of normal menstruation (spontaneous periods, resumption of periods using combination pills, progestins alone, or LHRH pump, or spontaneous pregnancy); social, marital (unmarried, living with someone, marriage), and occupational (working, not working, student) status after disease.

DATA COLLECTION

One person spent three months collecting data from two sources: review of medical records and a telephone survey to obtain missing and follow-up data. The telephone calls, which lasted an average of 5 minutes, provided information about the patient’s weight over time and made it possible to assess relapse (the criteria for which were not stipulated during the interview). Patients who could not be reached by telephone were considered lost to follow-up.

STATISTICAL DATA ANALYSES

We used Statview® software for the statistical analysis. Differences between subgroup means were assessed with a t test for unmatched series and a $\chi^2$ test to compare nominal variables. A Kaplan Meyer survival curve showed the risk of relapse. A p-value < 0.05 was considered statistically significant.

Results

Figure 1 describes the subgroups.

Description of the total population

The initial cohort, based on the hospital’s anorexia nervosa registry, included 326 persons. After reviewing the medical records, we excluded 15 young women defined as consti-
We attempted to reach 311 former patients for the telephone survey. Six patients refused to participate (1.9%), and 87 could not be reached at the telephone number in their file and were considered lost to follow-up (28%). We had complete data for 218 subjects. The mean duration of follow-up was 8.3 ± 5.3 years. Age at disease onset averaged 18 years (range: 9-41), and mean trough BMI 14.5 kg/m² (8.9-17.4). Overall, 172 patients (78.9%) maintained a BMI > 17.5 kg/m² for at least 1 year, while 46 (21.1%) never reached a BMI that high or maintained it for less than a year. Normal menstruation resumed for 120 patients (55%), either as resumption of spontaneous menstrual periods (98.3%), or as spontaneous pregnancy (1.7%), while 86 (39.4%) did not resume spontaneous hormonal activity (table 1). Excluding the 12 patients who took combination birth control pill before, during, or after disease (5%) raises the proportion who achieved resumption of normal hormone function from 55 to 58.3%. Combining the two recovery criteria (BMI > 17.5 kg/m² for at least a year and resumption of menstruation), 115 patients (52.8 %) recovered fully (table 2) and 53 (24.3%) improved, meeting only one of the criteria. Finally, 38 patients (17.4%) did not recover according to either criterion. Again excluding the 12 patients (5.5%) on combination birth control pills (cohort studied = 206), we observed a full recovery rate of 55.8%, an improvement rate of 25.7%, and a chronic illness rate of 18.5%. Five patients (2.3%) regained normal hormonal function despite a BMI < 17.5 kg/m². After they regained some weight, we classified them as constitutionally thin, because their periods returned despite their continued thinness. This new classification was not well defined at the time of Morgan and Russell. The overall recovery rate thus rose from 55.8 to 58.1%. Of 218 patients, 4 (1.8%) died, 3 directly of AN.

**RESULTS FOR THE POPULATION OF RECOVERED PATIENTS**

These patients returned to a BMI > 17.5 kg/m² for at least 1 year and achieved normal spontaneous menstruation. For this group, the mean duration of anorexic body weight was 2.4 ± 2.3 years (2 months-12.8 years), and the mean duration of amenorrhea was 3.5 ± 2.7 years (3 months- 16.8 years). Mean BMI at resumption of menstruation was 19.5 kg/m² ± 1.7 (16-24.8), thus within 0.7 ± 0.8 kg/m² of their mean normal BMI before the disease. During the study, we noted 23 cases of relapse; that is, 20% of the patients who had been considered cured (figure 2). The specifics of relapse varied: 8 had a recurrence of restricting anorexia and 15 of bulimic anorexia. The mean duration of recovery without relapse was 2.3 ± 2.0 years (1 month-9.5 years).

### Table 1

**Description of the population that did not spontaneously resume normal menstruation (including those who resumed menstruation with a birth control pill)**

<table>
<thead>
<tr>
<th>Hormonal characteristics</th>
<th>Number of patients</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amenorrhea</td>
<td>49</td>
<td>57.0</td>
</tr>
<tr>
<td>Resumed menstruation with combination birth control pills</td>
<td>22</td>
<td>25.5</td>
</tr>
<tr>
<td>Resumed menstruation with progestin-only pills</td>
<td>10</td>
<td>11.6</td>
</tr>
<tr>
<td>Resumed menstruation with LH-RH pump</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>Pregnancy during LHRH pump</td>
<td>4</td>
<td>4.7</td>
</tr>
</tbody>
</table>

### Table 2

**Outcome of anorexia nervosa according to recovery criteria**

<table>
<thead>
<tr>
<th>BMI &gt; 17.5 kg/m²</th>
<th>BMI &lt; 17.5 kg/m²</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resumption normal menstruation</td>
<td>115 (52.8%) (R)</td>
<td>5 (2.3%) (I)</td>
</tr>
<tr>
<td>No resumption of normal menstruation</td>
<td>48 (22%) (I)</td>
<td>38 (17.4%) (C)</td>
</tr>
<tr>
<td>Normal menstruation not determinable with estrogen-progestin</td>
<td>9 (4.1%)</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>172 (78.9%)</td>
<td>46 (21.1%)</td>
</tr>
</tbody>
</table>

**Figure 2** Kinetics of relapses in the population of recovered patients; 80% of the relapses took place during the first 3 years after recovery.
COMPARISON OF RECOVERED AND NON-RECOVERED SUBPOPULATIONS

These two populations did not differ significantly in terms of psychiatric follow-up, psychotropic medication, type of management, inpatient versus outpatient status, type of AN, occupational status, or duration of hospitalization. They differed significantly for four characteristics:

- **age at onset of disease**: patients who recovered were an average of 1.9 years younger at disease onset than those who did not (17.1±3.8 years versus 19.0 ± 5.3 years, p < 0.037);
- **time until treatment**: on average 15.6 months less for the patients who recovered (18.0 ± 31.2 months versus 31.6 ± 48.0 months, p < 0.004);
- **trough BMI**: the mean was 0.9 kg/m² higher in the group that recovered (14.9 ± 1.7 kg/m² versus 14.0 ± 1.9 kg/m², p < 0.0013);
- **number of consultations**: on average, two more in the group that recovered (6.2 ± 5.3 versus 4.1 ± 4.3, p < 0.022).

COMPARISON OF THE POPULATION CONTACTED BY TELEPHONE WITH THOSE LOST TO FOLLOW-UP

The group lost to follow-up (patients whom we could not reach by telephone) accounted for 28% of the initial population. It did not differ significantly from the population followed for any of the following criteria: age at onset, BMI before AN or trough BMI, time until treatment, or age at initiation of treatment.

Discussion

AN is recognized as a serious disease. Mortality may appear low in this study (1.8%) compared with data from the literature (table 3), which nonetheless vary quite substantially. In his review, Steinhausen mentions a standardized mortality rate for AN ranging from 1.36 to 17.8% according to a study and points out that it is highest in the first year, because of acute malnutrition, and after 15 years, from complications of chronic malnutrition. A retrospective study covering 63 years, published in 2003, found survival in a population of AN patients to be similar to that of a control population representative of the general population. Iacovino suggests, as did Steinhausen, that bias in current studies of mortality overestimates the number of deaths attributed to this disease. Fisher reports that mortality diminished during the 1970s because of better management.

Finally, it appears important to detect and treat comorbidity factors (such as alcohol, depression and anxiety) in order to improve positive outcome rates. Active management of AN is justified by its potential for causing death in young people.

Except for mortality, the results of our follow-up are similar to those from the literature (table 3). Several authors who have published follow-up studies consider uncurred patients to represent a chronic form of this disease. Characteristics affecting disease course can be divided into two groups. Early onset during adolescence is associated with a good prognosis, although the converse is true for onset before puberty. Criteria for poor prognosis include a low trough BMI, a long delay until treatment, and a relatively low number of consultations. Some of these data are found in the literature. The role of trough BMI remains controversial. We note that purging or vomiting, usually considered a poor prognostic factor, did not appear here. This may be related to the type of interview (telephone), which does not encourage people to discuss difficult topics.

### Table 3

**Outcome of anorexia nervosa applied to recent data from the literature**

<table>
<thead>
<tr>
<th>Author</th>
<th>Date of publication</th>
<th>Type of document</th>
<th>Number of patients per study</th>
<th>Recovered (%)</th>
<th>Improved (%)</th>
<th>Chronic illness (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. Fisher</td>
<td>February 2003</td>
<td>Literature review (100 studies)</td>
<td>nd</td>
<td>45.5</td>
<td>33.5</td>
<td>19.8</td>
<td>2-8</td>
</tr>
<tr>
<td>H.C. Steinhausen</td>
<td>August 2002</td>
<td>Literature review (119 studies)</td>
<td>6 - 151</td>
<td>46.9</td>
<td>33.5</td>
<td>20.8</td>
<td>5</td>
</tr>
<tr>
<td>B. Lowe et al.</td>
<td>July 2001</td>
<td>Article (prospective study)</td>
<td>84</td>
<td>51</td>
<td>21</td>
<td>10 + 16 (deaths)</td>
<td>16</td>
</tr>
</tbody>
</table>

*nd: results not available.

**Sources:**
Patients regained normal hormone function at a BMI of approximately 20 kg/m². Our study is the first to report this figure and its correlation with pre-disease stable BMI (within 0.7 kg/m²). This stable weight is a primary objective to be set at the beginning of treatment. It would be interesting to complement these weight data by various tests to improve our understanding of the components of the restoration of hormonal activity. Use of impedance measurements, for example, would make it possible to measure both body fat and hydration levels, which often distort real weight in AN. We know that body fat, acting through leptin secretion, plays a role in the regulation of food intake and in gonadotropin production. It seems clear that weight alone is insufficient to explain the resumption of menstruation and that body composition plays a role.

Only 20% of the patients in our study had relapses, although Carter et al. observed a rate of 35% in a prospective study. This difference is explained by our definition of recovery, which included a BMI > 17.5 kg/m² for at least one year. According to Carter et al. and our results (figure 2), relapses are especially frequent in the first 3 years. Authors have recommended multidisciplinary management combining psychotherapy, psychotropic medication, and treatment of the malnutrition. Hospitalization remains controversial. Some claim it increases the likelihood that the disease will become chronic. This argument can be refuted in view of the current management guidelines, because only patients for whom outpatient treatment is unsuccessful are hospitalized. It thus appears important to favor short hospitalizations and treatments and to reserve long hospitalization for chronic disease. Our results confirm the usefulness of early treatment, but do not provide information about types of treatment. This study uses retrospective methodology, the limitations of which are well known, especially the bias due to the variable rate of follow-up. Different authors propose different percentages to ensure reliability. Hsu et al. recommend less than 20% and Morgan and Russell less than 5%. Although our population of patients lost to follow-up was higher, these patients could not be distinguished from the population we could follow by any criterion (table 3).

This suggests that there is no selection bias but rather a random selection related to the type of interview used in this study. Consequently, elimination from the statistical analysis of the patients lost to follow-up has only a slight effect on the overall results, as Steinhausen reported in his literature review. Inversely, refusal to respond may be considered a defense mechanism related to non-recovery. The refusal rate in our study (1.9%) was too small to affect the results.

Anorexia nervosa is a disease whose severity depends more on its chronic nature than on its mortality. It appears that the number of deaths attributed to AN in the literature has been overestimated. Physicians treating patients with anorexia must bear in mind specific figures: approximately 50% recovery for the combined criteria, a mean duration of 3.5 years for recovery, resumption of menstruation associated with a BMI close to the pre-disease level.
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