The Clinical Significance of Amenorrhea as a Diagnostic Criterion for Anorexia Nervosa

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ABSTRACT

Objective: Amenorrhea is a DSM-IV criterion for the diagnosis of anorexia nervosa (AN). Several studies have reported few differences between patients who meet the full DSM-IV criteria for AN and those who meet all but the amenorrhea criterion. Although this suggests that the absence of menses does not provide critical diagnostic information, many of these studies are limited by small sample sizes. This study aims to examine the clinical utility of amenorrhea as a criterion for the diagnosis of AN.

Method: A chart review was conducted of 240 consecutive patients admitted for inpatient treatment at the NY State Psychiatric Institute from 1993 to 2006. Menstrual data were collected from the Eating Disorder Examination conducted upon admission. Independent samples *t*-tests were performed to evaluate differences in clinical variables, including age, lifetime lowest body mass index (BMI), admission and discharge BMI, previous number of hospitalizations, duration of

illness, Beck Depression Inventory total score, Beck Anxiety Inventory total score, and Eating Disorder Examination subscale scores.

Results: The amenorrheic and menstruating groups differed significantly only on lowest lifetime BMI and admission BMI, with individuals with amenorrhea having lower BMIs on both measures.

Conclusion: These results indicate that amenorrhea does not distinguish between groups on a number of important measures of clinical severity. It may be that amenorrhea reflects weight and nutritional status, rather than providing useful diagnostic information. Future studies are needed to examine the potential prognostic value of menstrual status. © 2008 by Wiley Periodicals, Inc.

Keywords: anorexia nervosa; amenorrhea; diagnosis

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With the fifth edition of the diagnostic and statistical manual of mental disorders[1] (DSM-V) on the horizon, the evolving diagnostic criteria for anorexia nervosa (AN) are being carefully considered. The suggested weight threshold and amenorrhea criteria have both been sources of debate for DSM-V.[2] Amenorrhea did not appear as a diagnostic criterion in the DSM-III,[3] but was observed frequently among individuals with AN. It also provides a clear and objective diagnostic criterion with important

medical significance. Amenorrhea is currently defined in the DSM-IV as "the absence of at least three consecutive menstrual cycles"[1] (p 589). In addition, DSM-IV explains that "a woman is considered to have amenorrhea if her periods occur only following hormone, e.g., estrogen, administration." Similarly, the international classification of diseases[4] (ICD-10) also includes the absence of menses as a diagnostic criterion, but does not provide parameters regarding duration of amenorrhea.

The DSM-IV is designed largely in part to guide clinicians towards making diagnoses in an effort to inform treatment decisions.[5] However, the requirement of amenorrhea as a criterion has yielded some clinical dilemmas. Some patients meet all the criteria for AN except for amenorrhea, giving them the diagnosis of Eating Disorder Not Otherwise Specified (EDNOS), yet there are no treatment guidelines for individuals with EDNOS. In addition, the diagnosis of EDNOS can result in the potential false sense that the severity of an individual's illness is less extreme and may make it difficult to obtain reimbursement for treatment from insurance companies. The amenorrhea criterion is also limited

since it cannot be applied to males with AN. Furthermore, it makes it difficult to categorize individuals using hormone replacements like oral contraceptives. Although research indicates that amenorrhea usually, but not always occurs following a reduction in body weight and body fat,[6–10] its utility in distinguishing individuals with AN from those without remains unclear.

Several studies reported few meaningful differences in demographics, disturbed eating behaviors, body image perceptions, illness history and psychiatric comorbidity between menstruating and non-menstruating patients, supporting the removal of the amenorrhea criterion.[11–15] Although the current evidence suggests that amenorrhea may not be clinically significant in differentiating individuals with all other features of AN, many of these studies are limited by small sample sizes. The current study looked specifically at clinically meaningful variables (e.g., demographic and psychological measures of illness severity) among individuals who meet all DSM-IV criteria for AN and those who meet all criteria except amenorrhea.

Method

The medical records of 240 inpatients consecutively admitted for treatment to the Eating Disorders Service of the New York State Psychiatric Institute from March 1993 to December 2006 were retrospectively reviewed. All patients provided informed consent for the use of physical and psychological assessment data for research purposes. An eating disorder diagnosis for each patient was established based on a clinical interview conducted by a staff psychiatrist or psychologist. Diagnostic criteria for AN, other than amenorrhea, were available and were verified with the Structured Clinical Interview for DSM-IV (SCID-I)[16] for 180 of the participants. Current menstrual activity was assessed via the Eating Disorder Examination (EDE) interview.[17] Menstrual history elicited on the admission EDE was confirmed against information obtained by a clinical admission interview or SCID-I or a phone screen form when this information was missing from either clinical interview. If a discrepancy in menstrual status between the EDE and the clinical interview was uncovered, the data were omitted. It was determined that a patient did not meet the amenorrhea criterion for the diagnosis of AN if she had any menstrual bleeding in the 3 months prior to hospital admission. If the information about menstrual function 3 months prior to hospitalization was missing from the EDE, then menstrual status was obtained from a clinical note. Patients who were taking oral contraceptives were excluded from the analysis as were patients who were not below 85% of

expected body weight based on mid-point for medium frame women, according to the Metropolitan Life actuarial tables.[18] In addition to menstrual status, we extracted data on the four subscales of the EDE, total scores on the Beck Depression Inventory (BDI) (versions 1 and 1A)[19] and the Beck Anxiety Inventory (BAI),[20] duration of illness, previous number of hospitalizations for the eating disorder and age. Height and weight data were obtained on admission and discharge from the hospital and self-reported lowest adult weight was also recorded. These were used to calculate body mass index (BMI) at each time point.

Statistical Analyses

All of the data were first examined for normality and variables that violated this assumption were transformed using a log transformation. Independent samples t-tests were then performed on normally distributed and transformed variables, but means for the non-transformed variables are reported. In an effort to control for an increase in the familywise error rate that accompanies multiple comparisons, significance was set at alpha less than 0.004 based on a Bonferroni correction. Effect sizes using Cohen's d were also calculated for each comparison. A chi square test was used to examine the relationship between menstrual status and AN-subtype (restricting versus binge-purge).

Results

There were 240 patients admitted for treatment of AN between 1993 and 2006. Forty-three patients were excluded from the analyses. Of the excluded patients, 17 patients were taking oral contraceptives, 13 patients had a discrepancy on menstrual status between the admission note and EDE, eight did not meet the weight threshold of less than or equal to 85% of ideal body weight based on the 1959 Metropolitan Life Insurance tables, three were males, and two were missing information about menstrual status. The final sample included 150 patients with amenorrhea and 47 patients who were menstruating at the time of hospital admission. Of those 47, 16 patients reported menstruating regularly in the 3 months prior to hospitalization, 15 reported having two periods, 13 reported having one period, one reported spotting, one reported some bleeding, though exact amount was unknown and one reported four menstrual periods over the course of 3 months. Five of the patients with amenorrhea and three of the menstruating patients were clinical admissions who were only eligible to participate in a research intake interview. While height and weight upon admission were

TABLE 1. Independent samples *t*-test results

	Amenorrhea			Menstruating						95% CI		Cohen's *d*
	N	Mean	SD	N	Mean	SD	t	df	P			
Age (years)	150	25.44	6.12	47	25.49	6.43	−0.005	195	0.996	−0.08	0.08	−0.01
Admission BMI[a] (kg/m^2)	150	14.91	1.89	47	16.44	1.19	−5.225	195	0.000	−2.11	−0.95	−0.97
Duration of illness (years)	149	8.09	5.99	46	8.25	6.09	−0.012	192	0.990	−0.28	0.27	−0.03
Lifetime lowest BMI[a] (kg/m^2)	144	14.00	1.79	46	15.09	1.63	−3.678	188	0.000	−1.68	−0.51	−0.64
No. previous hospitalizations	149	3.03	4.18	46	3.15	4.98	0.663	146	0.509	−0.21	0.41	−0.03
Discharge BMI (kg/m^2)	148	19.64	1.27	46	19.68	1.30	0.222	190	0.825	−0.11	0.13	−0.03
Beck Depression Inventory	144	26.36	13.42	42	24.18	11.57	0.955	184	0.341	−2.33	6.69	0.17
Beck Anxiety Inventory	102	18.56	13.24	30	21.82	12.90	−1.231	128	0.221	−0.60	0.14	−0.25
EDE												
Restraint	140	4.03	1.55	44	4.48	1.32	1.621	182	0.107	−0.03	0.32	−0.31
Eating	140	3.24	1.49	44	3.82	1.33	−2.320	182	0.021	−1.08	−0.09	−0.41
Shape	140	3.97	1.58	44	4.37	1.29	1.330	182	0.185	−0.06	0.29	−0.28
Weight	140	3.59	1.82	44	4.25	1.47	1.882	182	0.061	−0.01	0.39	−0.40

[a] Significant difference between amenorrheic and menstruating group at the *p* < 0.001 level.

recorded for all patients, **Table 1** indicates the number of participants with missing data for the other assessments.

The results from the independent samples *t*-tests indicate that the two groups differed significantly only on lowest lifetime BMI and admission BMI (see **Table 1**), with individuals with amenorrhea having lower BMIs on both measures. There was no significant difference in the number of hospitalizations, the duration of illness, or symptom severity. In the amenorrhea group, 72 individuals were binge/purge subtype and 78 were restricting subtype. In the menstruating group, 38 individuals were binge/purge subtype and nine were restricting subtype. A chi square analysis revealed a significant difference between group membership based on subtype, χ^2 (1) = 15.662, *p* < 0.001. In the menstruating group, the proportion of patients with restricting subtype was significantly smaller than in the amenorrheic group.

Conclusion

This retrospective analysis found that patients with all features of AN except amenorrhea did not differ from those with amenorrhea on most clinically important measures. No significant differences emerged on psychological variables that characterize AN including disturbed ideas about weight and shape, or affective symptoms. While not statistically significant in this analysis, individuals who were menstruating did have higher scores on the eating concerns subscale of the EDE (*p* = 0.021, *d* = −0.41), which is a difference in the opposite direction of what would be expected if menstruating signified less severe illness. This study did not find a difference in duration of illness or previous

number of hospitalizations between the two groups, indicating that these patients obtain similar amounts of intensive healthcare resources to treat their eating disorders. Furthermore, these patients did not differ in discharge BMI suggesting that amenorrhea may not be useful as a predictor of short-term treatment outcome. The fact that the larger proportion of individuals with menstrual activity are those with binge-purge sub-type may relate to factors associated with this sub-type, such as the possibility that these individuals are at higher weights because they may consume more calories through binge episodes.[21] Overall, the results suggest that amenorrhea may be a reflection of weight or nutritional status rather than a useful diagnostic criterion.

These findings are consistent with other reports. One study of a community-based sample examined 24 women meeting full criteria for AN and 44 meeting all criteria except for amenorrhea.[11] The authors reported that the groups did not differ significantly in age of onset, maximum and minimum weight, percent weight loss or bulimic behaviors. The menstruating group was reported to have higher rates of comorbidity and history of family problems. Cachelin et al.[12] also failed to uncover significant differences in disturbed eating, body image perceptions, and psychopathology among amenorrheic (*n* = 40) and menstruating (*n* = 12) women with AN. The authors did find that the non-amenorrheic group was significantly older and, as in the present study, weighed significantly more. Similarly, Gendall et al.[14] compared patients with a BMI of less than 17.5 who had amenorrhea (*n* = 16) to those without (*n* = 7) and found few meaningful differences between the groups. In their sample, amenorrheic patients were more likely to exercise, scored lower on novelty seeking and had

lower pulse rates and systolic blood pressure. A study by Abraham et al.[15] compared 90 inpatients with secondary amenorrhea to 19 with irregular periods, and 54 who had regular cycles, reporting that the best predictors of amenorrhea at admission were a current BMI less than or equal to 18.0 and having rules for exercising. However, the analyses included patients with AN or bulimia nervosa. Despite limitations, these studies consistently find that amenorrhea is related to low weight status, rather than reflecting a core feature of AN.

While not directly comparing patients with AN who are menstruating to those who are amenorrheic, Pinheiro et al.[22] conducted a retrospective review of data from 1,705 women with eating disorders including AN, BN, and EDNOS to compare menstrual status across these diagnostic groups. The authors found that menstruating participants had significantly higher values for highest and lowest lifetime BMI, greater binge and vomiting frequency, and more appetite suppressant use. Amenorrheic participants had the greatest caloric restriction and highest frequency of exercising and laxative use. The study did not reveal any significant differences in comorbid Axis I and II psychopathology. However, the normal menstruation group scored significantly lower on eating disorder rituals, personal standards, and harm avoidance, but higher on novelty seeking. The authors conclude that menstrual status does not discriminate between eating disorder diagnoses. Again, it appears that the majority of differences they uncovered are found in measures that reflect nutritional status (i.e. BMI, caloric intake, and exercise).

A study by Watson et al.[13] did find a small number of clinical differences based on menstrual status. They conducted a retrospective chart review of patients with full syndrome AN (n = 230) or EDNOS (n = 67) due to failure to meet either the weight or amenorrhea criteria. Within this sample, 28 individuals were menstruating and weighed less than 85% of ideal body weight. The authors reported that the menstruating group had a lower discharge percentage of expected body weight, shorter hospitalization and scored lower on the Eating Attitudes Test-26 and the Eating Disorder Inventory drive for thinness subscale than patients who were amenorrheic. Unlike the current study, the amennorheic and menstruating groups had comparable admission percentage of expected body weights. Importantly, though, they reported that the amenorrheic group and low-weight, menstruating group had comparable bone deficiency when measured on an age and gender matched bone mineral density test. Overall, the authors con-

cluded that the menstruating low-weight group was quite similar to the amenorrheic group.

The primary aim of this study was to compare patients with AN based on their menstrual status 3 months prior to inpatient hospital admission. We focused on this time period because it is the specified time frame identified in DSM-IV to consider when determining whether a patient's symptoms warrant a diagnosis of AN. However, while lifetime history of menstrual status is not taken into account when assessing a patient for a current diagnosis of AN, it is possible that individuals who have never experienced amenorrhea are distinct from individuals who may currently be menstruating, but have a history of amenorrhea. Therefore, we examined our sample of menstruating patients further by determining how many had a prior history of amenorrhea and how many had never experienced amenorrhea over the course of their lifetime. The results indicated that 28 of the menstruating patients had a history of amenorrhea, while only six of the patients had never experienced amenorrhea. In addition, five patients were missing this data and eight charts did not clearly specify the duration of past amenorrhea, making it difficult to classify those patients.

Although the number of menstruating women without a history of amenorrhea was very small, making it difficult to draw meaningful conclusions, we conducted two exploratory analyses. We performed t-tests to compare currently menstruating patients with and without a lifetime history of amenorrhea. The comparison revealed no significant differences. Finally, we compared the currently menstruating patients without a lifetime history of amenorrhea to those patients with current amenorrhea. Similar to our original analysis, none of these comparisons were significant except for admission BMI and lifetime lowest BMI [data not shown]. Although these findings do not completely rule out the possibility that the individuals who have never been ammenorrheic have a distinct psychopathology (given the small subgroup size), there is no suggestion that there are meaningful differences with respect to illness severity or treatment needs. However, future research with a larger sample size comparing individuals with AN who have never been amenorrheic and those who have a history of amenorrhea may be useful to better understand the importance of the amenorrhea criterion. In addition, it may also be useful to compare patients with and without amenorrhea who are matched for BMI.

The strength of the current study is the relatively large sample size, including a reasonable sample of both amenorrheic and menstruating individuals

with AN. As with all studies of amenorrhea in AN, the findings are limited by the self-report nature of menstrual status and clinical history (hospitalizations, lowest lifetime weight). However, the study is strengthened by the use of two interview measures (the SCID and EDE) as well as self-report assessments. In addition, the majority of patients in this study were participating in research, so it is possible that these findings differ from other clinical populations. No study to date has examined the predictive value of amenorrhea in long-term outcome. Nonetheless, taken together these findings suggest that presence of amenorrhea, while important in evaluating the health status of the patient, may not be a useful diagnostic criterion.

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