

# Early onset anorexia nervosa: Multidisciplinary hospital intervention in a 1-year follow-up study

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## Abstract

**Background:** Early onset anorexia nervosa (EOAN) is a subclassification of AN, defined by an onset before 14 years, and characterized by specific demographic, neuropsychological, and clinical features. The present study aims to provide naturalistic data on a wide sample with EOAN, focusing on psychopathological and nutritional changes occurring in the context of a multidisciplinary hospital intervention, as well as the rate of rehospitalizations during a 1-year follow-up.

**Method:** Observational, naturalistic study adopting standardized criteria for EOAN (onset before 14 years). EOAN were compared to adolescent-onset AN (AOAN) patients (onset after 14 years) by demographic, clinical, psycho and treatment variables. Psychopathology was assessed at admission (T0) and discharge (T1) with self-administered psychiatric scales for children and adolescents (SAFA) subtests for Eating Disorders, Anxiety, Depression, Somatic symptoms, and Obsessions. Then, potential differences of T0–T1 changes in psychopathological and nutritional variables were assessed. Finally, rates of re-hospitalizations at 1-year post-discharge follow-up were assessed with Kaplan–Meier analyses.

**Results:** Two-hundred thirty-eight AN individuals (EOAN = 85) were enrolled. When compared to AOAN, EOAN participants were more frequently males ( $X^2 = 5.360$ ,  $p = .021$ ), more frequently received nasogastric-tube feeding ( $X^2 = 10.313$ ,  $p = .001$ ), and risperidone ( $X^2 = 19.463$ ,  $p < .001$ ), obtained a greater T0–T1 improvement in body-mass index percentage ( $F[1.229] = 15.104$ ,  $p < .001$ ,  $\eta^2 = 0.030$ ), with higher 1-year freedom from re-hospitalization (hazard ratio, 0.47; Log-rank:  $X^2 = 4.758$ ,  $p = .029$ ).

**Conclusion:** In this study, describing the broadest EOAN sample available in literature so far, EOAN patients received specific interventions and obtained better outcomes at discharge and follow-up when compared to AOAN. Longitudinal, matched studies are required.

## KEYWORDS

adolescence, childhood, early onset anorexia nervosa, eating disorders, multidisciplinary hospital treatment

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## 1 | INTRODUCTION

### 1.1 | Anorexia nervosa and early onset anorexia nervosa

Anorexia nervosa (AN) is a mental health condition included in the Diagnostic and Statistical Manual of Mental Disorders, Fifth edition (DSM-5) among the feeding and eating disorders (FED), typically characterized by a restricted assumption of energy, fear of fat, and body weight, and a disturbed experience of body shape and weight (APA, 2013). This condition may be associated with several medical and mental health complications and comorbid diseases, such as cardiovascular (Borgia et al., 2021), nutritional (Skowrońska et al., 2019), and neurodevelopmental disorders (Westwood & Tchanturia, 2017).

The peak incidence of AN has been classically reported to occur during adolescence (Herpertz-Dahlmann & Dahmen, 2019). In a community-based prospective study presenting the annual incidence for different FED, Stice and colleagues documented, for AN, peak age for onset between 19 and 20 years (Stice et al., 2013). Despite this evidence, childhood AN has been reported in several case studies (Irwin, 1984; Russell, 1985). The recognition and treatment of childhood AN represent relevant challenges for mental health clinicians and researchers, due to the recently documented increase in the incidence of AN among younger persons (aged <15 years) (Van Eeden et al., 2021).

Early onset AN (EOAN) represents a subclassification of AN. While an established definition has not been reached, most studies on this condition refer to the definition advanced by Lask and Bryant-Waugh, which proposes an age at the onset before 14 years old as a defining criterion (Lask & Bryant-Waugh, 1992, 1993). Regardless of the heterogeneous boundaries that have been established so far, EOAN is currently considered a single entity in the spectrum of eating disorders (ED), carrying a relevant and specific burden (Clarke et al., 2021; Nicholls et al., 2011). Researchers have documented that EOAN may entail an epidemiological and clinical profile differing from AN with an onset during adolescence or early adulthood.

### 1.2 | Clinical features of EOAN

Researchers have raised concerns about the possibility to rely on present data to determine the exact prevalence and incidence of childhood AN since most studies report joint data for children and adolescents (Herpertz-Dahlmann & Dahmen, 2019). In a British surveillance study, the reported estimated incidence of AN in patients younger than 13 years was 1.09/100000 (Nicholls et al., 2011). In a registry study conducted in Germany, 25% of 289 patients admitted for the first time to inpatient care were <14 years of age (Jaite et al., 2019).

As for reported clinical features, patients with EOAN may display a more restrictive eating behaviour (van Noort et al., 2018), with a relevant prevalence of this symptom on binge-eating patterns (Fosson et al., 1987; Matsumoto et al., 2001). Psychopathological assessments

have revealed that EOAN, when compared to adolescent-onset AN, may present lower eating concerns (Cooper et al., 2002), self-esteem, and perfectionism impairments (van Noort et al., 2018), despite a high number of medical consultations for eating, weight, and shape may be found in EOAN patients, especially in the year before diagnosis (Lask, Bryant-Waugh, et al., 2005). Neuroradiological features have been proposed as well, with a single study reporting that patients with EOAN may display associations between regional cerebral blood flow and various aspects of a cognitive profile, including impaired visuospatial ability, impaired complex visual memory, and enhanced information processing (Lask, Bryant-Waugh, et al., 2005). Nonetheless, in a second study, children with EOAN showed no significant differences in flexibility, inhibition, planning, central coherence, visuospatial short- and long-term memory or recognition, when compared to healthy controls (van Noort et al., 2016). More recent research has not confirmed this evidence, with Jenkins and colleagues reporting that EOAN patients may demonstrate higher eating disorders symptomatology and dysmorphic concern compared to the later-onset controls, as well as significantly decreased cognitive flexibility (Jenkins et al., 2020). When considering medical complications of malnutrition, girls with EOAN have been found to display greater deficits in bone mineral content and density than controls (Clarke et al., 2021). The study of prognostic factors for EOAN has been attempted by a previous publication by Bryant-Waugh and colleagues, reporting early age at onset (<11 years), depression, and disturbed family life as potentially linked to the worst prognosis in this population (Bryant-Waugh et al., 1988).

The aims of the present research, considering previous literature data, may be summarized in three major topics that led the Authors to conceptualize the study: (a) Previous studies underline the importance of adopting a dynamic perspective in the diagnosis and treatment of AN, with possible early or partial presentations, and high-diagnostic instability (Herzog et al., 1993; Strober et al., 1997). In early presentations, clinical symptoms may overlap those of full-blown syndromes (Stein et al., 1997), and sometimes worse psychopathology with more restrictive eating behaviour than classic adolescent-onset diseases may be present (van Noort et al., 2018) or lower eating concerns reported (Cooper et al., 2002). A clearer characterization of the “Early Onset” presentation of AN would be important for prevention and taking charge of the disease. (b) The psychopathology associated with EOAN and AOAN has been documented, but the literature lacks data concerning potential changes of these parameters occurring in the context of a multidisciplinary hospital intervention. Our question is: may the psychopathological domain benefit from a structured hospital intervention, to prioritize treatment options in the identification of individualized management for EOAN? (c) Individuals with EOAN may sustain multiple and frequent clinical evaluations, especially eating, weight, and shape consultations (Lask, Bryant-Waugh, et al., 2005). It is noteworthy that children and adolescents receiving inpatient interventions for mental health conditions have been found to frequently suffer from restricted space, containment, limited access to healthy food, restrictions on cooking, and physical activities (Faulkner et al., 2009; Carney et al., 2021). Determining the intensity of treatment

received by individuals with EOAN may help clinicians in predicting the overall risk for these patients to be subjected to specific interventions during their illness, with a potential impact on the planning of long-term management plans.

This study provides naturalistic data on a wide sample with EOAN, as compared to a group of patients with AOAN. The study will compare both baseline and post-hospitalization features of these groups, highlighting potential co-occurring changes in nutritional and psychopathological measures, as well as follow-up data after a 12-month follow-up period following hospital discharge.

The Authors point out that, despite the previous literature providing interesting data on the psychopathological and neuropsychological features of EOAN, due to the scarcity of literature to form directional hypotheses on the themes relevant to this research, the nature of this study was exploratory and no predetermined hypotheses were made.

## 2 | METHODS

### 2.1 | Study design and participants

This is an observational retrospective study. This study was conducted in the context of an observational study investigating the use of psychopharmacological treatments in a third-level Italian Regional Center for FEDs in Children and Adolescents and was approved by the local ethical committee (code NPI-DAPSIFA2020). Strengthening the reporting of observational studies in epidemiology guidelines were observed during the planning and execution phases of the study (von Elm et al., 2007). This study was not sponsored or funded by any company.

The study was conducted in February 2021 by retrospectively considering patients assessed at the study Center between 01 January 2016 and 31 December 2020, and with at least one hospitalization for ED in the same Center. Hospitalization was defined as an inpatient or day hospital treatment. The day-hospital treatment program for patients with ED is comparably structured and as intensive as inpatient treatment. The hospital program adopted in our Center entails a multidisciplinary psychological, psychopharmacological, and nutritional intervention. All included patients were subjected to the same multidisciplinary program, performed by the same team, in the same Center, following clinical international guidelines (National Institute for Health and Care Excellence, 2017).

Inclusion criteria were: (a) a diagnosis of AN according to the DSM-5 criteria; (b) acquisition of informed consent. The exclusion criterion was: insufficient clinical documentation. Patients were then included in the EOAN group if they had an onset of AN before the age of 14, according to the definition by (Lask & Bryant-Waugh, 1992, 1993). Patients with an onset of AN after the age of 14 (14.1–17.9 years) were included in the adolescent-onset group (AOAN). Consistent with the few existing studies that provide specific criteria (Clarke et al., 2021; Matsumoto et al., 2001), “onset” was defined as the occurrence of food avoidance and weight loss. As a notable

difference, however, we allowed onset dates reported by the patients and their caregivers, but only when they were confirmed by a clearly documented clinical record produced by an expert in the field of FED. Whenever a disagreement between the patient and caregivers regarding onset emerged, data provided by the clinicians were used to discriminate the most reliable date. The selection of the two groups was performed including all the patients undergoing the same hospital treatment during the selected period, to provide an unbiased and naturalistic observation. Given the naturalistic nature of the study, missing data were not replaced.

### 2.2 | Assessment methods

The primary objective of the study was to describe a sample of patients with EOAN in the context of a multidisciplinary hospital intervention for FED. Thus, psychopharmacological treatment variables were assessed by thoroughly reviewing clinical documentation, which included the dates and duration of treatment, initial and maximum dosages, any reasons for treatment interruption, and possible emerging adverse drug reactions. During hospitalization, patients received repeated standard laboratory exams (including blood counts, electrolytes, liver enzymes, lipid profiles, and coagulation) and repeated electrocardiograms. Nutritional interventions were collected and coded as well, including the use of nasogastric tube (NGT) feeding. All the participants received multidisciplinary hospital treatment for AN, including individual and group psychotherapeutic interventions.

All the patients received an assessment for FED, including psychopathological, nutritional, and biochemical screening at hospital admission. Besides pharmacological and nutritional interventions, the considered variables included demographics (gender, age), clinical variables (AN subtype, comorbidities, duration of illness before the hospitalization, duration of hospitalization, FED symptoms), and anthropometric variables (admission, T0, and discharge, T1 %BMI and BMI). Bodyweight and its changes were assessed as %BMI. The use of this measure is indicated by the report Junior MARSIPAN: Management of Really Sick Patients under 18 with AN. Percentage BMI is calculated as  $(\text{BMI}/\text{median BMI for age and gender} \times 100)$  (Royal College of Psychiatrists, 2012). The World Health Organization BMI-for-age charts for girls and boys were used as reference values in this study (WHO, 2005). Data concerning an admission before/after the COVID-19 pandemic were collected as well, given the potential confounding effect of this variable on the onset and duration of illness before the hospitalization of patients referred for FED. Notably, the COVID-19 pandemic had a significant impact on FED in Italy, both in terms of post-traumatic symptomatology and interference with the recovery process (Castellini et al., 2020). Despite this evidence, we decided to collect data both from the pre-pandemic and pandemic periods, unitedly and separately. The interpretation of the resulting numbers belonging to the two historical cohorts should consider the almost complete closing of paediatric mental health services in the months between March and May 2020.

Diagnoses of AN, AN subtypes, and comorbidities were performed by paediatric neuropsychiatrists and clinical psychologists trained in the field of FED following DSM-5 diagnostic criteria (APA, 2013). The diagnostic process was supported by the administration of the tests described below, all validated for the assessment of children and adolescents with ED in the Italian language. These tests were all administered at both hospital admission (T0) and discharge (T1).

1. All patients were assessed with the Self-Administered Psychiatric Scales for Children and Adolescents (SAFA), a validated psychometric instrument used to assess psychiatric comorbidities in children and adolescents with eating disorders (Cianchetti & Sannio Fascello, 2001; Franzoni et al., 2009). Five subtests were administered, assessing specific psychopathological domains: eating disorders psychopathology (SAFA-P), anxiety (SAFA-A), depression (SAFA-D); obsessive-compulsive symptoms (SAFA-O), somatic symptoms (SAFA-S) (Franzoni et al., 2009).

The diagnostic process was supported by the Eating Disorders Inventory-3 (Garner, 2004) and the Eating Disorders Questionnaire in Childhood (Franzoni et al., 2017).

For this study, only the results of the SAFA scales were reported and compared with statistical analyses.

The two groups (EOAN and AOAN) were compared for demographics (gender, age), clinical variables (AN subtype, comorbidities, duration of illness before the hospitalization, duration of hospitalization), anthropometric variables (admission, T0 and discharge, T1 % BMI and BMI), the pre- or post-pandemic moment of hospitalization, treatment variables (NGT, psychopharmacology).

To report potential differences between the two groups as regards the occurrence of new hospitalizations for FED in the 12 months, data concerning the follow-up for all the patients after 1 year of discharge were collected.

## 2.3 | Statistical analysis

Descriptive analyses were provided for the entire sample and the two included groups. The significance level was set at .05, and all tests were two-tailed. Shapiro-Wilk's and Levene's tests were used to assess the normality of data distribution and homogeneity of variance. Bonferroni correction was applied for multiple comparisons.

Then, possible differences between the two groups regarding T0-T1 changes in weight and psychopathology during the hospital treatment were considered. To this end, multiple analyses of covariance were conducted, using BMI and each psychopathological measure at T1 as a dependent variable, and the group status (EOAN, AOAN) as independent variables. All the analyses were controlled for the respective T0 weight/psychopathological measures. Since different age groups were included, separate analyses were conducted for

SAFA subscales (%BMI, BMI, SAFA-A, SAFA-D, SAFA-O, SAFA-D and SAFA-S).

The rate of re-hospitalizations for the EOAN and the AOAN group was calculated through the Kaplan-Meier method and the Log-rank test was performed to assess potential differences between the two groups. The Cox proportional hazards model was used to estimate the hazard ratio and 95% confidence interval for EOAN as compared with that for AOAN. The sample size was determined based on the number of participants enrolled within the study period. All the statistical analyses were performed using R 4.1.2 (The R Foundation for Statistical Computing) for Windows.

## 3 | RESULTS

### 3.1 | Patient characteristics

A total of 301 children and adolescents with FED, who accessed our Center during the indicated period, were identified and considered for this study (mean age 15.9 years  $\pm$  2.1 years,  $F = 277$ , 92.0%). After applying the inclusion criteria, 44 patients with diagnoses other than AN were removed and not considered for the following analyses, while 257 children and adolescents with AN were included in the study. Nineteen patients were removed from this sample after applying exclusion criteria (partial/insufficient clinical documentation), while a total of 238 patients met the selected criteria and were retained for the final analyses.

Descriptions verbally reported by the patients and their caregivers indicated an age at the onset before the age of 14 years in 107 patients (45.0%). Upon systematically assessing the clinical documentation of the included patients, 22/107 had a clearly documented onset of AN symptomatology only after the age of 14. Thus, 85 (35.7%) patients were finally included in the EOAN group (mean age  $\pm$  standard deviation, 12.8  $\pm$  1.5 years; females, 88.2%) and 153 (64.3%) were included in the AOAN group (17.3  $\pm$  2.5 years; females, 96.1%). As reported in Table 1, mental health comorbidities (Obsessive-Compulsive Disorder and Major Depressive Disorder) were documented, while no major physical comorbidity emerged. No significant difference in comparisons of specific FED symptoms between the two groups (restrictive eating, hyperactivity, binge eating, purging behaviours) was documented.

Early-onset patients were more frequently males ( $X^2 = 5.360$ ,  $p = .021$ ) and were at a younger age at admission ( $U = 12503.0$ ,  $p < .001$ ) when compared to the adolescent-onset group. Clinically, EOAN individuals were at a younger age at onset ( $U = 9158.5$ ,  $p < .001$ ), had a lower BMI at admission ( $U = 7346.5$ ,  $p < .001$ ) and discharge ( $U = 8463.5$ ,  $p < .001$ ), and a higher %BMI at discharge ( $U = 3779.5$ ,  $p < .001$ ), were more frequently treated with NGT ( $X^2 = 10.313$ ,  $p = .001$ ), and more frequently received risperidone ( $X^2 = 19.463$ ,  $p < .001$ ), while fluoxetine was administered more frequently to AOAN participants ( $X^2 = 12.677$ ,  $p < .001$ ). Patients' characteristics at baseline are summarized in Table 1.

**TABLE 1** Demographic and clinical characteristics of the two groups. Data are reported as total numbers (percentage) or means (+/– standard deviation)

Variables	EOAN (n = 85)	AOAO (n = 153)	Statistics	Effect size (CI)
<b>Demographics (1)</b>				
Gender	F = 75 (88.2%) M = 10 (11.8%)	F = 147 (96.1%) M = 6 (3.9%)	X <sup>2</sup> = 5.360, p = .021	Phi = 0.150
Age at admission (years)	12.8 ± 1.5	17.3 ± 2.5	T = 15.127, p < .001	d = 2.054 (1.727–2.377)
<b>Clinical (2)</b>				
Age at onset (years)	11.9+/-1.4	15.2+/-1.7	U = 9158.5, p < .001	d = 2.128 (1.774–2.478)
DUI (months)	13.7+/-12.5	13.5+/-8.1	U = 2150.5, p = .014	d = 0.362 (-0.005–0.728)
Access during the COVID-19 pandemic	5 (5.9%)	12 (7.8%)	X <sup>2</sup> = 0.317, p = .574	Phi = -0.036
AN subtype	ANR = 79 (93.0%) ANBP = 3 (3.5%) ANA = 3 (3.5%)	ANR = 123 (80.3%) ANBP = 17 (11.1%) ANA = 13 (8.6%)	X <sup>2</sup> = 7.099, p = .069 (3-groups comparison)	V = 0.173
Restrictive eating	85 (100%)	153 (100%)	X <sup>2</sup> = 0.000, p = 1.000	/
Physical hyperactivity	81 (95.3%)	134 (87.6%)	X <sup>2</sup> = 3.723, p = .054	Phi = 0.125
Binge eating	3 (3.5%)	17 (11.1%)	X <sup>2</sup> = 4.081, p = .043	Phi = 0.131
Purging behaviours	5 (5.9%)	28 (18.3%)	X <sup>2</sup> = 7.056, p = .008	Phi = -0.172
OCD	9 (10.6%)	11 (7.2%)	X <sup>2</sup> = 0.820, p = .365	Phi = 0.059
MDD	2 (2.4%)	13 (8.5%)	X <sup>2</sup> = 3.493, p = .062	Phi = -0.121
Admission %BMI	74.9+/-10.7	71.7+/-10.4	U = 5077.0, p = .014	d = -0.299 (-0.567–0.030)
Discharge %BMI	85.1+/-10.3	78.7+/-11.4	U = 3779.5, p < .001	d = -0.584 (-0.856–0.310)
Admission BMI	14.2+/-2.2	15.2+/-2.4	U = 7346.5, p < .001	d = 0.512 (0.242–0.782)
Discharge BMI	15.9+/-1.8	16.6+/-2.5	U = 8463.5, p < .001	d = 0.296 (0.027–0.555)
NGT	39 (45.9%)	39 (25.5%)	X <sup>2</sup> = 10.313, p = .001	Phi = 0.208
<b>Psychopharmacological treatment variables (3)</b>				
Any AAP	57 (67.1%)	56 (36.6%)	X <sup>2</sup> = 0.321, p = .571	Phi = 0.037
Risperidone	26 (30.6%)	13 (8.5%)	X <sup>2</sup> = 19.463, p < .001	Phi = 0.286
Olanzapine	22 (25.9%)	59 (38.6%)	X <sup>2</sup> = 3.913, p = .048	Phi = -0.128
Aripiprazole	18 (21.2%)	34 (22.2%)	X <sup>2</sup> = 0.035, p = .852	Phi = -0.012
Quetiapine	2 (2.4%)	14 (9.2%)	X <sup>2</sup> = 4.026, p = .045	Phi = -0.130
Any SSRI	63 (74.1%)	131 (85.6%)	X <sup>2</sup> = 4.798, p = .028	Phi = -0.142
Sertraline	59 (69.4%)	98 (64.1%)	X <sup>2</sup> = 0.699, p = .403	Phi = 0.054
Fluoxamine	6 (7.1%)	9 (5.9%)	X <sup>2</sup> = 0.128, p = .720	Phi = 0.023
Fluoxetine	10 (11.8%)	50 (32.7%)	X <sup>2</sup> = 12.677, p < .001	Phi = -0.231

Note: Multiple comparisons: (1) Bonferroni corrected significance value for a number of 2 ( $p = .05/2 = 0.0250$ ); (2) Bonferroni corrected significance value for a number of 12 ( $p = .05/10 = 0.0042$ ); (3) Bonferroni corrected significance value for a number of 9 ( $p = 0.005/9 = 0.0055$ ). Statistically significant differences after Bonferroni correction are marked in bold and italicized. Abbreviations: AAP, atypical antipsychotics; AN, Anorexia Nervosa; ANR, AN, restrictive subtype; ANBP, AN, binge-purging subtype; ANA, atypical AN; BMI, body-mass index; %BMI, Body-mass index percentage; DUI, duration of illness before the hospitalization; MDD, major depressive disorder; NGT, nasogastric tube feeding; OCD, obsessive compulsive disorder; SSRI, selective serotonin reuptake inhibitors.

### 3.2 | Admission - discharge changes of clinical and psychopathological variables

Table 2 presents the changes in clinical and psychopathological parameters between admission and discharge. Since different age groups were included, the table refers to variables addressing individuals of any age (%BMI, BMI, SAFA-A, SAFA-D, SAFA-O, SAFA-D and SAFA-S). %BMI improved significantly more in EOAN than in AOAN patients ( $F[1.229] = 15.104, p < .001, \eta^2 = 0.030$ ). No other statistically significant difference was documented between the two groups.

### 3.3 | Freedom from re-hospitalization

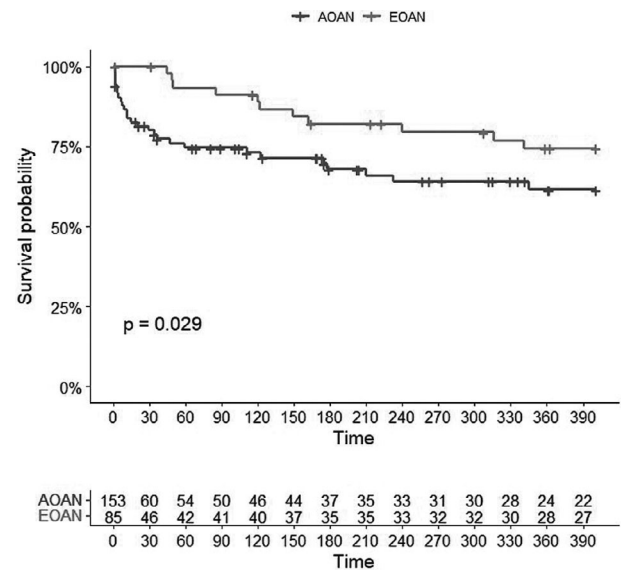
Kaplan Meier curves for EOAN and AOAN groups are reported in Figure 1. The mean time of freedom from re-hospitalization was 338.7 (95% CI, 303.9–373.5) days for the EOAN group and 277.8 (95% CI, 240.7–314.9) days for the AOAN group. The cumulative freedom from re-hospitalization at 12 months was 74.4% (95% CI, 61.3–87.5) for the EOAN group and 61.5% (95% CI, 49.7–73.2) for the AOAN group. EOAN patients had a significantly higher rate of freedom from rehospitalization than AOAN (hazard ratio, 0.47; 95% CI, 0.24–0.94; Log-rank test:  $X^2 = 4.758, p = .029$ ).

## 4 | DISCUSSION

The present study describes a sample of 85 patients with EOAN in the context of a multidisciplinary hospital intervention for FED, as compared to a group of patients with AOAN. This sample represents the largest cohort of individuals with this condition described in the literature so far.

Despite EOAN has been recently acknowledged as a distinct condition within the spectrum of the DSM-5 description of AN (Clarke et al., 2021; van Noort et al., 2016), the research on EOAN is still hampered by methodological differences in diagnostic criteria. Most studies (Jenkins et al., 2020; Lask, Bryant-Waugh, et al., 2005; Lask,

Gordon, et al., 2005; Matsumoto et al., 2001; van Noort et al., 2016; van Noort et al., 2018) have broadly referred to the classic “before the age of 14 years” defining criterion (Lask & Bryant-Waugh, 1992, 1993). The same criterion was adopted in the present study, where “onset” data provided by patients and caregivers were retained only when confirmed by a documented clinical record. Relevantly, the criterion here adopted included 35.7% of the overall sample in the EOAN group. This should be compared to recent German data, reporting that 25% of 289 patients admitted for the first time to inpatient care were <14 years of age (Jaite et al., 2019). Nonetheless, the literature describes a progressive lowering of peak age at the onset of AN: Steinhausen and Jensen documented that, in 2010, the most frequent age of onset of AN was 12–15 years, while the peak age of onset in 1995 ranged between 16 and 19 years (Steinhausen & Jensen, 2015).



**FIGURE 1** Re-hospitalization rates calculated by the Kaplan-Meier for the EOAN and AOAN groups. AOAN, adolescent onset anorexia nervosa; EOAN: early onset anorexia nervosa

**TABLE 2** Admission - discharge changes of clinical and psychopathological variables

Variables	F (df) for EOAN/AOAN status	p-value for EOAN/AOAN status	Effect size ( $\eta^2$ ) for EOAN/AOAN status
%BMI	15.104 (1229)	<b>&lt;.001</b>	0.030
BMI	0.566 (1230)	.453	0.001
SAFA-A	0.045 (1,93)	.833	2.544 <sup>-4</sup>
SAFA-D	0.170 (1,92)	.681	0.001
SAFA-O	7.106 <sup>-4</sup> (1,90)	.979	5.530 <sup>-6</sup>
SAFA-P	0.069 (1,88)	.794	4.808 <sup>-4</sup>
SAFA-S	0.026 (1,83)	.871	1.784 <sup>-4</sup>

Abbreviations: AOAN, adolescent onset Anorexia Nervosa; BMI, body-mass index; %BMI, body-mass index percentage; EOAN, early onset anorexia nervosa; SAFA, self-administered psychiatric scales for children and adolescents; SAFA-A, anxiety subtest; SAFA-D, depression subtest; SAFA-O, obsession subtest; SAFA-P, eating disorders subtest; SAFA-S, somatic symptoms subtest. Statistically significant differences are marked in bold and italicized.

Thus, our data seem to confirm a progressive shift in the peak age at onset for patients with AN.

In our sample, males were significantly more represented in the EOAN than in the AOAN group. Nicholls and colleagues conducted a British national surveillance study on new cases of early-onset eating disorders (<13 years), reported 18% frequency of males across all FED, and a 12% frequency for AN (Nicholls et al., 2011). Notably, some studies on EOAN deliberately excluded males, to prevent unequal gender distributions (van Noort et al., 2018), or to assess specific endocrine variations (Clarke et al., 2021). Given the insufficient information still available in the medical literature on these patients (Strobel et al., 2018), we suggest the inclusion of males in studies addressing the clinical and neuropsychological features of EOAN and recommend specific longitudinal research targeting these samples.

Data on administered treatments failed to show differences between EOAN and AOAN in the overall frequency of prescription of atypical antipsychotics, and although SSRIs were prescribed more frequently to AOAN, this result failed to reach statistical significance after applying Bonferroni correction. When addressing specific treatments, fluoxetine ( $n = 50$ , 32.7%) was used more frequently in AOAN and risperidone ( $n = 26$ , 30.6%) in EOAN. Insufficient reports have been produced on psychopharmacological treatment in EOAN so far. Our findings may be compared to the findings of Nicholls and Colleagues in early-onset ED, which document the use of SSRI (fluoxetine for nine individuals, sertraline for four, and one not stated) and atypical antipsychotics (olanzapine for four individuals and risperidone for eight) in a sample of 208 individuals (76 with AN) (Nicholls et al., 2011). However, the number of participants fed by NGT differs in the two studies, with 23 (11%) patients in the British sample (Nicholls et al., 2011) and 39 (45.9%) in our research. According to these data, our results failed to identify marked differences between EOAN and AOAN concerning the treatment delivered. Nonetheless, the greater, although not statistically significant, frequency of patients with binge-purging behaviours in the AOAN than in the EOAN group in our study (see Table 1), may be partially responsible for the higher documented use in AOAN of fluoxetine, a drug that has been licensed for the treatment of Bulimia Nervosa (Sohel et al., 2022). Even though these numbers seem to indicate a high-absolute frequency of use of psychopharmacological and NGT interventions in our sample with EOAN, severe methodological differences (diagnostic criteria, use of different versions of the DSM, age threshold, mixed vs homogeneous diagnoses) hinder the possibility to establish direct comparisons, and demand further targeted research.

In our study, participants with EOAN showed a significantly lower rate of re-hospitalization than those with AOAN at 1 year of follow-up, showing that 74.4% of EOAN participants remained free from re-hospitalization. Moreover, EOAN patients obtained a greater %BMI improvement between admission and discharge when compared to AOAN. These results should be compared with those reported in 30 children by Bryant-Waugh and Colleagues, describing a good outcome in 18/30, a moderate to severe impairment in 10/30, and two deaths, after a long-term (mean 7.2 years) follow-up (Bryant-Waugh et al., 1988). Nicholls and colleagues, in a sample of 208 patients with early onset eating disorders, reported that 50% were admitted to the hospital;

outcome data were available for 76%, documenting that at 1 year, 73% improved, 6% worsened and 10% remained unchanged (Nicholls et al., 2011). According to these data, our results managed to provide new insights on the risk of rehospitalization of EOAN, highlighting a better outcome than that reported in patients with AOAN. Given that our two groups differed for age at onset, but not for the duration of untreated illness, we may hypothesize that a multidisciplinary hospital intervention may more positively influence the medium-term (1 year) outcome of patients with an early onset, independently from the previous duration of AN. The relevant differences between our study and this research (different versions of the DSM, heterogeneous diagnoses) limit the possibility to draw direct comparisons. Distinct subgroups or differences in psychopathological traits between EOAN patients may be implicated in determining the trajectories of the outcome of this population. Relevantly, no particular improvement in psychopathology was documented in our sample with EOAN when compared to AOAN, suggesting the need for specific outcome measures.

The data here reported may carry relevant implications for the early detection, early intervention, and prognosis of AN. The evidence of a lack of significant differences in the distribution of FED-specific symptoms and psychopathology between EOAN and AOAN in the two included groups, despite being negative data, may directly impact the early recognition of EOAN. The evidence that EOAN may manifest with a series of the typical key features of AN may help clinicians in correctly categorizing these patients, potentially reducing the risk of misdiagnosis, and delayed time to diagnosis and treatment.

Our data reporting a reduced risk for rehospitalization carries implications for the early management of this condition. Inpatient admissions represent a critical event in child psychiatry, given the documented findings of frequently insufficient options for suitable step-down (post-discharge) care (Thompson et al., 2021) and the high and socially impacting economic costs (Herndon et al., 2020). A high risk of rehospitalization directly impacts the medical decisions and early management in clinical practice with children and adolescents with AN, since major international guidelines advise against the indiscriminate use of inpatient treatments for these patients (Couturier et al., 2020; National Institute for Health and Care Excellence, 2017).

The first 3 years of illness, in patients with AN, represent a critical window for recovery, beyond which outcomes are poorer (Treasure et al., 2015). Nonetheless, evidence in this field is contradictory. In a systematic review of the literature, Schoemaker pointed out that the prognostic value of early intervention in AN cannot be estimated based on the treatment-outcome literature, since most of the studies considered the duration of the illness and not the occurrence of early intervention (Schoemaker, 1997). The relevance of early intervention, nonetheless, has been pointed out by Treasure and Russel, who reported how patients with an onset in adolescence who had been ill for over 3 years had a poor response to both family and individual therapy, suggesting a poor outcome unless treatment is delivered within the first 3 years of illness (Treasure & Russell, 2011). These issues have been targeted by research by Fukutomi and Colleagues prioritizing patients aged 18–25 years old, with a duration of illness <3 years, reporting a more complete recovery in patients with AN at

24 months when compared to treatment as usual (Fukutomi et al., 2020). Based on these considerations, we think that the precocious identification and recognition of patients with EOAN and their follow-up outcomes could represent the clinical basis for the development of target interventions.

This study has some limitations. First, its retrospective nature and the specific setting (a third-level Center for FED in developmental age) may limit the possibility to draw direct comparisons with other studies. Second, aside from a comparison group with AOAN, no specific control group from the general population was available for psychopathological measures. Third, the follow-up period was limited to 12 months. However, this study also presents significant strengths. The sample included represents the widest available in the literature so far on EOAN, followed up for a 1-year long period. Its real-world nature permitted the thorough description of psychopharmacological, nutritional, and psychopathological parameters. Our use of a standardized definition for EOAN and clear clinical records documenting its onset provide a stronger characterization of this condition, which will be helpful in further studies.

## 5 | CONCLUSION

This study reports the clinical, psychopathological, and treatment characteristics of a wide sample of patients with EOAN, as compared to a group of AOAN individuals assessed in the same third-level Center for FED in the developmental age. EOAN participants were more frequently males, received more frequently NGT and risperidone, obtained a greater T0-T1 improvement in weight measures, and had a higher 1-year rate of freedom from re-hospitalization. Further studies, conducted using standardized definitions, are required to clearly identify the distinctive features of EOAN, and to plan for directed clinical interventions.

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## CONFLICT OF INTEREST

The authors have no competing interests/conflict of interest.

## DATA AVAILABILITY STATEMENT

The datasets used and analyzed during the study are available from the corresponding author on reasonable request.

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