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ORIGINAL ARTICLE

Suicidality in adolescents with onset of anorexia nervosa

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Abstract

Objectives The mortality rate in patients with anorexia nervosa (AN) is 5 to 10 times higher than in general population and, suicide is one of the main causes of death. We evaluated the prevalence of suicidality (ideation, self-injurious behaviour, suicidal attempts) in 100 adolescents with onset of AN and we explored the correlation between suicidality, severity of AN symptoms and psychiatric comorbidity.

Methods We subdivided AN patients into restrictive (R-AN; $n=66$) and restrictive atypical (A-AN; $n=34$), according to the European Guidelines criteria. Assessment was performed using the eating disorder inventory 3rd version, the schedule for affective disorders and schizophrenia for school-age children-present and lifetime version interview, and the Columbia-suicide severity rating scale. Fisher's exact test and Mann–Whitney test (with correction for multiple testing) were used to compare the distribution of categorical and continuous variables between R-AN and A-AN patients, and between patients with vs. without suicidal behaviours.

Results Twenty-seven patients (27%) presented suicidality as clinical feature, expressed as at least one of the following: suicidal ideation (24%), self-cutting (19%), and suicidal attempt (6%). Patients with suicidality showed greater severity of psychiatric symptoms related to AN psychopathology and presented psychiatric comorbidity, especially depression, more often than patients who did not reported suicidality (70,4% vs 29,6%). No significant differences in terms of suicidal behaviours and AN-specific psychopathology were found between R-AN and A-AN.

Conclusions Suicidality in adolescent patients with R-AN and A-AN seems to be related to ED symptoms. These data highlight the importance of screening for suicidality among adolescents at onset of AN, and confirms that A-AN should not be considered a milder disease.

Level of evidence Level IV: Evidence obtained from multiple time series analysis such as case studies. (NB: Dramatic results in uncontrolled trials might also be regarded as this type of evidence)

Keywords Adolescents · Anorexia nervosa · Atypical anorexia nervosa · Suicidality · Self-cutting

Introduction

The term "suicidality" is used to describe a wide spectrum of suicidal manifestations, which extends from ideation to acts (self-aggressive behaviours, parasuicide, and suicide attempts) [1] and represent a condition of health urgency, particularly in adolescence and young adulthood [2]. The prevalence rates for suicidality in adolescence are between 15 and 30% according to both American [3] and European [4] data. In patients with anorexia nervosa (AN), suicide can be considered the most frequent cause of death, much more frequent than hunger and complications of weight loss [5]. In detail, about half of ED patients report suicidal ideation, with up to 26% of patients eventually attempting

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suicide [6, 7]. Anorexia nervosa (AN) is the most prevalent ED type among adolescents, primarily involving female, with a reported mortality rate 5 to 10 times higher than in the general population [8, 9], and with a high prevalence of suicidality and risk of death for complete suicide [10, 11]. Some authors [12, 13] reported that ED could be considered an indirect manifestation of self-aggressive behaviours that can be precursors of suicide, much more than the presence of overt psychopathologies. The scientific literatures indicate that bulimia or binge-purging AN (BP-AN) [14] represent the pathologies more at risk of suicide due to the apparently "active" nature of these ED types [15]. In fact, vomiting, laxative use, and excessive exercise can increase suicidal risk while other factors typical of restrictive AN (R-AN), such as dietary restriction, may not [16]. These considerations were mostly made based on findings from studies conducted mainly in adult patients. Furthermore, suicidal behaviour has rarely been studied and described in the literature among patients suffering from atypical restrictive AN (A-AN), which refers to those patients that fulfill all the diagnostic criteria for R-AN except for being underweight [17, 18].

Compared to R-AN patients, those suffering from atypical AN usually present for treatment after a longer duration of illness [19] and are less likely to receive inpatient care [20], suggesting that the severity of their illness often goes unnoticed for a longer period, most likely because of their normal weight. Yet patients with A-AN can be just as medically ill as those with R-AN, and can actually report worse eating disorder-specific psychopathology [21]. By and large, differences between A-AN and R-AN patients are still underestimated, and our study aims to help fill this knowledge gap. Moreover, it is known that adolescents who suffer from AN have increased risk of experiencing depression [22], and a vast body of literature shows that suicidal thoughts are associated with depression in adolescents [23], yet how anorexia and depression interact in determining one's tendency to suicidal behaviours remains unclear.

The general objective of the present study is to better clarify the relationship between AN and suicidality in a group of adolescents at the onset of AN symptoms, taking into account illness severity and psychiatric comorbidity. We specifically focused on adolescents because relatively little is known about this topic in developmental age in comparison to adult individuals, for which an extensive literature already exists. For the same reason, we opted to focus on restrictive AN (typical and atypical) instead of other ED types, which are more studied in relation to suicidal behaviour. Therefore, our aim in this study was in particular to: (a) determine the prevalence of suicidality among children and adolescents diagnosed with AN (either R-AN, or restrictive A-AN); and (b) study the association between severity of AN symptoms, psychiatric comorbidity, and suicide, overall and in relation to the diagnostic subtype (R-AN vs. A-AN). In line with other studies [24, 25] that conceptualize the severity of AN regardless of weight, our initial hypothesis was that suicidality is not related to the severity of underweight, as assessed by the BMI, but rather to the psychopathological aspects of the patients.

Methods

Selection of patients

The study was approved by the Pediatric Ethics Committee of the Tuscany Region. We obtained written informed consent by parents or legal guardian and patients. We enrolled 100 adolescent inpatients (11 male and 89 female) consecutively admitted to the CAPU of the Meyer Children's Hospital in Florence between January 2016 and December 2020.

A retrospective chart review was completed. All patients under the age of 18 years who received a primary diagnosis of R-AN, according to DSM-5 criteria [17] were considered as potentially eligible for inclusion. Patients were included if they met the following criteria: (a) age $\leq$ 18 years; (b) current diagnosis of AN (either R-AN or A-AN); (c) absence of significant current and/or lifetime substance abuse disorder; (d) absence of intellectual disability; (e) no history of endocrine disorders; (f) early stage of disease evaluated with illness duration < 3 years, according to literature data [26].

A detailed psychiatric, family, psychopathological, and nutritional interview, involving both patients and caregivers, were performed by a multidisciplinary team at hospital admission. A clinical and anthropometric evaluation was also performed.

Sociodemographic and clinical variables at admission

Sociodemographic and clinical variables used for the study included: nationality, age, biological sex, vital signs, presence of coexisting medical conditions, history of psychiatric diagnosis, family history of ED or other psychiatric diagnosis. For each patient, we retrospectively collected data from the medical reports at the time of the assessment.

Anthropometrics

Weight and height were measured by nursing staff and the percentile Body Mass Index (pBMI) was calculated with the 2000 Centers for Disease Control and Prevention (CDCP) growth charts [27]. All patients were subdivided, in R-AN

or A-AN based on their BMI being below (R-AN) or above (A-AN) the 10th percentile [18].

Psychometric measures

The diagnostic assessment included the following tests administered by psychiatrists in the first 2 days after admission to the CAPU: (a) the Eating Disorder Inventory, 3rd version (EDI-3) to the 13–18 year-old age group, according to the questionnaire administration criteria [28]; (b) the Italian version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children/Present and Lifetime Version (K–SADS–PL) [29] which follows DSM-5 criteria [17] and was administered both to patients and caregivers; and (c) the Italian version of Columbia-suicide severity rating scale (C-SSRS) [30].

The EDI-3 is a self-report measure of psychological traits in individuals with EDs aged 13–53 years [28]. It has 91 items organized into 12 primary scales, three of which are ED specific: drive for Thinness, Bulimia, and Body Dissatisfaction. Nine are general psychological scales: low Self-Esteem, Personal Alienation, Interpersonal Insecurity, Interpersonal Alienation, Interoceptive Deficits, Emotional Dysregulation, Perfectionism, Asceticism, and Maturity Fears. The Italian version of EDI-3 has demonstrated very good day test–retest reliability, cross-informant agreement and a good discriminating validity. Analysis of the EDI-3 questionnaire profiles is limited to the 13–18-year-old age group, according to the questionnaire administration criteria.

Age at onset was defined as the age at which each patient first met the DSM-5 diagnostic criteria [17] for AN. The AN diagnosis and psychiatric comorbidities were assessed through a direct clinical interview and with the administration of K–SADS–PL [29]. The K-SADS-PL is a semi-structured interview used to determine Axis I psychiatric diagnoses. The interview, which was administrated by a trained psychologist to the patient and his/her parents, consists of an introductory interview, a screen interview, and five diagnostic supplements. Items are scored using a 0 to 3 or 0 to 2 point rating scale: 0 indicates no information is available, one suggests the symptom is not present, two indicates subthreshold levels of symptomatology, and three represents threshold criteria. Moreover, the C-GAS scale evaluates the global functioning of the patient.

Suicidality that occurred after the emergence of AN symptoms was evaluated during the clinical interview using the C-SSRS [30]. Based on the C-SSRS scores, we differentiated the presence of ideation, intensity of ideation, self-injurious behaviours, suicide attempts, and lethality of suicide attempts as follows based on actual mortality/medical harm:

0: no suicidal ideation or suicidal behaviour with no damage;
1: thoughts of death but not suicidal ideation and not suicidal behaviour;
2: sporadic unstructured suicidal ideation or minor suicidal behaviour, such as superficial self-cutting with minor physical damage (slight bleeding, scratching, bruising);
3: unplanned suicidal ideation or persistent thoughts of death or suicidal behaviour with moderate physical damage, need for medical attention (e.g., second degree burns, major vessel bleeding);
4: active suicidal ideation with some intent to act, without specific plan or preparatory acts or behaviour (anything beyond verbalization or thought, like assembling specific method (e.g., buying pills or gun) or preparing for death by suicide (e.g., giving things away, writing suicide note);
5: Active suicidal ideation with specific plan and intent or suicide attempt with minor physical damage and medical hospitalization required;
6: repeated major self-injurious behaviours, suicide attempts with severe physical harm and repeated suicide attempts with number 6.

Statistical analysis

The distribution of demographic, anamnestic, and clinical variables were reported using percentages for categorical variables and, medians and interquartile ranges for continuous variables. Differences between subgroups (between AN-R and AN-A, and between patients with vs. without suicidal behaviours) were assessed using the Fisher's exact test and the Wilcoxon test for categorical and continuous variables, respectively. Correction for multiple testing was performed by means of a false discovery rate (FDR) procedure.

Results

Anthropometrics, clinical, and psychopathological features

In the study period, 100 patients (89 females and 11 males) with onset of AN according to DSM-5 criteria were selected. Age ranged between 11.4 and 17.9 years (mean 15.0, median 14.6). The patients' mean weight, height, and BMI at admission were 42.8 kg, 163.5 cm, and 15.2 kg/m^2, respectively, and the mean percentage of weight loss, from the beginning of eating disorder symptoms to hospital admission, was 21.7%. Of the 100 patients included, 66 and 34 were

Table 1 Sociodemographic and anthropometric characteristics of the study population

	All patients	AN subtype according to European guidelines		
		R-AN	A-AN	*p* value
Age (years)				
Median	15.2	15.2	15.1	
IQR	(14.2–16.0)	(14.1–16.0)	(14.2–16.0)	0.746
Gender (*N* of patients)				
Female	89	62	27	
Male	11	4	7	**0.042**
Height (cm)				
Median	163	163	165	
IQR	(157–169)	(157–167)	(159–171)	0.100
Weight at onset (Kg)				
Median	55	51	59	
IQR	(50–59)	(46–55)	(55–68)	**< 0.001**
Weight at hospital admission (Kg)				
Median	42	39	49	
IQR	(38–47)	(35–42)	(44–53)	**< 0.001**
Percentage of weight loss (%)				
Median	20.6%	21.3%	19.9%	
IQR	(15.9–28.0)	(17.6–27.9)	(13.4–28.0)	0.298

Significant differences between restrictive (R-AN) and atypical anorexia nervosa (A-AN) patients are marked with *p* values in bold

classified as R-AN or as A-AN according to the European Guidelines criteria. The percentage of weight loss at admission did not significantly differ between R-AN and A-AN patients. Sociodemographic and anthropometrics features are detailed in Table 1.

Suicidality

Twenty-seven patients (27%) presented suicidality as clinical feature, expressed as at least one of the following manifestations: suicidal ideation, clinical evidence of self-cutting, or suicidal attempt (Table 2). Among the latter group, five patients reported a suicide attempt in their clinical history, and one patient reported multiple suicidal attempts. All these 27 patients showed a positive C-SSRS score. Notably, there were no differences in suicidality between patients with R-AN and A-AN (Table 2). Table 3 shows the number of patients that presented specific suicidal behaviours and any possible combination of them.

Patient's suicidality tended to associate with higher scores to the EDI-3 questionnaire, both in some of the single scales (eating disorder-specific and psychological trait scales) and in most of composite ones (Table 4). Instead, the scores to the EDI-3 questionnaire did not differ between R-AN and A-AN patients (Table 4). Finally,

Table 2 Comparison between restrictive anorexia nervosa (R-AN) and restrictive atypical anorexia nervosa (A-AN)

	Type of diagnosis		
	R-AN	A-AN	*p* value
Suicidality			
No	46	27	0.349
Yes	20	7	
Self-cutting			
No	51	30	0.282
Yes	15	4	
Suicidal ideation			
No	48	28	0.332
Yes	18	6	
Suicidal attempt			
No	63	31	0.561
One	3	2	
Multiple	0	1	
C-SSRS scores			
C-SSRS = 0	46	27	0.349
C-SSRS ≥ 1	20	7	

C-SSRS (dichotomized into 0 vs. ≥ 1) was used as parameter to evaluate the presence of suicidality

anthropometric parameters did not differ between patients who reported vs. did not show suicidality (Table 5).

Psychiatric comorbidity

Forty-seven patients (47%) included in the study presented psychiatric comorbidity associated with AN: of these, 39/47 (83%) had only one comorbidity, while 8/47 patients (17%) showed two or more comorbidities (Table 5). Anxiety (49%) and depression (38%) were the most frequently

Table 3 Detailed description of suicidality

Description of suicidality	No of patients (%)
Suicidality in general	*n* = 27 (27)
Suicidal ideation (SI)	*n* = 6 (6)
Self-cutting (SC)	*n* = 3 (3)
SI and SC	*n* = 12 (12)
Suicidal attempt (SA) and SI	*n* = 2 (2)
SA, SI and SC	*n* = 3 (3)
Multiple SA, Si, and SC	*n* = 1 (1)
C-SSRS = 1	*n* = 2 (2)
C-SSRS = 2	*n* = 12 (12)
C-SSRS = 3	*n* = 8 (8)
C-SSRS = 4	*n* = 0 (0)
C-SSRS = 5	*n* = 1 (1)
C-SSRS = 6	*n* = 4 (4)

Table 4 Comparison of EDI-3 questionnaire scores (reported as median and 25th–75th percentiles) between patients with R-AN vs. A-AN, and between patients with or without suicidality, self-cutting, suicidal ideation, and suicidal attempt

Single scales	AN type			Suicidality			Self-cutting			Suicidal ideation			Suicidal attempt		
	R-AN ($n=66$)	A-AN ($n=34$)	FDR-adj p value	No ($n=73$)	Yes ($n=27$)	FDR-adj p value	No ($n=81$)	Yes ($n=19$)	FDR-adj p value	No ($n=76$)	Yes ($n=24$)	FDR-adj p value	No ($n=94$)	Yes ($n=6$)	FDR-adj p value
Eating disorder-specific scales															
Drive for thinness	80 (45–90)	89 (75–99)	0.132	80 (50–90)	90 (77–99)	0.044	80 (50–90)	90 (82–99)	0.020	80 (50–91)	87 (78–99)	0.081	85 (56–91)	78 (71–90)	0.965
Bulimia	42 (0–61)	62 (29–75)	0.132	42 (0–73)	52 (42–69)	0.355	42 (0–69)	61 (42–73)	0.201	42 (0–73)	52 (42–65)	0.438	52 (0–69)	47 (42–73)	0.965
Body dissatisfaction	59 (39–91)	79 (62–92)	0.212	66 (39–88)	83 (48–94)	0.044	62 (42–88)	85 (75–94)	0.017	69 (40–87)	83 (46–95)	0.068	75 (42–91)	75 (45–80)	0.965
Psychological scales:															
Low self-esteem	64 (28–89)	79 (52–86)	0.585	61 (28–84)	89 (67–95)	0.006	61 (28–86)	89 (67–95)	0.017	61 (31–86)	89 (64–95)	0.030	72 (35–89)	66 (47–89)	0.965
Personal alienation	71 (23–89)	71 (44–89)	0.585	58 (23–83)	83 (71–94)	0.012	58 (23–86)	86 (75–94)	0.012	58 (23–88)	81 (57–95)	0.036	71 (31–89)	62 (44–86)	0.965
Interpersonal insecurity	77 (40–93)	85 (47–92)	0.769	77 (34–92)	90 (73–95)	0.021	78 (34–92)	92 (77–95)	0.017	77 (34–92)	90 (75–95)	0.036	84 (40–92)	77 (62–90)	0.965
Interpersonal alienation	66 (26–89)	76 (36–89)	0.572	59 (19–89)	76 (59–89)	0.067	61 (19–88)	76 (66–97)	0.024	60 (22–89)	76 (62–89)	0.112	66 (29–89)	85 (76–89)	0.612
Interoceptive deficits	81 (46–90)	77 (56–90)	0.946	71 (46–88)	90 (82–96)	0.006	74 (46–88)	90 (82–95)	0.017	72 (46–88)	90 (75–96)	0.024	77 (46–90)	90 (56–95)	0.636
Emotional dysregulation	64 (35–86)	66 (35–86)	0.985	59 (26–84)	74 (50–91)	0.223	58 (26–84)	84 (50–91)	0.101	64 (26–85)	64 (46–90)	0.444	64 (35–86)	49 (34–84)	0.965
Perfectionism	55 (19–79)	55 (27–84)	0.595	55 (19–82)	55 (27–74)	0.837	55 (22–79)	55 (37–79)	0.679	55 (19–81)	55 (32–77)	0.793	55 (27–79)	50 (22–84)	0.965
Asceticism	75 (31–92)	82 (57–93)	0.572	75 (40–90)	92 (57–98)	0.067	75 (40–90)	92 (57–98)	0.075	72 (35–88)	93 (57–98)	0.036	75 (40–92)	86 (57–95)	0.965
Maturity fears	59 (39–83)	65 (32–92)	0.366	65 (39–88)	59 (32–82)	0.338	65 (39–88)	59 (39–79)	0.201	65 (39–88)	59 (35–76)	0.353	65 (46–88)	28 (16–46)	0.204

Table 4 (continued)

Single scales	AN type			Suicidality			Self-cutting			Suicidal ideation			Suicidal attempt		
	R-AN ($n=66$)	A-AN ($n=34$)	FDR-adj p value	No ($n=73$)	Yes ($n=27$)	FDR-adj p value	No ($n=81$)	Yes ($n=19$)	FDR-adj p value	No ($n=76$)	Yes ($n=24$)	FDR-adj p value	No ($n=94$)	Yes ($n=6$)	FDR-adj p value
Composite scales															
Eating concerns composite	67 (41–85)	81 (71–90)	0.030	71 (42–84)	84 (68–90)	0.027	67 (42–84)	88 (76–90)	0.008	71 (42–85)	82 (68–90)	0.036	73 (45–89)	74 (56–77)	0.890
Ineffectiveness composite	70 (33–91)	81 (53–89)	0.416	66 (38–85)	87 (71–95)	0.005	69 (38–88)	87 (73–95)	0.008	69 (38–88)	87 (68–95)	0.022	74 (40–89)	72 (62–88)	0.890
Interpersonal problems composite	75 (26–90)	84 (53–94)	0.402	74 (26–90)	88 (67–96)	0.022	77 (26–90)	89 (70–96)	0.025	75 (26–93)	87 (68–96)	0.036	79 (30–93)	82 (74–98)	0.965
Affective problems composite	76 (46–93)	78 (52–89)	0.762	70 (42–86)	87 (80–95)	0.005	72 (42–88)	88 (82–95)	0.009	72 (44–88)	87 (73–95)	0.023	77 (46–89)	84 (52–90)	0.890
Overcontrol composite	65 (42–87)	77 (57–91)	0.402	73 (42–84)	80 (52–92)	0.108	73 (42–84)	82 (57–92)	0.079	67 (42–83)	83 (54–94)	0.036	73 (42–87)	79 (37–80)	0.890
Global psychological maladjustment	77 (40–93)	79 (60–89)	0.838	75 (42–89)	85 (69–94)	0.054	76 (42–89)	92 (73–94)	0.038	75 (42–89)	87 (65–95)	0.075	78 (56–92)	66 (57–94)	0.862

P values were from Wilcoxon's test for median comparison, and corrected for multiple comparison using a false discovery rate (FDR) procedure

Table 5 Anthropometrics features, psychiatric comorbidities, anxiety, and depression: comparison between patients with or without suicidality, self-cutting, suicidal ideation/attempt, and C-SSRS positive scores at hospital admission

	Suicidality			Self-cutting			Suicidal ideation			Suicidal attempt			C-SSRS at admission		
	No	Yes	*p* value	No	Yes	*p* value	No	Yes	*p* value	No	Yes	*p* value	No	Yes	*p* value
Initial weight, kg	54 (50–58)	55 (50–60)	0.534	55 (50–60)	53 (47–58)	0.529	53 (49–59)	55 (51–59)	0.462	54 (50–58)	57 (52–61)	0.266	54 (50–58)	55 (50–60)	0.534
Weight at admission, kg	42 (38–47)	43 (37–47)	0.370	42 (38–47)	42 (37–46)	0.676	42 (38–47)	43 (37–47)	0.526	42 (37–46)	49 (42–53)	0.070	42 (38–47)	43 (37–47)	0.370
Weight loss, %	20 (16–28)	22 (16–28)	0.858	21 (16–28)	19 (16–27)	0.871	21 (16–28)	21 (15–29)	0.897	21 (16–28)	17 (13–26)	0.313	20 (16–28)	22 (16–28)	0.858
Psychiatric comorbidities															
None	45 (61.6%)	8 (29.6%)		47 (58.0%)	6 (31.6%)		46 (60.5%)	7 (29.2%)		53 (56.4%)	0 (0%)		45 (61.6%)	8 (29.6%)	
One	25 (34.3%)	14 (51.9%)		30 (37.0%)	9 (47.4%)		27 (35.5%)	12 (50%)		36 (38.3%)	3 (50%)		25 (34.3%)	14 (51.9%)	
Two or more	3 (4.1%)	5 (18.5%)	0.004	4 (4.9%)	4 (21.1%)	0.024	3 (3.9%)	5 (20.8%)	0.007	5 (5.3%)	3 (50%)	0.001	3 (4.1%)	5 (18.5%)	0.004
Anxiety															
No	58 (79.4%)	19 (70.4%)		63 (77.8%)	14 (73.7%)		61 (80.3%)	16 (66.7%)		73 (77.7%)	4 (66.7%)		58 (79.5%)	19 (70.4%)	
Yes	15 (20.6%)	8 (29.6%)	0.423	18 (22.2%)	5 (26.3%)	0.764	15 (19.7%)	8 (33.3%)	0.176	21 (22.3%)	2 (33.3%)	0.619	15 (20.5%)	8 (29.6%)	0.423
Depression															
No	64 (87.7%)	18 (66.7%)		71 (87.7%)	11 (57.9%)		65 (85.5%)	17 (70.8%)		79 (84%)	3 (50%)		64 (87.7%)	18 (66.7%)	
Yes	9 (12.3%)	9 (33.3%)	0.021	10 (12.3%)	8 (42.1%)	0.006	11 (14.5%)	7 (29.2%)	0.129	15 (16%)	3 (50%)	0.070	9 (12.3%)	9 (33.3%)	0.021

C-SSRS (dichotomized into 0 vs. ≥ 1) was used as parameter to evaluate the presence of suicidality

associated comorbidities. In detail anxiety was found as isolated comorbidity in 17/47 patients (36%) and depression in 25% of patients. The other isolated comorbidities were less representative, and are described in detail in Table 6. There were no significant differences in the frequency of psychiatric comorbidities between R-AN and A-AN patients (results not shown).

Of the 27 patients showing suicidality, a total of 19 (70.4%) presented at least one psychiatric comorbidity associated with AN. Patients with any psychiatric comorbidity associated with AN reported suicidality more often than those without psychiatric comorbidity (p value = 0.004) (Table 5). Suicidality was more frequent and statistically significant only among patients with depression (p value = 0.021) (Table 5). This result was not confirmed for patients with anxiety, the other most representative comorbidity in our sample (Table 5).

Discussion

In this paper, we aimed to study suicidality and the correlation with severity of AN-specific symptoms and psychiatric comorbidity, in a group of adolescents at the onset of AN. It is known that suicide represents a major health risk among AN patients [31], however, unlike for patients with bulimia nervosa or binge eating disorders [32, 33], there is limited evidence on the prevalence of suicidal behaviours among adolescents with recent onset AN, and this was the rationale for our decision to focus on this particular subset of patients.

Table 6 Detailed description of psychiatric comorbidities associated with AN

Type of psychiatric comorbidity	No of patients (%)
Psychiatric comorbidity in general	n = 47 (47)
One psychiatric comorbidity	n = 39 (39)
Two or more psychiatric comorbidities	n = 8 (8)
Anxiety	n = 17 (17)
Depression	n = 12 (12)
Obsessive compulsive disorder (OCD)	n = 5 (5)
Mood disorder not otherwise specified (MDNOS)	n = 1 (1)
Bipolar disorder (BP)	n = 1 (1)
Post-traumatic stress disorder (PTSD)	n = 1 (1)
Gender dysphoria (GD)	n = 1 (1)
Other psychiatric comorbidities	n = 1 (1)
Anxiety and depression	n = 4 (4)
Anxiety and MDNOS	n = 1 (1)
Anxiety and GD	n = 1 (1)
Depression and PTSD	n = 1 (1)
Depression, OCD, and other psychiatric comorbidities	n = 1 (1)

In addition, we tried to understand if patients with A-AN, had a milder suicidality compared to R-AN patients: while A-AN is increasingly being considered as a form of anorexia possibly as severe as the typical, restrictive forms of it [34], more evidence is useful to further substantiate this view.

In our study, 27% of patients showed suicidality, which was related to AN psychopathology (drive for thinness, body dissatisfaction, low self-esteem, personal and interpersonal alienation, interpersonal insecurity, emotional dysregulation, and perfectionism) regardless of diagnosis (R-AN or A-AN). This is fairly in line with literature data [35–37], although it should be highlighted that a peculiarity of our study is the lack of association between underweight and suicidal behaviours. Instead, a clear link emerged between the suicidality and the psychiatric comorbidity. Patients with any psychiatric comorbidities associated with AN reported suicidality significantly more often than those without psychiatric comorbidities (70.4% vs 29.6%). When examining the different types of psychiatric comorbidities, suicidality was found to be significantly more frequent only among patients with depression. Instead, there was no evidence that suicidal behaviours were associated with anxiety, which was only slightly less frequent than depression in our study population. These data do not surprise us, as it is clear that depressive symptoms can increase the individual's alienation from himself and others, thus contributing to increasing suicidal ideation and behaviour [38]. Overall, these findings are of clinical interest as they can help doctors identify the subset of patients who are more likely to present suicidal behaviours and who need, therefore, closer care. Notably, there were no differences in the prevalence of both psychiatric comorbidities and suicidality between patients with R-AN or A-AN, confirming that the latter form should not be considered as a milder form of disease, at least as regards the prevalence of suicidality [39–41].

Our results could partially be explained through the Interpersonal Psychological Theory of Suicide (IPTS) [42, 43]. The IPTS poses that the ability to die from suicide builds up over time through repeated experiences with painful and/or frightening events, which progressively lead to a habit of pain and fear [16]. The frequent involvement of patients with AN in painful stimuli (dietary restriction) associated with a sense of ineffectiveness, interpersonal and emotional problems, general psychological discomfort, may eventually enhance one's suicide capacity. In line with this theory and according to recent literature [44], feeling a burden for others and the lack of sense of belonging in AN patient seem to be able to increase the insensitivity to pain and subsequent suicidal risk. The IPTS may be especially relevant for patients who are older of those included in our study (i.e., adults instead of adolescents at an early AN stage), since time is needed, according to this theory, to acquire the capability of suicide. Since, however, interpersonal difficulties

and comorbid psychiatric symptoms gradually worsen as the disease progresses, assessing the severity and implication of these factors in patients at symptoms onset may help shed light on how AN and suicidal behaviours develop over one's lifetime (i.e., in the transition from adolescent to early adulthood), and could have significant clinical and treatment implications.

Strength and limits

Our study also has limitations, particularly its retrospective nature, the limited sample size and variability (e.g., with a limited number of males included), the use of BMI at first encounter for ED evaluation (instead of repeated measurements of it or lowest lifetime BMI), and some others, which all limit the generalizability of our conclusions. A carefully designed prospective study, with a larger study size, a wider age distribution and a good representativeness of both sexes, aiming to evaluate treatment outcomes in patients diagnosed with R-AN or A-AN at onset of symptoms would be helpful in filling some of the gaps still existing in the scientific literature on the topics. Finally, while we were especially interested in restrictive AN because these were less studied in the scientific literature, future studies may want to extend the focus to binge-purging AN as well, to have a broader picture of individuals with the different types of AN:

What is already known on this individuals?

It is already known the linkage between AN and suicide, without specific correlation with A-AN in adolescent population.

What this study adds?

This study provides new information on the association between A-AN and suicidality among adolescents. The scientific literature on suicidality among adolescents with A-AN is still sparse. Our findings highlight that clinicians should keep in mind the importance of studying suicidality and considering suicidal risk in all patients with onset of AN, particularly in those who have psychiatric comorbidities, independent from the severity of underweight. These considerations have significant clinical applications, as they could improve the care pathways of patients with AN, improve symptoms and reduce the risk of suicide. By having it clear that it is necessary to investigate suicidal behaviours at the very onset of AN symptoms (regardless of the degree of underweight), treating doctors may improve their ability to care for these patients and effectively prevent suicide attempts and complete suicide. Thus, we believe that our findings have significant clinical applications, highlighting the importance of screening for suicidal risk among adolescent patients with AN, particularly those who have psychiatric comorbidities.

Conclusions

We observed that suicidality among patients with AN is associated with the severity of AN symptoms (as assessed by means of the EDI-3 questionnaire) and with the psychiatric comorbidity, regardless of underweight. We remark the concept that A-AN should not be considered as a milder form of AN, and we highlight the importance to evaluate suicidal risk in adolescents at onset of R-AN and A-AN.

Author contributions All authors contributed to the study conception and design. Material preparation and data collection were performed by TF, ST ER, and FM: The first draft of the manuscript was written by AM and TF: and all authors commented on previous versions of the manuscript. Conceptualisation, review, supervision and, editing were performed by TP and SL: Statistical analysis, review, and editing were performed by SC: all authors read and approved the final manuscript.

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Data availability The dataset generated during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. The study was approved by the Pediatric Ethics Committee of the Tuscany Region. 2nd August 2021/ N°AN2021.

Informed consent Written informed consent was obtained from the parents.

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