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A prospective observational study comparing rates of medical instability between adolescents with typical and atypical anorexia nervosa

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Abstract

Background: Recognition of atypical anorexia nervosa (AAN) has challenged underweight as a defining factor of illness severity in anorexia nervosa (AN). The present study aimed to compare rates of medical instability in adolescents with underweight (AN) and non-underweight (AAN) anorexia nervosa.

Methods: The study examined assessment data from specialist eating disorder services in the UK between January and December 2022. Participants ($n = 205$) aged 11–18 years were recruited across eight eating disorder clinics and diagnosed with AN ($n = 113$) or AAN ($n = 92$) after clinical assessment. Parameters associated with risk of medical instability were compared between AN and AAN groups, using t tests and regression analysis.

Results: Rates of bradycardia and hypotension did not differ significantly between AN and AAN groups ($p = 0.239$ and $p = 0.289$). Although white blood cell counts were lower in the AN group, rates of leukopaenia could not be statistically compared as a result of there being too few counts in at least one group. No incidences of hypophosphataemia were found in the sample. A significant regression equation was found for percentage median body mass index, but not rate of weight loss, as a predictor of blood pressure, serum phosphorous and magnesium.

Conclusions: Our findings indicate that medical instability occurs across a range of body weights in young people with AN and AAN. Although certain parameters of risk such as blood pressure, serum phosphorous and magnesium may be worsened at lower weight, both AN and AAN are serious mental health conditions that can lead to medical instability.

KEYWORDS

anorexia nervosa, eating disorders, malnutrition, medical instability, mental health

Funding information
None

Highlights

- The study compared rates of medical instability in adolescents with underweight (AN) and non-underweight (AAN) anorexia nervosa.
- The findings support the conclusion that, although certain parameters of risk (e.g., blood pressure) may be worsened by lower weight, both AN and AAN are serious illnesses that can lead to medical compromise.

INTRODUCTION

Atypical anorexia nervosa (AAN) describes patients resembling all characteristics of anorexia nervosa (AN), but, despite having lost significant amounts of weight, they are not clinically underweight [1,2]. The 5th Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) lists AAN as an example under the Otherwise Specified Feeding and Eating Disorders (OSFED) diagnostic category [2]. In comparison, the first medical descriptions of anorexic illness date back to 1689, with AN becoming widely recognised and accepted by the medical profession over a century ago, and it was first listed in the DSM in the 1950s [3,8]. A core feature, common to both AAN and AN, is an intense fear of weight gain that drives potentially harmful weight control behaviours, such as severe dietary restriction, self-induced vomiting, excessive exercise and abuse of medications (e.g., laxatives or diuretics) [4,5]. Traditionally, degree of underweight was recognised as the definitive factor of illness severity in AN [6,7]. However, recognition of AAN, has challenged this definition with rapid weight loss being identified as a predictor of medical risk, independent of underweight [6,8,9].

Cardiovascular complications and electrolyte disturbances are common causes of medical instability in AN and AAN[10–12]. Bradycardia and hypotension are both well-established consequences of starvation[13,14]. In low body weights, or bodies that have lost significant weight, bradycardia is explained by mechanisms such as parasympathetic predominance, increased or decreased intracardiac glycogen stores and myocardial atrophy causing structural changes[15,16]. Hypotension results from purging or insufficient food and fluid intake, causing reduced blood volume or autonomic dysfunction related to disturbances in key hormones. Hypotension can also result from low electrolyte concentration, leading to low concentration gradient and loss of circulating blood volume[17,18]. Cardiovascular complications leading to medical instability have been shown to affect up to 80% of adolescents with AN and AAN[16].

Deranged biochemical parameters are also often observed in both AN and AAN, and are caused by malnutrition, dehydration and eating disorder related behaviours such as purging and misuse of medications (e.g., diuretics or laxatives)[19]. Common abnormalities reported in the literature include hypokalaemia (related to purging)[20] and leukopaenia[21]. Hyponatraemia, hypomagnesaemia, hypocalcaemia and hypoglycaemia also often occur as a result of malnutrition and disordered behaviours employed in AN and AAN to manage weight[20]. Leukopaenia is well described in children with protein-energy malnutrition, as a result of suppression of the production of the haematopoietic cells in the bone marrow [22].

Rates and severity of physical and psychological morbidity in AAN have been described and compared to that of AN [4,5,8]. Similar rates of cardiac complications, electrolyte disturbances and eating disorder cognitions have been reported in adolescents with AAN, with comparable severity of symptoms as observed in AN [23,24]. Research studies that have focused on the comparison of AN and AAN have identified rapid weight loss as one of the defining factors of increased medical risk in the absence of being underweight [4,9,23]. Recognition and treatment of AAN poses challenges because of the historic reliance on low weight as the primary indicator of malnutrition and increased medical risk [25].

The number of adolescents being diagnosed with AAN is growing, and approximately one-third of adolescents presenting to eating disorder services have a history of overweight or obesity [9,26]. Historically, eating disorders in adolescents presenting to specialist services in larger bodies have been missed and treatment has been delayed. These adolescents are at risk of poorer clinical outcomes as a result of delays in diagnosis [27]. Kennedy et al.[28] found that adolescents with a history of overweight took 10 months longer to be diagnosed with an eating disorder compared to those without. Improved awareness of AAN among care providers has been recommended, and the perception that adolescents with AAN are less unwell challenged in line with current evidence showing similar rates of medical and psychiatric morbidity [26].

Advancements in research in AAN have confirmed that risks, including medical and psychiatric, are not limited to the underweight [4,8,26]. Recommendations for future work have focused on exploration of the physical risks arising in adolescent AAN [9,16,23]. Further research is essential in this area to help clinicians to develop a greater understanding of the medical risks arising in the absence of underweight and to ensure that adolescents with AAN are not missed by eating disorder services. The present study aims to compare rates of medical instability in adolescents with AAN and AN.

The hypothesis that medical instability can occur in the absence of underweight (i.e., in adolescents with AAN) was tested.

METHODS

Sample

Participants were prospectively recruited from eight child and adolescent outpatient eating disorders services in London. Inclusion criteria were age 11–18 years, diagnosis of AN or AAN and first episode of eating disorder treatment (i.e., those who had previously received a diagnosis and/or treatment for AN or AAN were excluded). Eating disorder diagnosis was made by clinician assessment at specialist outpatient eating disorder services by a multidisciplinary team comprising of psychologists, psychiatrists, nurses, dietitians and family therapists. Patients meeting full criteria as per the Diagnostic and Statistical Manual, version 5, or the International Classification of Diseases Manual, version 10, including the presence of significant underweight were diagnosed with AN, those meeting criteria but in the absence of significant underweight, were diagnosed with Otherwise Specified Feeding and Eating Disorder and classified as AAN.

Percentage median body mass index (%mBMI) between 95% and 105% is the expected normal weight range for children and adolescents; below this range is classed as underweight and above this range is typically classed as overweight. In the previous DSM-IV, AN diagnosis in those under 18 years of age, was limited to those considered to be significantly underweight, with mBMI < 85% being listed as an example of this[29]. The DSM-5 does not identify a weight threshold for AAN and, as such, mBMI > 85% was used in the present study. Patients were excluded if they had a comorbid physical health condition, were presenting for a subsequent episode of treatment, or did not receive a diagnosis of AN or AAN.

Research governance

Ethics approval was sought through the Integrated Research Application System. The study was approved by the Health Research Authority following successful Research Ethics Committee review (study identification number 298190). The research and development review boards at each site reviewed and provided local approval for the study.

Data collection

Patients assessed between January 2022 and December 2022, and meeting inclusion criteria were recruited to the study. Two trained researchers on each site collected data and recorded this on standardised proformas which was then checked by the main researcher for quality assurance. Data were collected at the initial assessment with the specialist eating disorders team. Data collected included demographic and clinical characteristics including weight (kg), weight loss rate per week prior to the initial assessment, and cardiovascular and biochemical parameters (Table 1). Weight loss rate (kg per week) was defined as average weight lost per week (kg) in the months (i.e., for all participants, this was a minimum of 1 month and maximum of 3 months) leading up to the eating disorder assessment. Sample size, means and standard deviations were described for each parameter. Parameters and references ranges were informed by UK national guidance (MEED report) for eating disorders [30]. The MEED report contains a risk assessment tool whereby parameters associated with increasing risk of medical instability and reference ranges are stated. This tool is intended to guide clinician level of concern regarding acute medical risk. In cases where reference ranges were absent from guidance, international published eating disorder guidance was used to inform ranges [31].

Analysis plan

Data were recorded and entered into SPSS, version 28 (IBM Corp., Armonk, NY, USA). Two independent groups were created: these were adolescents diagnosed with AN and those diagnosed with AAN at the initial assessment. Participants with missing data were excluded from statistical tests. A Shapiro–Wilk test was used to determine whether data were normally distributed and Levene's test for homogeneity of variance was used to identify whether normally distributed variables had equal variance across groups. Independent samples *t* tests were used to compare mean differences between groups for those normally distributed variables, whereas the Mann–Whitney *U* test compared variables that did not follow normal distribution. The Bonferroni test was applied to correct for multiple comparisons in *t* tests as a result of the increased risk of type 1 errors. Effect size of significant results was reported using Cohens classification: $d = 0.2$ (small), $d = 0.5$ (medium) and $d > 0.8$ (large).

Parameters of medical compromise and instability were compared between AN and AAN groups. Parameters analysed were; bradycardia (heart rate < 60 beats/min), severe bradycardia (heart rate < 40 beats/min), hypotension (systolic blood pressure < 90 mmHg), hypothermia (temperature < 35.5°C), hypoglycaemia (serum glucose < 3.0 mmol/L), hypophosphataemia (serum phosphorous < 0.8 mmol/L), hypocalcaemia (serum calcium < 2.2 mmol/L), hypomagnesaemia (serum magnesium < 0.6 mmol/L), hypokalaemia (serum potassium < 3.0 mmol/L) and leukopaenia (white blood cell [WBC] count $< 3.8 \times 10^9$/L).

Pearson correlation was used to identify the strength of association between variables. Simple linear regression models were used to analyse parameters with significant

TABLE 1 Comparison of physical health parameters of adolescents with anorexia nervosa (AN) to those with atypical anorexia nervosa (AAN).

	AN ($n = 113$)		AAN ($n = 92$)		
	Mean ± SD	*n* (%)	Mean ± SD	*n* (%)	*p*
Age (years)	14.8 ± 0.2	108 (96)	14.7 ± 0.2	92 (100)	0.263
Gender					
Male	–	4 (4)	–	6 (7)	–
Female	–	109 (96)	–	86 (93)	–
mBMI (%)	76.9 ± 0.6	108 (96)	95.3 ± 1.0	91 (99)	< 0.001
Weight loss (kg/week)	0.7 ± 0.1	68 (60)	0.7 ± 0.1	48 (52)	0.168
Intake (kcal/day)	840 ± 51	86 (76)	735 ± 50	70 (76)	0.105
Fluid intake (ml/day)	1182 ± 86	62 (55)	1437 ± 103	55 (60)	0.072
Temperature (°C)	36.3 ± 0.1	41 (36)	36.4 ± 0.1	23 (25)	0.381
Hypothermia (<35.5°C)	35.2 ± 0	1 (2)	35.1 ± 0	1 (4)	–
QTc (ms)	406 ± 6	17 (15)	387 ± 7	15 (16)	0.038
Heart rate (beats/min)	68 ± 1.8	72 (64)	73 ± 1.7	66 (72)	0.024
Bradycardia (<60 beats/min)	52 ± 5	22 (31)	50 ± 2	11 (17)	0.239
Severe bradycardia (<40 beats/min)	–	0 (0)	36 ± 0	1 (2)	–
Blood pressure (mmHg)	103 ± 1.3	72 (64)	111 ± 1.4	72 (78)	< 0.001
Hypotension (<90 mmHg)	87 ± 3	14 (10)	85 ± 2	2 (3)	0.298
Glucose (mmol/L)	4.4 ± 0.2	36 (32)	4.3 ± 0.1	26 (28)	0.915
Hypoglycaemia (<3.0 mmol/L)	2.8 (0)	2 (6)	2.6 (0)	1 (4)	–
Phosphate (mmol/L)	1.3 ± 0.1	44 (39)	1.3 ± 0.1	37 (40)	0.126
Hypophosphataemia (<0.8 mmol/L)	–	0 (0)	–	0 (0)	–
Calcium (mmol/L)	2.4 ± 0.1	47 (42)	2.4 ± 0.1	40 (44)	0.378
Hypocalcaemia (<2.2 mmol/L)	1.9 ± 0.5	4 (7)	2.1 ± 0.1	2 (3)	–
Magnesium (mmol/L)	0.9 ± 0.1	39 (35)	0.8 ± 0.1	35 (38)	0.057
Hypomagnesaemia (<0.6 mmol/L)	4.2 ± 0.1	49 (43)	4.2 ± 0.1	44 (48)	0.911
Potassium (mmol/L)	–	0 (0)	–	0 (0)	–
Hypokalaemia (<3.0 mmol/L)	1.0 ± 0	1 (3)	–	0 (0)	–
WBC ($\times 10^9$/L)	4.9 ± 0.3	31 (27)	5.8 ± 0.3	26 (28)	0.028
Leukopaenia ($<3.8 \times 10^9$/L)	3.4 ± 0.50	8 (26)	3.5 ± 0	1 (4)	–

Note. Bonferroni adjusted critical $p < 0.003$.

Abbreviations: AN, anorexia nervosa; AAN, atypical anorexia nervosa; WBC, white blood cell count.

correlations. Missing data were coded and excluded from the analysis by pairwise deletion. $p < 0.05$ (corrected for all ties) was considered statiutically significant for all tests.

RESULTS

Demographic and physical health parameters

Data were collected from participants ($n = 205$) at first presentation to their local eating disorder services. Parameters of adolescents diagnosed with AN ($n = 113$) were compared with those diagnosed with AAN ($n = 92$) (Table 1). After correcting for multiple comparisons using the Bonferroni test, the critical p value was adjusted to $p < 0.003$.

Adolescents with AN by definition had significantly lower percentage mBMIs, with large effect size (76.9% vs. 95.3%, $p < 0.001$, $d = 2.326$). The mean age, rate of weight loss, and dietary and fluid intake, did not differ significantly between groups. Mean systolic blood pressure and mean heart rate were significantly lower in

TABLE 2 Correlations between clinical parameters and weight parameters of adolescents with both anorexia nervosa (AN) and atypical anorexia nervosa (AAN).

	Percentage median BMI (%)			Rate of weight loss (kg/week)		
	n	*r*	*p*	*N*	*r*	*p*
Temperature	63	0.844	0.025	42	0.107	0.501
QTc	32	−0.255	0.158	20	−0.267	0.255
Blood pressure	142	0.313**	<0.001*	95	−0.179	0.082
Heart rate	137	0.162	0.059	91	0.023	0.829
WBC	54	0.237	0.084	38	−0.061	0.717
Phosphate	78	0.246*	0.030*	55	−0.105	0.446
Glucose	61	−0.012	0.928	41	−0.021	0.895
Calcium	84	0.048	0.667	58	0.185	0.165
Magnesium	72	−0.247*	0.037	50	−0.202	0.159
Potassium	91	0.093	0.380	93	−0.131	0.302

Abbreviations: *r*, correlation coefficient; WBC, white blood cell count.

the AN group compared to the AAN group, with a medium effect size for both parameters (103 vs. 111 mmHg, $p < 0.001$, $d = 0.623$ and 68 vs. 73bpm, $p = 0.024$, $d = 0.645$). Although mean WBC count was significantly lower in the AN group compared to the AAN group (4.9 vs. 5.8 $\times 10^9$/L, $p = 0.028$), there were too few counts in the AAN group to statistically compare rates of leukopaenia between groups. No significant differences were found between groups in all other clinical parameters.

Rates of medical instability

Rates of medical instability were compared between AN and AAN groups (Table 1). One participant in each group had hypothermia. Rates of bradycardia did not differ significantly between AN and AAN groups ($p = 0.239$). One participant in the AAN group had severe bradycardia (HR = 36 beats/min). Rates of hypotension did not differ significantly between groups ($p = 0.289$) and rates of leukopaenia could not be statistically compared as a result of there being less than five counts in at least one group. No incidences of hypophosphataemia or hypomagnesaemia were found in the sample, and there were no significant differences in rates of hypoglycaemia. Rates of hypocalcaemia and hypokalaemia could not be compared due to there being too few counts in one or more groups.

Predictors of medical instability

A Pearson correlation was used to determine the relationship between clinical parameters and weight parameters (%mBMI and rate of weight loss) (Table 2). The percentage mBMI was positively correlated with blood pressure ($r = 0.313$, $p < 0.001$) and serum phosphorous (r = 0.246, $p = 0.030$), and negatively correlated with serum magnesium (r = −0.247, $p = 0.037$). No significant correlations were found between other variables and % mBMI. No correlations were identified between rate of weight loss and clinical parameters.

A simple linear regression was calculated to predict blood pressure, serum phosphorous and magnesium based on %mBMI. The linear regression was also calculated for these parameters based on rate of weight loss (Table 3). A significant regression equation was found for %mBMI as a predictor of blood pressure, serum phosphorous and magnesium. No significant regression equation was found for rate of weight loss as a predictor of any clinical parameters analysed.

DISCUSSION

The findings of the present study not only suggest several similarities, but also key differences in the rates of medical stability and compromise in adolescents presenting to eating disorder services with AN and AAN. Medical instability was observed in both AN (underweight) and AAN (non-underweight) groups, although certain parameters of risk were predicted by decreasing %mBMI.

Cardiovascular complications are well reported in adolescent AN and AAN [15,32,33]. Bradycardia and hypotension are common symptoms, observed in up to 40% of adolescent inpatients. This is caused by the profound parasympathetic predominance of low body weights, or bodies that have lost significant amounts of weight [14].

TABLE 3 Linear regression analysis of weight parameters as predictors of blood pressure, serum phosphorous and magnesium in adolescents with typical and atypical anorexia nervosa.

	Blood pressure (mmHg)					Serum phosphorous (mmol/L)					Serum magnesium (mmol/L)				
Variables	***B***	**SE**	**Beta**	***t***	***p***	***B***	**SE**	**Beta**	***t***	***p***	***B***	**SE**	**Beta**	***t***	***p***
%mBMI	0.301	0.770	0.313	3.902	<0.0001	0.003	0.001	0.246	2.217	0.030	−0.001	0.001	−0.247	−2.132	0.037
Weight loss	−4.038	2.300	−0.179	−1.756	0.082	−0.027	0.036	−0.105	−0.768	0.446	−0.030	0.021	−0.202	−1.430	0.159

Note: *B,* unstandardised coefficients; Beta, standardised coefficients; *t*, test statistic; significance, $p < 0.05$; %mBMI, percentage median body mass index; weight loss is kg/week.

Although higher incidences of hypotension and orthostatic changes have been observed in underweight adolescents with AN [24,25,34], non-underweight adolescents with AAN also frequently present with these symptoms [4,26]. In the present study, modest rates of bradycardia ($n = 33$) and very low rates of severe bradycardia ($n = 1$) were observed in the overall sample. No significant differences were identified between AN and AAN groups in rates of bradycardia. Significantly lower blood pressures were observed in the AN group compared to the AAN group. The findings of the present study mirror those of previous research, with significant underweight increasing risk of lower blood pressure in adolescents with AN [35], but with overall rates of cardiovascular complications being similar between groups.

Biochemical derangements are frequently reported in low weight adolescents with AN [5,8]. Between 29% and 39% of patients with AN have been observed to present with leukopaenia [36]. Leukopaenia has been related to changes in the bone marrow, such as bone marrow atrophy, that result from chronic malnutrition in AN [37]. In this sample, underweight adolescents with AN had significantly lower mean white blood cell counts than those with AAN, supporting current research highlighting chronic malnutrition as a key factor leading to low white blood cell count. Although those with AN were also observed to have greater rates of leukopaenia, groups could not be statistically compared as a result of their being too few counts in at least one group.

Hypophosphataemia typically occurs in adolescents with AN or AAN as a consequence of refeeding syndrome (RS). RS is a potentially fatal clinical condition that can occur during the nutritional rehabilitation of malnourished patients with AN,[38] its hallmark feature is hypophosphataemia [39]. Studies that have examined rates of RS in adolescents with AN have identified hypophosphataemia in 6%–22% of subjects [40]. Adolescents with <70% mBMI have been identified as being at significantly greater risk of developing this symptom compared to those of higher weights.[40,41] In the present study, although no significant differences were identified between AN and AAN groups in serum phosphorus, and no participants presented with hypophosphataemia, lower %mBMI did predict decreasing serum phosphorus. Our findings support the hypothesis that rates of hypophosphataemia are low in this patient group, and that those at lowest weights are at greatest risk of the complication.

Over the past decade, greater magnitude and speed rate of weight loss has received much attention as a predictor of physical risk in AAN, independent of other factors.[5,6,9,23] Current research studies on this topic, comparing these two diagnostic groups, have reported upon the significance of rate and amount of weight loss when assessing physical risk.[9,23] Whitelaw et al.[9] compared total weight loss and recent weight loss to admission weight as predictors of physical risk in adolescents with AN and AAN, and concluded that a greater total or recent weight loss was a stronger predictor of many physical complications that cause hospital admission than admission weight. Similarly, Garber et al.[23] also found that a history of weight loss was associated with markers of malnutrition across a range of body weights, independent of underweight status.

In the present study, the findings support our hypothesis that medical instability occurs in the absence of underweight in adolescents with AAN. One crucial difference between the findings from our study and those of other recent research is the absence of significant difference between rates of weight loss between AN and AAN groups within our sample. Furthermore, our sample was recruited in the outpatient setting, where illness severity is typically lower. Previous research studies that highlight similarities in risks associated with AN and AAN have been predominantly based in the inpatient setting.

A key strength of the present study was its large sample size, with data being collected from a number of sites. The study also had a number of limitations, such as the large volume of missing data. Missing data were removed by pairwise deletion from all analysis to reduce the effect of this limitation on the power of the study results. Similarly, data related to weight loss did not consider total lifetime weight loss or history of premorbid overweight or obesity. Because only recent weight loss was recorded, the study could only investigate this parameter in relation to the effect of weight loss rate on physical risk. Ethnicity was not collected for the sample, which may also have impacted the study's results as a result of possible %mBMI cutoffs differing across different ethnicities. Weight parameters used within the study do not consider individual differences, such as ethnicity. Because of the small number of males present

in the sample, the results may or may not be applicable to males with AN or AAN.

CONCLUSIONS

We conclude that physical risk assessment should not be limited to the underweight young people with AN. Medical instability can occur across a range of body weight, although certain parameters of risk are predicted by %mBMI and are worsened by lower weight. Further research is required to investigate the differences in presentation between diagnoses and to guide evidence-based treatment in AN and AAN.

ETHICAL STATEMENT

Ethics approval was sought through the Integrated Research Application System. The study was approved by the Health Research Authority following successful Research Ethics Committee review (study identification number 298190). The research and development review boards at each site reviewed and provided local approval for the study.

AUTHOR CONTRIBUTIONS

Cliona Brennan was responsible for conception and design of the study, recruitment of participants, data collection and analysis, and preparation of drafts and final versions of the manuscript and associated tables and documents. Dee Bhakta contributed to the conception, design and supervision of the study, as well as editing of the draft and final manuscript and tables. Mima Simic, Sarah Illingworth, Erica Cini, Simon Chapman, Dasha Nicholls and Victoria Chapman contributed to the design and supervision of the study, as well as the editing of the final manuscript. Ellen Hayes, Sarah Fuller, Jade Orpwood, Nicola Tweedy, Tahmida Baksh, Conor Simms, and Emma Astaire were responsible for the recruitment of participants, collection of study data and editing the final draft of the manuscript.

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CONFLICTS OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

TRANSPARENCY DECLARATION

The lead author affirms that this article is an honest, accurate and transparent account of the study being reported.

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PEER REVIEW

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REFERENCES

1. Hay P. Current approach to eating disorders: a clinical update. Intern Med J. 2020;50(1):24–9.
2. The American Psychiatric Association. The diagnostic and statistical manual of mental disorders. 5th ed. 2013. pp. 307.
3. Dell'Osso L, Abelli M, Carpita B, Pini S, Castellini G, Carmassi C, et al. Historical evolution of the concept of anorexia nervosa and relationships with orthorexia nervosa, autism, and obsessive-compulsive spectrum. Neuropsychiatr Dis Treat. 2016; 12:1651–60.
4. Vo M, Golden N. Medical complications and management of atypical anorexia nervosa. J Eat Disord. 2022;10(1):4–9. https://doi.org/10.1186/s40337-022-00720-9
5. Brennan C, Illingworth S, Cini E, Bhakta D. Medical instability in typical and atypical adolescent anorexia nervosa: a systematic review and meta-analysis. J Eat Disord. 2023;11(1):58.
6. Neale J, Hudson LD. Anorexia nervosa in adolescents. Br J Hosp Med. 2020;81(6):1–8.
7. Norrington A, Stanley R, Tremlett M, Birrell G. Medical management of acute severe anorexia nervosa. Archiv Dis Childhood Educ Pract Ed. 2012;97(2):48–54.
8. Walsh BT, Hagan KE, Lockwood C. A systematic review comparing atypical anorexia nervosa and anorexia nervosa. Int J Eat Disord. 2022;56:798–820.
9. Whitelaw M, Lee KJ, Gilbertson H, Sawyer SM. Predictors of complications in anorexia nervosa and atypical anorexia nervosa: degree of underweight or extent and recency of weight loss? J Adolesc Health. 2018;63(6):717–23. https://doi.org/10.1016/j.jadohealth.2018.08.019
10. Hudson LD, Nicholls DE, Lynn RM, Viner RM. Medical instability and growth of children and adolescents with early onset eating disorders. Arch Dis Child. 2012;97(9):779–84.
11. Bako A, Yeo M, Sawyer SM, Hughes E. 98. How low can you go? The significance of bradycardia for acute clinical outcomes in hospitalised adolescents with anorexia nervosa. J Adolesc Health. 2019;64(2):S52. https://doi.org/10.1016/j.jadohealth.2018.10.114
12. Golden NH, Keane-Miller C, Sainani KL, Kapphahn CJ. Higher caloric intake in hospitalized adolescents with anorexia nervosa is associated with reduced length of stay and no increased rate of refeeding syndrome. J Adolesc Health. 2013;53(5):573–8. https://doi.org/10.1016/j.jadohealth.2013.05.014
13. Costa J, Moreira A, Moreira P, Delgado L, Silva D. Effects of weight changes in the autonomic nervous system: a systematic review and meta-analysis. Clin Nutr. 2019;38(1):110–26.
14. Chidiac CW. An update on the medical consequences of anorexia nervosa. Curr Opin Pediatr. 2019;31(4):448–53.
15. Morris R, Prasad A, Asaro J, Guzman M, Sanders L, Hauck A, et al. Markers of cardiovascular dysfunction in adolescents with anorexia nervosa. Glob Pediatr Health. 2017;4:2333794X1772742.
16. Assalone C, Leonardi L, Franceschi R, Fumanelli J, Maines E, Marini M, et al. Determinants of severe bradycardia in

adolescents hospitalized for anorexia nervosa. Pediatr Int. 2022;64(1):e14967.
17. Mehler PS, Brown C. Anorexia nervosa—medical complications. J Eat Disord. 2015;3(1):11.
18. Quesnel DA, Cooper M, Fernandez-del-Valle M, Reilly A, Calogero RM. Medical and physiological complications of exercise for individuals with an eating disorder: a narrative review. J Eat Disord. 2023;11(1):1–18. https://doi.org/10.1186/s40337-022-00685-9
19. Katzman DK. Medical complications in adolescents with anorexia nervosa: a review of the literature. Int J Eat Disord. 2005;37(SUPPL):S52–9.
20. Winston AP. The clinical biochemistry of anorexia nervosa. Ann Clin Biochem Int J Lab Med. 2012;49(2):132–43.
21. Gibson D, Watters A, Cost J, Mascolo M, Mehler PS, et al. Extreme anorexia nervosa: medical findings, outcomes, and inferences from a retrospective cohort. J Eat Disord. 2020;8(1):25.
22. Getawa S, Getaneh Z, Melku M. Hematological abnormalities and associated factors among undernourished under-five children attending University of Gondar Specialized Referral Hospital, Northwest Ethiopia. J Blood Med. 2020;11:465–78.
23. Garber AK, Cheng J, Accurso EC, Adams SH, Buckelew SM, Kapphahn CJ, et al. Weight loss and illness severity in adolescents with atypical anorexia nervosa. Pediatrics. 2019;144(6):e20192339.
24. Sawyer SM, Whitelaw M, Le Grange D, Yeo M, Hughes EK. Physical and psychological morbidity in adolescents with atypical anorexia nervosa. Pediatrics. 2016;137(4):e20154080.
25. Whitelaw M, Gilbertson H, Lee KJ, Sawyer SM. Restrictive eating disorders among adolescent inpatients. Pediatrics. 2014;134(3):e758–64.
26. Freizinger M, Recto M, Jhe G, Lin J. Atypical anorexia in youth: cautiously bridging the treatment gap. Children. 2022;9(6):837.
27. Lebow J, Sim LA, Kransdorf LN. Prevalence of a history of overweight and obesity in adolescents with restrictive eating disorders. J Adolesc Health. 2015;56(1):19–24. https://doi.org/10.1016/j.jadohealth.2014.06.005
28. Kennedy GA, Forman SF, Woods ER, Hergenroeder AC, Mammel KA, Fisher MM, et al. History of overweight/obesity as predictor of care received at 1-year follow-up in adolescents with anorexia nervosa or atypical anorexia nervosa. J Adolesc Health. 2017;60(6):674–9.
29. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (4th ed., Text Revision). 4th ed. 2000.
30. Royal College of Psychiatrists. CR 233: Medical emergencies in eating disorders (MEED) Guidance on recognition and management. 2022;(May):185. Available from: https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr233-medical-emergencies-in-eating-disorders-(meed)-guidance.pdf?sfvrsn=2d327483_50
31. Cini E, Cuntz U, Westphal B, Voderhozer U, Garber A. Emergency and general hospital treatment for eating disorders. In: Robinson P, Wade T, Herpertz-Dahlmann B, Fernandez-Aranda F, Treasure J, Wonderlich S, editors. Eating disorders: an international comprehensive view. 1st ed. Springer; 2023.
32. Spaulding-Barclay MA, Stern J, Mehler PS. Cardiac changes in anorexia nervosa. Cardiol Young. 2016;26(4):623–8.
33. Giovinazzo S, Sukkar SG, Rosa GM, Zappi A, Bezante GP, Balbi M, et al. Anorexia nervosa and heart disease: a systematic review. Eat Weight Disord. 2019;24(2):199–207. https://doi.org/10.1007/s40519-018-0567-1
34. Peebles R, Hardy KK, Wilson JL, Lock JD. Are diagnostic criteria for eating disorders markers of medical severity? Pediatrics. 2010;125(5):e1193–201.
35. Misra M, Aggarwal A, Miller KK, Almazan C, Worley M, Soyka LA, et al. Effects of anorexia nervosa on clinical, hematologic, biochemical, and bone density parameters in community-dwelling adolescent girls. Pediatrics. 2004;114(6):1574–83.
36. Hütter G, Ganepola S, Hofmann WK. The hematology of anorexia nervosa. Int J Eating Disord. 2009;42(4):293–300.
37. De Filippo E, Marra M, Alfinito F, Di Guglielmo ML, Majorano P, Cerciello G, et al. Hematological complications in anorexia nervosa. Eur J Clin Nutr. 2016;70(11):1305–8.
38. Kohn MR, Madden S, Clarke SD. Refeeding in anorexia nervosa: increased safety and efficiency through understanding the pathophysiology of protein calorie malnutrition. Curr Opin Pediatr. 2011;23:390–4.
39. Araujo Castro M, Vázquez Martínez C. The refeeding syndrome. Importance of phosphorus. Med Clin (Barc). 2018;150(12):472–8.
40. Ornstein R, Golden N, Jacobson M, Shenker I. Hypophosphatemia during nutritional rehabilitation in anorexia nervosa: implications for refeeding and monitoring. J Adolesc Health. 2003;32(1):83–8.
41. Garber A, Cheng J, Accurso E. Short-term outcomes of the study of refeeding to optimize inpatient gains for patients with anorexia nervosa: a multicenter randomized clinical trial. JAMA Pediatr. 2021;10:19–27. Available from: https://jamanetwork.com/journals/jamapediatrics/article-abstract/2771984?utm_campaign=articlePDF%26utm_medium%3DarticlePDFlink%26utm_source%3DarticlePDF%26utm_content%3Djamapediatrics.2020.3359

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