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Traumatic stress, mental health and quality of life in adolescents with esophageal atresia

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ABSTRACT

Introduction: We aimed to investigate QoL in EA patients in relation to comparison groups and to clinical factors including experienced traumatic stress.

Material and Methods: Adolescents with EA in Norway born between 1996 and 2002 were included. Clinical assessment and patient's characteristics were collected. Quality of life (PedsQL), traumatic stress (IES-13) and mental health (SDQ-20) were compared to groups of healthy controls, children with acute lymphoblastic leukemia (ALL) and kidney transplanted children (TX).

Results: 68 EA adolescents participated. Total scores for PedsQL were not different from the healthy group and ALL patients, but significantly better than the TX patients. The subscale for physical performance was significantly lower than in healthy adolescents, and nine (17%) patients had scores ≤ 70 indicating reduced health status. Five EA adolescents (12%) had mental health scores suggesting a psychiatric disorder, and six (9%) reported high traumatic stress scores with a significant correlation to days on ventilator in the neonatal period. The strongest predictors for quality of life among EA adolescents were self-reported mental health, posttraumatic stress and GERD symptoms.

Conclusion: Scores for Quality of life in the EA group are good except for subscale for physical performance. Symptoms of posttraumatic stress, mental strain and gastroesophageal reflux are predictors of reduced QoL.

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1. Introduction

Esophageal atresia (EA) is a severe congenital malformation with a prevalence of 2.4 per 10 000 births [1]. Until the last decades EA was associated with significant mortality, but as the majority of infants now survive neonatal corrective surgery the focus has shifted from mortality to morbidity and long-term prognosis [2]. Dysphagia, gastro-esophageal reflux (GER), tracheomalacia and esophageal stenosis represent long-term problems reported in EA patients, often requiring long-lasting hospitalizations with repeated invasive diagnostic and treatment procedures throughout childhood [3]. Although prior studies have demonstrated that chil-

dren with neonatal surgical malformations may experience negative effects on neurodevelopment and psychological development with long-term risk of developing mental health and psychosocial problems [4-10], it is still unclear how neonatal treatment and long-term morbidities impact behavior and emotional health [4, 11-15]. Studying one year old infants with EA, Faugli et al. diagnosed mental health disorder in 31% of the infants [16]. The predicting factors were more than one operation, mechanical ventilation beyond one day, mother-reported posttraumatic stress symptoms and moderate-to-severe chronic family strain. Yet, the reports on mental health and psychosocial functioning in EA children and adolescents are few and divergent. Whereas there are reports on mental health and psychosocial functioning not different from comparison groups [10], other report impaired quality of life (QoL) and psychosocial dysfunction in a significant proportion of EA adolescents [17].

Level of Evidence: Level II prognosis study.

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We hypothesized that adolescents with EA face increased mental strain and reduced QoL, notably if they have serious comorbidities and have experienced traumatic stress.

2. Material and methods

2.1. Participants

All children born in Norway with EA between January 1996 and December 2002 [median age 16 (range 13–20)] were retrospectively selected from medical registers at the three tertiary University hospitals. Exclusion criteria included genetic syndromes and diagnoses associated with growth disorder (i.e. cerebral palsy, muscular dystrophy, trisomy 21), or mental retardation leaving the EA adolescent unable to answer questionnaires. Patients were also excluded if Norwegian was not spoken by the adolescent and by the mother.

2.2. Recruitment of comparison groups

For comparison on the psychometric methods (PedsQL, SDQ), we used previously presented groups: 42 healthy adolescents [median age 11 years (range 8.9–15.0)] recruited from two elementary schools and two junior high schools in Norway [18], 40 children with acute lymphoblastic leukemia (ALL) [median age 11 years (range 8.5–15.4)] [19] and 38 kidney transplanted children (TX) [median age 13 years (range 3.0–19.0)] [20].

Methods

2.3. Study design

A descriptive cross-sectional study was conducted. The EA adolescents and their mothers visited the out-patient clinic of the national hospital during two consecutive days for examination and follow-up assessment. Clinical assessment was performed by a pediatric surgeon, a pediatric nurse, a physiotherapist and a dietitian.

2.4. Clinical data

Clinical characteristics of EA adolescents were retrieved from medical records and during follow-up; gestational age at birth, birthweight, VACTERL (defined as having ≥ 3 of the characteristic abnormalities: vertebral defects, anal atresia, cardiac defects, trachea-esophageal fistula, renal anomalies, and limb abnormalities), number of days on ventilator, length of first hospital stay (LOFHS), esophageal stenosis, number of esophageal dilatations, previous gastrostomy, frequent dysphagia and symptoms of gastroesophageal reflux (GER). Standard deviation score weight-for-age (SDS-WFA) and standard deviation score height-for-age (SDS-HFA) were estimated according to Norwegian reference data on growth [21].

2.5. Psychometric instruments

2.5.1. Traumatic stress (IES-13)

Children's Revised Impact of Event Scale (IES-13) is a 13-item instrument measuring traumatic stress in children [22]. The instrument is based on the adult Impact of Event Scale [23]. The child version consists of 4 items measuring intrusion, 4 items measuring avoidance and 5 items measuring arousal. All items of the IES are anchored to a specific event and stressor: 'Hospital admission with surgery' [24]. The instrument is designed for children aged 8 years and above who are able to read independently. Each item is scored on a five level likert scale (0–4). The IES is a reliable and valid diagnostic screening tool for post-traumatic stress disorder (PTSD) in

children, and is useful in identifying children requiring further assessment or intervention [22]. For screening purposes the sum of Intrusion and Avoidance items are added. A sum of scores ≥ 17 is defined as cases, suggesting PTSD [25].

2.5.2. Mental health (SDQ-20)

The Strengths and Difficulties Questionnaire (SDQ-20) is used to assess mental and psychosocial health in children and adolescents [26]. The SDQ is a screening questionnaire consisting of 25 items in addition to a supplement on the impact of the difficulties for the child and family. Each item is scored on a three-point ordinal Likert scale from "not true", "somewhat true" or "certainly true", rated 0–2 for negatively worded items and rated inversely 2–0 for positively worded items. A higher score indicates more problems. The instrument has five subscales: Conduct problems, Hyperactivity, Emotional problems, Peer problems, Pro-social behavior, with the first four adding up to the Total Difficulties Score. Sub scores for each subscale range 0–10. Total difficulties score of ≥ 19 defines symptom "cases" according to Goodman (www.sdqinfo.com) and adjusted to Norwegian cut-offs [27]. As such, symptom score >90 percentile predicts a substantially raised probability of being diagnosed with a psychiatric disorder. A raw score of 16–18 is defined as "borderline", i.e., symptom score within percentile 80–90. The extended version of the SDQ includes a brief "impact supplement" concerning overall distress and social impairment. The impact questions have four response categories which correspond with a point scale 0–0–1–2. A total impact score of ≥ 2 defines impact "caseness", i.e. having variable functioning with sporadic difficulties or symptoms in several but not all social areas, and a score of 1 is defined as borderline, i.e. having difficulty in a single area but generally functioning pretty well.

The proxy-report assesses the parental perception of their child's mental health. Each subscale consists of five items. The SDQ shows satisfactory reliability and validity [28].

Results from a former study by our group in TX children, children with ALL and healthy adolescents have been introduced for comparison [20]. The SDQ scores for the healthy adolescents have previously been presented as not being significantly different than the SDQ norms or reference values from the normative data based on a large representative Norwegian sample [20, 27–29].

2.5.3. Health related quality of life (PedsQL)

The Pediatric Quality of Life Inventory (PedsQLTM) 4.0 [30, 31] is a 23-item instrument for measuring health status in children and adolescents, and it is grouped into four subscales: (1) physical functioning (8 items), (2) emotional functioning (5 items), (3) social functioning (5 items) and (4) school functioning (5 items). In addition to the four subscales, a total summary health score (23 items) can be computed. A psychosocial health summary score (15 items) can be computed as the sum of the items divided by the number of items answered in the emotional, social, and school functioning subscales, and a physical health summary score (8 items) is the same as the physical functioning subscale. The items for the self-report and proxy-report are essentially identical, differing in developmentally appropriate language and first- or third-person tense suitable in age groups from 2 to 18 years. It has achieved excellent reliability differentiating between healthy children and children with chronic health conditions. The instructions ask how much of a problem each item has been during the past 1 month. (0=never a problem; 1=almost never a problem; 2=sometimes a problem; 3=often a problem; 4=almost always a problem). Subjects are requested to rate how many problems they experienced during the past month with health (e.g. I hurt or ache), activities (e.g. It's hard for me to run) or feelings (e.g. I feel afraid or scared). Items are reverse-scored and linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25,

4 = 0) so that higher scores indicate better health status. Scale scores are computed as the sum of the items divided by the number of items answered (this accounts for missing data). The proxy-reports assess the parents' perception of their child's health status. The psychometric properties of the Norwegian version of PedsQL 4.0 have been evaluated in the general population and found satisfactory [32]. Cut-off value for PedsQL total score were set at ≤ 70 , with a lower score indicating reduced health status [33].

2.6. Ethics

After written and oral information, all participants signed the consent prior to visiting the outpatient clinic. Information that could identify patients directly to the study was erased, and each patient was given a random study number to prevent identification of individuals by researchers. All collected data was electronically stored at the hospital server. The study was approved by the Regional Ethical Committee (REK) in Norway, reg.no: 2014/1224, and Data protection officer (PVO), reg. no: 2014/9344.

2.7. Statistics

All analyses were performed by SPSS version 25 (SPSS, Chicago, IL). Continuous normal distributed variables are presented as means with standard deviation (SD), or if skewed as median (range, percentiles). Categorical variables are given as proportions and percentages. Differences in continuous variables between independent groups were analysed using a two-sample *t*-test (Student *t*-test) for Gaussian distributed data and otherwise with the non-parametric Mann-Whitney-Wilcoxon test (Mann-Whitney U).

Due to missing individual original data from the comparison groups (TX, ALL, Healthy) we chose to calculate by ANOVA significant differences in total scores between the EA group and the comparison groups only. Post hoc tests (Statpages) determined which total score means were statistically significantly different. The strength of associations between normally distributed continuous variables was measured using Pearson's correlation coefficient, or Spearman's correlation coefficient when appropriate. Forward and backward multiple linear regression analysis (*p*-value 0.05) was used to analyze possible explanatory variables as predictors of quality of life. Only independent variables statistically significant from univariate correlation to the dependent variable were included in the regression models. To further confirm the relationship between the dependent and the independent variables also a forced entry regression model was applied. We chose a 5% statistical significance level.

3. Results

We identified 125 EA patients born consecutively in Norway between 1996 and 2002. Sixteen (13%) patients died in the neonatal period because of associated major anomalies or serious complications, 7 met exclusion criteria. Enrolment details are shown in Fig. 1. Out of 102 eligible EA adolescents and mothers invited to the follow-up study, 68 (67%) participated. The only statistical difference in adolescent baseline data between participants (*n* = 68) and non-participants (*n* = 34) was that the participants were median one year younger (*p* = 0.018) (table 1).

Clinical data

Clinical data are presented in table 2. Baseline data are in line with other EA populations [34–38]. 15% of the adolescents were regarded stunted (z-score-HFA < -2), 10% were underweight (z-score-WFA < -2) and 12% were overweight (z-score-WFA > 1).

3.1. Traumatic stress (IES-13)

Traumatic stress scores ranged from 0 to 40, with a median of 10. The sum score of intrusion and avoidance was median 3 (range 0–28), resulting in 6 (9%) EA adolescents being categorized as cases (table 3).

Traumatic stress scores correlated significantly to birthweight (*p* = 0.025), Nissen fundoplication (*p* = 0.016), present GERD symptoms (*p* = 0.023) and dysphagia (*p* = 0.032) (table 4). Presence of high stress scores (case), suggesting PTSD, was significantly correlated to number of days on ventilator in the neonatal period (*p* = 0.010) (table 4).

3.2. Mental health (SDQ-20)

Total scores for mental health (self-report and proxy) showed significantly impaired mental performance in the EA group compared to healthy adolescents (table 3). The total scores in the EA group were not significantly different from the TX- and the ALL-groups.

Self-report on emotional problems was not different from comparison groups, but the EA mothers reported significantly more emotional problems in the EA-adolescents than the mothers of healthy adolescents.

Out of 43 EA adolescents eligible for SDQ, thirty eight (88%) had self-reported scores within normal range (< 16). Five patients (12%) were classified as cases or borderline cases (table 3), suggesting a substantially raised likelihood of being diagnosed with a psychiatric disorder [39]. Looking at impact scores, concerning overall distress and social impairment, 10 patients (23%) were cases or borderline cases. Mental strain was not related to dysphagia or GERD symptoms (table 4). The total SDQ score and the emotional sub score were significantly correlated to gender, with females reporting more problems than males. SDQ scores were also positively and significantly correlated to presence of VACTERL and overweight (SDS-WFA > 1) (table 4).

3.3. Health related quality of life (PedsQL)

The EA group reported the same total scores for PedsQL as the healthy group and the ALL patients, but had significantly better scores than the TX patients (table 3). Looking at the proxy total scores the mothers of the EA patients scored their adolescents significantly lower than the mothers of the healthy group. Overall the EA patients reported PedsQL at the same level as the ALL patients, with levels showing significantly better QoL than TX adolescents.

The EA group and their mothers reported significantly lower scores on subscale for physical performance. The school performance subscales also showed a tendency (*p* = 0.06) to be lower than healthy adolescents, while EA group scored at the same level as healthy adolescents on emotional and social subscales. Nine (17%) EA adolescents had scores ≤ 70 indicating reduced health status.

PedsQL total score and sub scores for physical performance were highly negatively correlated to dysphagia and GERD symptoms (table 4). We also noticed that psychosocial health summary score was significantly negatively correlated to dysphagia, GERD and to body length (table 4). Social performance was, as scored both by the EA adolescents and their mothers, negatively correlated to number of days on ventilator (*p* = 0.014, *p* = 0.018), respectively.

The adolescents rated their own health status not significantly different from their mothers rating, except for the emotional subscale where the mothers scored the adolescents significantly lower than the self-score (table 3). However, there was a significant posi-

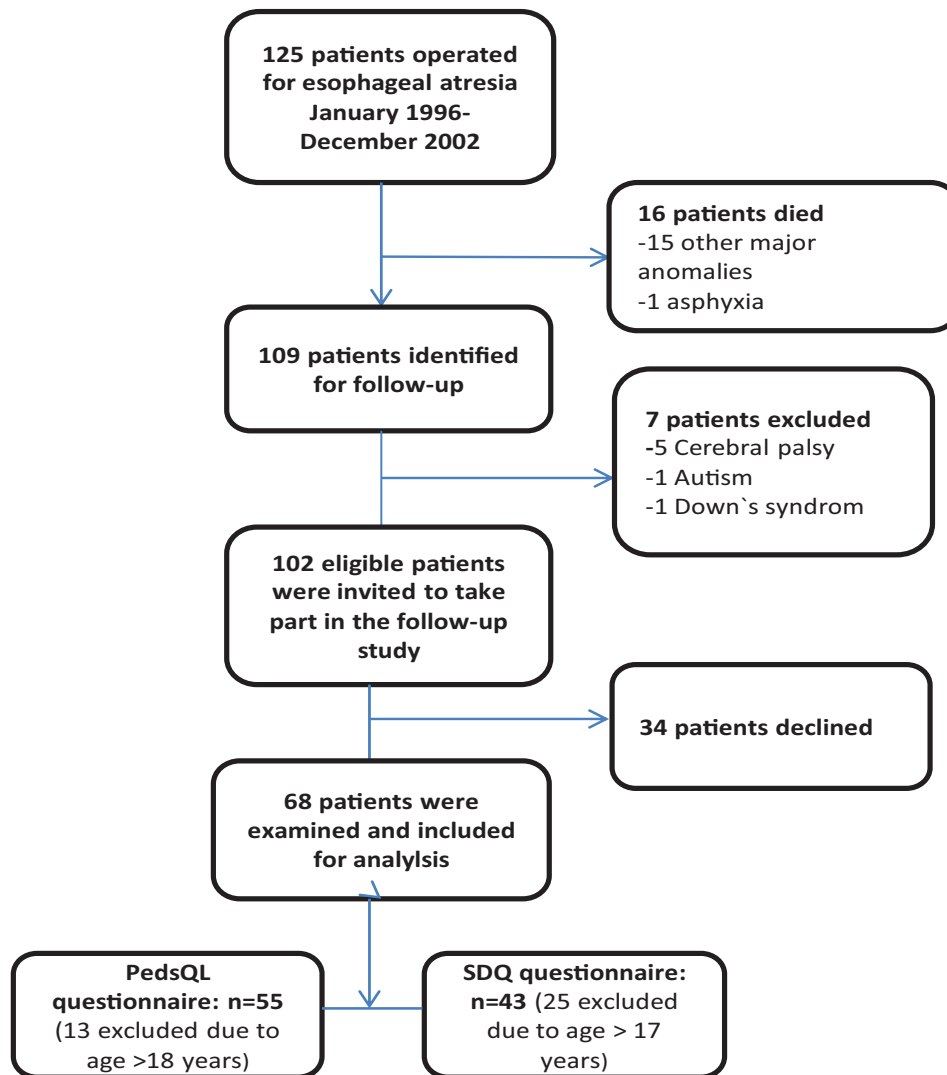


Fig. 1. Enrolment of patients with esophageal atresia (EA) ($n = 68$).

Table 1

Baseline characteristics of invited EA adolescents ($n = 102$).

Baseline characteristics EA adolescents	Participants $n = 68$	Non-participants $n = 34$	p-values*
Prematurity (<37 weeks GA); n (%)	24 (35)	7 (21)	0.130
Boys; n (%)	40 (59)	20 (59)	1.00
EA type C; n (%)	58 (85)	29 (85)	0.666
VACTERL association; n (%)	14 (21)	4 (12)	0.273
LOFHS (length of first hospital stay); days, median (range)	22 (8–264)	20 (11–140)	0.529
Age at invitation; years, median (range)	16 (13–20)	17 (13–20)	0.018

* P values are based on comparison of attending- and non-attending EA adolescents (Mann-Whitney U test).

tive correlation demonstrated between patient and mother in PedsQL total summary score ($p < 0.001$) and in all PedsQL subscales (table 4).

Relations between scores for quality of life and mental health are presented in table 4, showing significant correlations between almost all parameters, total scores as well as sub scores, for psychological health and wellbeing.

Using the PedsQL total score as the dependent variable, we entered traumatic stress (IES-13), GERD symptoms and mental health (SDQ) total score as explanatory variables into a multiple linear regression analysis. The results indicated that the model explained 55.9% of the variance and that the model was a significant predictor of QoL, $F(3,50) = 21.132$, $p < 0.001$. While SDQ total

score was the most significant contributor to the model ($B = -1.387$, $p < 0.001$), GERD symptoms (total score) and traumatic stress (IES intrusion + avoidance) were also significant predictors of QoL (table 5).

4. Discussion

Total scores for health related Quality of life in the EA group were not different from the healthy group and the ALL patients, but significantly better than the TX patients. The EA group, however, scored significantly lower than healthy adolescents on subscale for physical performance, and 9 (17%) EA adolescents had scores ≤ 70 indicating reduced health status.

Table 2
Demographics and clinical data.

	Participants n = 68
Previous gastrostomy; n (%)	12 (18)
Treated for esophageal stenosis; n (%)	30 (44)
Number of esophageal dilatations; n, median (range)	6 (1–108)
Nissen fundoplication; n (%)	9 (13)
Age at Nissen fundoplication; months, median (range)	10 (4–59)
SDS-Height for age; z-score, median (range)	−0.65 (−4.56 – 1.77)
Stunting (SDS-Height For Age < −2); n (%)	10 (15)
SDS-Weight for age; z-score, median (range)	−0.42 (−6.03 – 2.60)
Body Mass Index (BMI); kg/m ² , median (range)	21 (13–33)
Underweight (SDS-Weight For Age < −2); n (%)	7 (10)
Overweight (SDS-Weight For Age > 1); n (%)	8 (12)
Frequent dysphagia; n (%)	58 (85)
Symptoms of gastro-esophageal reflux disease; n (%)	44 (65)

According to Gross' EA classification 3 (4%) attending adolescents had type A, none type B, 58 (85%) type C, 4 (6%) type D and 3 (4%) type E.

Mental strain in EA adolescents was significantly higher than in healthy adolescents and 6 (9%) EA adolescents were categorized

as cases suggesting PTSD. The strongest predictors for quality of life among EA adolescents in our study were self-reported mental health, posttraumatic stress and GERD symptoms.

4.1. Posttraumatic stress

The adolescents with EA have obviously ever since birth been exposed to pain and stressful treatment procedures. These factors may induce posttraumatic stress affecting mental health and quality of life. All items of the IES were in our study anchored to previous or recent hospital visits involving surgery as the specific stressor. Conscious or unconscious thoughts related to the stressor were expected to give a higher IES-questionnaire score. Six (9%) of the EA adolescents reported a high level of stress indicating a severe reaction related to hospital admissions and surgery. The scores for posttraumatic stress were strongly related to number of days on ventilator in neonatal period, to dysphagia and to symptoms and treatment for gastroesophageal reflux. Increased number of days on ventilator may in this context also reflect a longer period of neonatal intensive care treatment devoid of physical contact with

Table 3

Health-related quality of life (PedsQL) and Mental- and Psychosocial health (SDQ) of respectively 54 and 43 adolescents with esophageal atresia (EA) and their mothers, and impact of event scale (IES) of 68 EA adolescents. The results in EA group are compared to children and mothers with kidney transplantation (TX), Acute Lymphoblastic Leukaemia (ALL) and healthy controls. Differences between other groups are not shown.

Mental health and quality of life scales	EA	TX	ALL	Healthy
PedsQL child self-report	n = 55	n = 30	n = 40	n = 42
Total score	83.7 (13.4)	69.1 (17.9) ^{***}	81.7 (12.6)	88.9 (7.6)
Psychosocial health	84.1 (13.7)	67.0 (18.1)	79.3 (14.0)	87.2 (9.2)
Physical functioning	83.1 (18.2)	74.9 (17.0)	86.3 (12.1)	92.3 (6.5) ^{**}
Emotional functioning	82.3 (19.0)	69.5 (15.8)	75.1 (18.7)	83.2 (12.7)
Social functioning	92.6 (12.6)	73.7 (21.5)	86.0 (14.1)	92.5 (7.7)
School functioning	77.3 (18.9)	63.1 (17.8) ^{***}	76.6 (16.4)	86.0 (13.0) [#]
PedsQL mother proxy-report	n = 55	n = 32	n = 36	n = 38
Total score	81.1 (16.0)	68.4 (19.2) ^{***}	79.4 (12.5)	89.6 (10.3) [*]
Psychosocial health	80.4 (15.7)	67.7 (18.9)	75.9 (14.2)	88.1 (11.3)
Physical functioning	82.4 (19.0)	69.4 (23.1) ^{**}	86.1 (13.7)	92.5 (10.5) [*]
Emotional functioning	76.8 (19.8)	70.0 (21.4)	70.3 (15.6)	85.0 (13.5)
Social functioning	86.9 (17.1)	67.8 (27.1) ^{***}	82.8 (15.5)	93.2 (9.9)
School functioning	77.5 (19.0)	62.9 (23.2) ^{**}	74.4 (19.9)	86.1 (14.6)
SDQ child self-report	n = 43	n = 26	n = 39	n = 41
Total difficulties	8.7 (5.0)	11.6 (5.7)	7.4 (4.8)	5.7 (4.3) [*]
No.(%) caseness, 19–40	1 (2,3)	2 (8)	1 (3)	0 (0)
No.(%) borderline, 16–18	4 (9,3)	6 (23)	0 (0)	1 (2)
Emotional problems	2.7 (2.3)	3.6 (2.1)	2.5 (2.1)	1.8 (2.2)
Conduct problems	1.1 (1.1)	1.9 (1.6)	2.1 (1.5)	1.8 (1.4)
Hyperactivity problems	3.4 (2.3)	3.6 (2.2)	3.1 (1.9)	3.3 (2.3)
Peer problems	1.5 (1.5)	2.5 (2.2)	2.3 (1.9)	1.6 (1.7)
Prosocial behavior	8.4 (1.5)	7.9 (2.1)	7.6 (1.8)	7.9 (1.8)
Impact score	0.7 (1.5)	0.8 (0.8)	0.2 (0.7)	0.2 (1.1)
No.(%) caseness, 2–10	7 (16)	6 (23)	3 (8)	2 (5)
No.(%) borderline, 1	3 (7)	1 (4)	2 (5)	0 (0)
SDQ mother proxy-report	n = 43	n = 31	n = 36	n = 38
Total difficulties	7.8 (5.3)	10.7 (6.3)	7.6 (5.2)	4.2 (3.6) ^{**}
No.(%) caseness, 19–40	2 (4,7)	4 (13)	2 (6)	0 (0)
No.(%) borderline, 16–18	2 (4,7)	3 (10)	3 (8)	0 (0)
Emotional problems	2.3 (2.3)	2.7 (2.0)	1.6 (1.8)	0.8 (0.9) ^{***}
Conduct problems	0.8 (1.0)	1.8 (1.5)	1.5 (1.3)	1.0 (1.2)
Hyperactivity problems	3.0 (2.2)	3.7 (2.5)	2.8 (2.7)	1.7 (2.0)
Peer problems	1.7 (2.0)	2.6 (2.5)	1.6 (1.9)	0.8 (1.0)
Prosocial behavior	8.6 (1.6)	7.8 (2.2)	8.0 (1.9)	8.9 (1.4)
Impact score	0.7 (1.7)	1.2 (2.0)	1.6 (2.4)	0.0 (0.2)
No.(%) caseness, 2–10	6 (14)	9 (29)	7 (19)	0 (0)
No.(%) borderline, 1	5 (12)	0 (0)	0 (0)	1 (3)
IES-13	n = 68			
Total score; median (range)	10 (0–40)			
Caseness/prevalence of PTS symptoms; n (%) ⁶	6 (9)			

Values are reported as the mean, with the SD in parenthesis unless stated otherwise.

¹ As measured by a total IES-score (Intrusion + Avoidance) ≥ 17.

* Significant different from EA group at the 0.05 level.

** Significant different from EA group at the 0.01 level.

*** Significant different from EA group at the 0.001 level.

P = 0.06.

Table 4
Relation between psychometric scores (PedsQL, SDQ-20, IES-13), somatic factors and proxy scores.

Variables/ outcomes	Gender	Number of days on ventilator	Prematurity	VACTERL association	Previous gastrostomy	Nissen Fundopli- cation	Dysphagia	GERD- symptoms	SDS-HFA	SDS-WFA	PedsQL proxy	SDQ proxy
PedsQL self												
Total			−0.262*			−0.301*	−0.395**	−0.372**			.616**	
Psychosocial			−0.254*			−0.280*	−0.308*	−0.305*	−0.260*		.525**	
Physical			−0.245*	.303*	−0.412*		−0.408**	−0.469***			.662**	
Emotional						−0.327*	−0.276*				.333*	
Social	−0.344*	−0.281*			−0.276*			−0.265*			.494**	
School						−0.286*	−0.301*	−0.307*			.591**	
PedsQL proxy												
Total	−0.306*				−0.408**	−0.278*	−0.347**	−0.280*				
Psychosocial	−0.284*				−0.332*	−0.269*	−0.351**					
Physical					−0.412**		−0.263*	−0.392**				
Emotional							−0.347**					
Social	−0.335*				−0.362**		−0.263*					
School					−0.402**	−0.303*	−0.272*					
SDQ self												
Total	−0.301*											.459**
Emotional	−0.423**											.599**
Conduct										.358*		
Hyperactivity												.379*
Peer												.528**
Prosocial				.347*								
Impact												
(Caseness)												
SDQ proxy												
Total												
Emotional												
Conduct												
Hyperactivity												
Peer					.304*							
Prosocial												
Impact												
(Caseness)												
IES-13												
Total												
Caseness†		.330**				.290*	.261*	.276*				

*Significant at the 0.05 level (two-tailed), **significant at the 0.01 level (two-tailed), ***significant at the 0.001 level (two-tailed).

† Sum of IES-13 subscores Impact + Avoidance ≥ 17 .**Table 5**

Forward multiple regression model with significant predictor variables; SDQ (total self-report), GERD symptoms, IES-13 (intrusion + avoidance) and PedsQL (total self-report) as outcome variable.

Dependent variable	Independent variable	B	95% Confidence interval	Beta	p value	R ²
PedsQL	Mental health (SDQ)	−1.387	−1.86, −0.910	−0.579	<0.001	.559
	GERD symptoms	−2.274	−4.106, −0.442	−0.247	.016	
	Traumatic stress (IES)	−0.482	−0.881, −0.084	−0.229	.019	

the parents. This may support the theory that children often experience medical treatment procedures as traumatic, leading to early age onset of mental problems [16], as well as a long-lasting impact of the traumas related to neonatal treatment [9, 40]. Further down the line this posttraumatic stress was related to adolescents' reported mental health and identified as a predictor of the adolescents' quality of life. Thus, we may interpret this as a cascade of factors influencing each other on the way from neonatal treatment to impaired adolescent psychological wellbeing.

Faugli et al. studied one year old EA children and diagnosed mental health disorders in one third of the children including traumatic stress disorder, disorders of affect, regulatory disorders and eating behavior disorders [16]. More than half of the mothers reported that the child had experienced medically induced trauma and observed PTS symptoms in their infants. The mental health di-

agnosis in the infants was predicted by the posttraumatic stress symptoms and duration of intensive care [16], which seem to be in accordance with the present study. Faugli's work was the first to demonstrate these impairments in EA infants. Our study confirms that there is still a significant impairment in mental health in the adolescent EA-population.

Confirming the suspicion of a posttraumatic stress mechanism related to impaired mental health does not exclude other mechanisms affecting neurodevelopmental outcome and mental health. In a recent review Schiller et al. looked at reports on memory impairments and academic problems after neonatal critical illness and suggest that these defects are related to common factors associated to the neonatal critical illness and not to underlying diagnosis [41]. Chandler et al. did MRI studies in infants after thoracic non-cardiac surgery and critical care and demonstrated brain at-

rophy in both full-term and pre-term patients [42]. On the other hand a recent study by Rudisill and coworkers demonstrated brain injury both before and after reconstructive surgery in EA patients and point out the need for knowledge about the pre-anesthesia intrinsic brain status to understand the mechanisms and the time of onset of the possible brain injury in EA patients [43]. Thus, even though the mechanisms of possible brain injury still need to be explored, recent research may seem to identify morphological substrates to the symptoms of trauma and mental impairment we register with the psychometric methods.

4.2. Mental health

Mental health in EA adolescents was significantly impaired on both self-reports and proxy-reports compared with those of healthy adolescents, comparable to the ALL patients, and better than TX patients. Low mental health scores at long term follow up in EA patients is in accordance with Koivusalo reporting low scores in 8.6% of adults [8]. The lower mental health in EA adolescents compared to the healthy adolescents could be related to more frequent hospital visits and/or unpleasant medical experiences during childhood. Faugli et al. used CBCL and YSR to assess behavioral and emotional problems as indicator for mental health in EA adolescents. In that previous study low birth weight and esophageal dilations had negative effect on mental health which seems to be in accordance with the present study showing the long term effects of traumatic experiences in early life [10]. Both studies add to the knowledge about impact of early traumatic experiences on long term mental health and psychosocial functioning [9, 44]. On the other hand another previous study have demonstrated normal self-reported mental health in EA children and adolescents aged 6–18 years, lower mental health reported in proxy-reports, but no relationship between mental health, clinical symptoms and complaints [45].

4.3. Quality of life

Total PedsQL scores as reported by the EA adolescents were not different from the healthy group. The EA mothers' proxy report, however, showed significantly lower scores than the mothers of the healthy group. Self-reported good quality of life is in accordance with the literature on EA follow-up, because even though there is a great heterogeneity of QoL assessment tools, almost none of the tools demonstrate significant differences between EA patients and comparison groups, nor between subgroups of EA [46].

Mental health followed by GERD symptoms and traumatic stress were the determinants for the EA adolescents' reported quality of life. These results are supported by previous studies where adult EA patients experienced impaired QoL related to gastrointestinal symptoms [6, 16, 39, 45, 47–49]. In our study, EA adolescents reported significant gastrointestinal problems with frequent dysphagia in 85% and symptoms of gastrointestinal reflux disease in 65%. Dysphagia was correlated to all sub-scales of PedsQL, reporting a negative impact on both the adolescents' own perceived health status as well as on the proxy-ratings. Previous reports also demonstrate the great impact dysphagia has on health status in EA patients, and may be explained by the great influence dysphagia has on daily activities such as eating and activity [6]. Both in Deurloo's and in our study the physical components of QoL were the subscales most significantly associated to dysphagia.

On the other hand, Deurloo et al. looking specifically at the association between complaints, esophageal function and QoL in adult EA patients found no association between QoL and complaints of gastroesophageal reflux which is in contrast to our results [6].

Among clinical factors prematurity was significantly correlated to PedsQL scores which is in accordance with Rozensztrauch also reporting lower quality of life in patients born before 37th week of pregnancy [49]. Ten (15%) adolescents were stunted (SDS-HFA < -2), and short stature correlated negatively to PedsQL which seem to be in accordance with our former study of EA adolescents aged 13 years stating that psychosocial functioning as assessed by Children's Global Assessment Scale (CGAS) was negatively affected by declined height [10].

Quality of life instruments measure an individual's perception on functioning. To assess children's QoL the parental perspective of the child is needed for a comprehensive and entire view. Our study demonstrated good correlation between mothers' and adolescents' ratings on quality of life. On the other hand, our results also show higher health status subscale scores in the adolescent report compared with the proxy-report which is in accordance with reports of parents' perception of their sick children underestimating the patient's own perception [50, 51]. One explanation might be that children with chronic conditions have previously been shown to cope better with everyday stressors compared to healthy comparison groups, in addition to applying coping strategies for use in disease-related contexts [34, 52, 53].

The child's perspective has previously been found to diverge from the parental perception especially in the emotional and social domains [19], which is also demonstrated in our study. There are also previous studies on both healthy and sick children that in contrast to our study report a total lack of agreement between child and proxy-reports, suggesting that the information presented by the proxy report is not equivalent to that reported by the patient [19, 34, 54].

4.4. Implications

Our results show that EA adolescents carry a significant burden lasting several years after EA surgery and hospital stay, reflecting the documented impact functional problems and clinical symptoms may have on mental health and psychological functioning. Neonatal surgery and hospital stay early in life may affect infant mental health, parental mental state, parent-child interaction and attachment. Long term morbidities in other domains (i.e. respiratory, school functioning, sports participation) may also affect growing up normally. It is important from the neonatal period to be aware that these risk factors are determinants for patients' long time adjustment to life, and to incorporate this in multidisciplinary care and follow-up procedures including care and information for the parents. The emphasis should be put on identifying the patients at risk of developing reduced health status and to intervene timely.

4.5. Strength and limitations

The strengths of the present study was the inclusion of a well-defined national sample of EA adolescents born during a given time period. Through a descriptive cross-sectional study we were able to assess the long-term perspective in adolescents with EA. We used validated and reliable questionnaires assessing mental and psychosocial health, enabling us to do comparative studies across different patient populations. Limitations to our study was that 34 (33%) EA adolescents declined follow-up, which may weaken our findings and conclusions. Apart from the attending EA adolescents being one year younger than the non-attending there were no other statistical differences in the clinical baseline data, but the current health status of the latter is not known.

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Declaration of Competing Interest

None

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