Original article

Psychological outcome and quality of life in children born with congenital diaphragmatic hernia

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ABSTRACT

Objective: To assess psychological and social functioning and health related quality of life and its early determinants in children born with congenital diaphragmatic hernia (CDH).

Design: Cross-sectional follow-up study.

Setting: Outpatient clinic of a tertiary care hospital.

Participants: 33 CDH survivors aged 6–16 years.

Main exposure: Patients who developed CDH associated respiratory distress within 24 h after birth.

Main outcome measure: Psychological and social functioning assessed with the Wechsler Intelligence Scale for Children (WISC-R), Bourdon-Vos test, Beery Developmental Test of Visual Motor Integration, Child Behavior Checklist (CBCL) and Teacher Report Form (TRF), and health related quality of life assessed with the Child Health Questionnaire (CHQ) and Health Utilities Index (HUI).

Results: Normal mean (SD) total IQ (100.0 (13.2)) and normal visual-motor integration, but significantly lower results for sustained attention (Bourdon-Vos test, 38.8 (11.2) points) were found. Learning difficulties were reported by 30% of parents. Eight children had scores in the clinical range on the CBCL and/or TRF, indicating clinically significant behavioural problems. Except for the CHQ scale General Health, health status was not different from the reference population. No significant correlations between test results and severity of CDH were found, except for an association of general health and physical functioning with length of hospital stay.

Conclusion: CDH patients are at risk for subtle cognitive and behavioural problems, probably not related to CDH severity. Perception of general health is reduced compared to the reference population, indicating that CDH survivors and their parents believe their health is poor and likely to get worse.

What is already known on this topic

► Small studies have shown significantly more emotional and behavioural problems than expected in congenital diaphragmatic hernia (CDH) survivors.
► CDH patients not treated with extracorporeal membrane oxygenation might also be at risk for cognitive problems.
► Despite significant CDH associated symptoms, a few quality of life studies in older patients suggest that the majority of patients enjoy quite healthy lives.

What this study adds

► CDH survivors have a near-normal level of cognitive functioning but are at risk for attention and concentration deficits.
► Many CDH survivors can have significant emotional and behavioural problems which may contribute to school failure.
► Perception of general health is reduced, indicating that parents and CDH survivors believe their health is poor and is likely to get worse.

Congenital diaphragmatic hernia (CDH) is a life threatening anomaly with a mortality rate ranging from 10% to 50%, depending on case selection.[1–3] Long term follow-up studies have shown that patients born with high risk CDH (ie, patients who develop CDH associated respiratory distress within the first day of life) experience significant CDH associated complications including respiratory problems, gastroesophageal reflux disease, nutritional problems and growth retardation.[4–7]

The first days of life of a CDH patient are a critical period in which the child is at risk of developing neurological damage from hypoxia, hypercapnia and acidosis due to the combination of pulmonary hypoplasia and pulmonary hypertension.[8] Most follow-up studies are limited to the first 5 years after CDH repair and include a heterogeneous group of CDH patients treated with and without extracorporeal membrane oxygenation (ECMO). Neurological morbidity has been reported in 10–30% of these patients.[9–14] CDH patients are predisposed to several factors, such as perinatal and postnatal hypoxia, hypercapnia and acidosis, that can interfere with central nervous system development[15] and serious problems in long-term psychosocial functioning and behaviour can be expected.[8 16–18]

Due to high co-morbidity, health related quality of life in a significant proportion of CDH patients may be compromised. However, little is known about the impact of long term health problems on the overall health related quality of life of these patients. Only two studies have assessed health related quality of life in CDH survivors, and they suggest a favourable health related quality of life for the majority of patients.[19 20]

The primary objective of this study was therefore to assess cognitive, behavioural and psychological outcome as well as the health related quality of life of children not treated with ECMO 6–16 years after surgical repair of high risk CDH. The secondary objective was to investigate whether the

neonatal characteristics of CDH were related to severity of cognitive deficits and health related quality of life.

METHODS

Patients

All patients born with high risk CDH (CDH associated respiratory distress within the first day of life) referred to the Pediatric Surgical Centre of Amsterdam between 1987 and 1999 were considered eligible. The patient's history was reviewed, in particular several perinatal and postnatal variables, through the use of standardised forms. Ethics permission for the study was granted by the local ethics committee. Written informed consent was obtained from all patients and their parents or guardians prior to participation.

Eighty five children born with CDH were referred to the Pediatric Surgical Centre of Amsterdam. Thirty three patients died. Eleven patients were excluded because of late CDH. To prevent confounding, CDH patients treated with ECMO were excluded (n = 1).

Of the remaining 40 high risk CDH patients, 33 (83%) agreed to participate (fig 1), while four refused to participate because of lack of time.

There were no significant differences between the basic characteristics of participants and non-participants (table 1).

Study design

Patients who gave informed consent visited the outpatient clinic, where a detailed medical history and information concerning school and school performance were obtained. Neurocognitive functioning was assessed with the Wechsler Intelligence Scale for Children Revised for the Netherlands (WISC-R), the Bourdon-Vos test and the Beery Developmental Test of Visual Motor Integration (Beery VMI). Behaviour was assessed with the Child Behavior Checklist (CBCL).
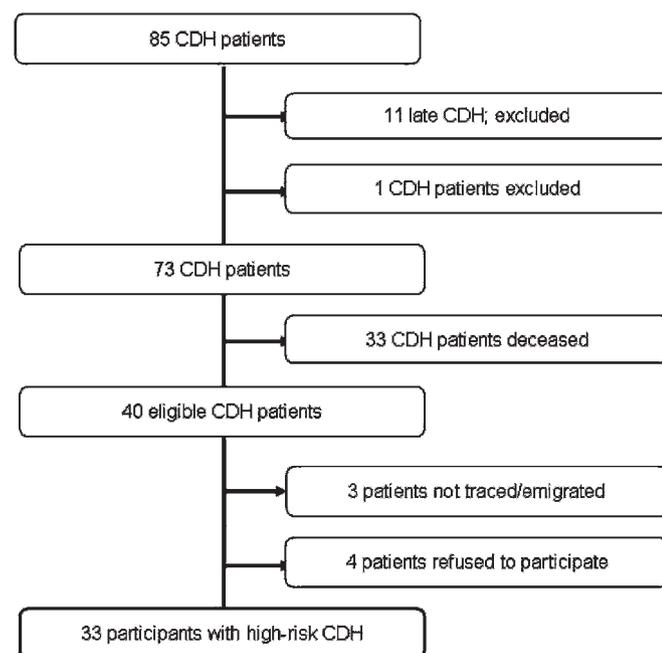

Figure 1 Exclusion and enrolment of patients. Eleven patients had late presenting CDH and were therefore excluded. One patient was excluded because of ECMO treatment. CDH, congenital diaphragmatic hernia; ECMO, extracorporeal membrane oxygenation.

Health related quality of life and health status were assessed with the Child Health Questionnaire (CHQ) and the Health Utilities Index 3 (HUI-3).

In order to create optimal conditions, all tests were performed in the morning and all children were tested by the same experienced child psychologist.

Neurocognitive functioning
WISC-R

The WISC-R is the Dutch version of the Wechsler Intelligence Scale for Children-Revised and yields three IQs: full scale, verbal and performance IQ. The test has Dutch norms, standardised with a mean (SD) of 100 (15) for all three IQ scores[21] and is validated for the Dutch population.[22]

Bourdon-Vos test

Selective attention was assessed with the Bourdon-Vos test. This paper-and pencil test measures sustained selective attention and concentration in terms of speed and accuracy.[23] The validity, sensitivity and reliability of the Bourdon-Vos test appear to be highly acceptable.[24]

Beery VMI test

The Beery VMI test is a paper-and-pencil test for children aged 3–18 years and measures integration of visual perceptual and motor abilities.[25] The test has proven to be valid and reliable.[26] The computed raw item scores are transformed into standard scores (T scores).

Behaviour
CBCL

The CBCL comprises a parent form and a teacher report form (TRF) and contains 120 items which are scored on a three-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very or often true) and was completed by the mother. A total problem score and two broad-band groupings were scored: an internalising grouping containing items such as withdrawn behaviour, somatic complaints without physical cause, and anxious-depressed feelings and an externalising grouping containing items such as aggressive and delinquent behaviour. All scores were converted into T scores. The CBCL has a Dutch version with Dutch norms with good reliability and validity. Teachers completed the teacher's report form (TRF) which is a teacher version of the CBCL. For the CBCL and the TRF, proportions of children with scores in the normal and the clinical range are given. Total T scores ⩾63 classify children in the clinically significant range (upper 10% of population norm groups).[27]

Health related quality of life and health status
CHQ

Health related quality of life was assessed using the CHQ-PF50 (for parents) and the CHQ-CF87 (for children ⩾10 years of age).[28] Results of the CHQ-PF50 and the CHQ-CF87 were compared with norm scores based on a representative sample of 353 Dutch schoolchildren aged 5–13 years[29] and norm scores based on a sample of 475 Dutch adolescents,[30] respectively, using the unpaired t test (see online supplementary data for more information about the CHQ).

In order to indicate clinical relevance of statistically significant differences, Cohen's effect sizes were calculated. Effect sizes (d) were calculated as follows: [mean (a)−mean (b)]/largest standard deviation. According to Cohen, effect sizes

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Table 1 Comparison of participating and non-participating CDH survivors

	Participating (n = 33)	Non-participating (n = 7)	p Value
Male	21 (64%)	3 (43%)	0.41
Age at follow-up (years)	10.2 (3.3)	11.4 (3.6)	0.63
Gestational age (weeks)	38.9 (2.0)	40.1 (1.6)	0.16
5 min AS $\leqslant$5	6 (18%)	1 (14%)	1.0
Left sided CDH	28 (85%)	7 (100%)	0.55
Ventilation (days)	15.3 (15.0)	12.3 (8.7)	0.96
LOS hospital (median days)	24	27	0.77
LOS ICU (median days)	13.5	12.5	0.53
GERD	7 (21%)	2 (29%)	1.0
Cardiac abnormalities	11 (33%)	4 (57%)	0.22
Neurologic deficits	9 (27%)	1 (14%)	0.66
Recurrent CDH	2 (6%)	0 (0%)	1.0

AS, Apgar score; CDH, congenital diaphragmatic hernia; GERD, gastroesophageal reflux disease; ICU, intensive care unit; LOS, length of stay.
Numbers indicate numbers of patients, except age at follow-up, gestational age, ventilation and length of stay. Variables are expressed as mean (SD) unless otherwise stated. Cardiac abnormalities were diagnosed in the neonatal period and included atrial septal defect, ventricular septal defect or a combination. All patients with neurological deficits had (motor) developmental delay in the first 2 years of life. GERD was demonstrated by gastrointestinal x ray series, pH-metry and/or endoscopy in the first 2 years after CDH repair. No significant differences were observed.

between 0.2 and 0.5 indicate a small effect, an effect size between 0.5 and 0.8 indicates a moderate effect, and effect sizes of 0.8 or larger are considered to be a large effect.[31]

HUI-3
The HUI-3 is a generic multi-attribute health status classification system, consisting of eight attributes. Each attribute consists of five to six levels representing the range of functioning from normal (one) to severely impaired (five or six) (see online supplementary data for more information about the HUI).

Statistical analysis
The unpaired t test was used for normally distributed continuous data and non-parametric tests for non-normally distributed continuous data. The Fisher exact test or the χ^2 test was used for comparing categorical data. Test results were compared with population norms using the one sample t test. Bonferroni correction was performed in order to correct for multiple testing.

We used the following independent variables, estimating the severity of the CDH, that could predict psychological test results and health related quality of life (dependent variables): length of stay in the hospital (LOS), Apgar score after 5 min (AS5), duration of ventilation and use of a patch. After an univariate regression analysis was carried out, multivariate regression analysis was performed entering all independent variables that had a p value of less than 0.1 on univariate analysis. This was done only for the dependent variables psychological test results and CHQ item scales with significant differences between the study population and the reference population or when there was a trend towards significance (p<0.1). Statistical significance was reached when p<0.05. All procedures were performed with SPSS 15.0.

RESULTS

Patients
The mean (SD) gestational age of the participants was 38.9 (2.0) weeks. Three children were born before or at a gestational age of 36 weeks (one at 32 weeks, one at 34 weeks and one at 36 weeks). Twenty one (64%) of the participants were male.

CDH repair was performed 1.8 (SD 2.3) days (median 1 day; range 0–12 days) after birth. All patients reported to have neurological abnormalities had a mild (motor) developmental delay in the first 2 years of life.

One patient was discharged with oxygen and needed it for 3 months after discharge due to persistent pulmonary hypertension.

Mean (SD) age at follow-up was 10.2 (3.3) years (table 1).

Neurocognitive and school functioning and behaviour
The majority of the participants (61%) attended primary school and nine children (27%) went to secondary school. Four children (12%) required special educational services. Learning problems were reported by the parents of 10 children (30%).

WISC-R
Thirty of 33 patients completed the WISC-R (table 2). One patient had already performed the test at school, but the results were not complete and could not be used. Two children did not complete the test because of concentration failure and visual incapacity, respectively. Four children had a total IQ that was significantly lower than the Dutch norm score (<−1 SD).

Bourdon-Vos test
The same two children who did not complete the WISC-R did not complete the Bourdon-Vos test either and for the same reasons. The mean (SD) score was significantly lower in CDH patients when compared to population norms (38.8 (11.2) points; 95% CI of the difference: −15.4 to −7.11; p<0.001). The difference remained significant after Bonferroni correction. Twelve children (39%) had a score at or below −1 SD.

Beery VMI test
All patients completed the Beery VMI test. Mean (SD) score was 47.8 (10.9) (95% CI of the difference: −6.00 to 1.70; p = 0.26); no significant difference was found compared to the mean population norm group scores.

CBCL
Twenty eight mothers and 24 teachers of 28 children completed the CBCL and/or TRF. In five children no CBCL or TRF was

Table 2 Results of the WISC-R

WISC-R, n = 31	Score, mean (SD)	95% CI	
		Lower bound	Upper bound
Total verbal IQ	99.5 (14.0)	94.3	104.8
Total performance IQ	100.6 (14.5)	95.2	106.0
Total IQ	100.0 (13.2)	95.0	104.9

WISC-R, Wechsler Intelligence Scale for Children Revised for the Netherlands.
No significant differences were found when compared to the norm score.

returned. Responders and non-responders did not differ as regards the peri- and postnatal variables mentioned in table 1. Six CDH patients (21%) had total problem scores in the clinical range on the CBCL, which is significantly more than the expected 10% of the reference population (χ^2; p = 0.003)[32] (table 3). There were no differences between patients in the normal and in the clinical range of the CBCL for Apgar score after 5 min, LOS or duration of ventilation.

Health related quality of life
CHQ
Parents of all 33 children completed the CHQ-PF50 (table 4). Only (Cohen's) effect sizes for general health perceptions were 0.87 indicating a large effect on this domain (fig 2).

Sixteen of 17 children completed the CHQ-CF87 and one patient refused (table 4).

HUI-3
The parents of all 33 patients completed the HUI-3 questionnaire. Only cognition was significantly lower in the CDH group. Vision was lower in CDH survivors, although this was not significant (table 5).

Explaining outcome based on neonatal characteristics
In linear regression analysis associations were found only for the domain General Health Perceptions and the domain Physical Functioning of the CHQ-CF87. General Health Perceptions decreases 0.12 points for every day the child stayed in hospital (constant 92.70; $R^2 = 0.259$), and Physical Functioning decreased 0.06 points for every day the child stayed in hospital (constant 95.42; $R^2 = 0.799$) when corrected for AS5, duration of ventilation and use of a patch for closure of CDH.

DISCUSSION
In general, we found subtle cognitive problems in patients 6–16 years after CDH repair. Although CDH patients had a normal level of cognitive functioning, since mean IQ scores were comparable to the healthy population, the Bourdon-Vos test showed a significantly lower score in CDH patients, implying CDH survivors might be at risk for attention and concentration deficits. Although mean behaviour problem scores were comparable to reference norms, it was remarkable that 20% of

the CDH patients (versus 10% of the Dutch general population) appeared to have clinically relevant behavioural problems.

So far only a few studies have reported on the long term cognitive development of CDH patients not treated with ECMO (roughly 50% of the high risk CDH patients are not treated with ECMO[33 34]) and most of these studies describe children with a maximum age of only 4 years.[8] Bouman *et al* studied a small sample of CDH survivors (11 patients, aged 8–12 years) with comparable patient characteristics and found a mean IQ of 85, while almost half of the children obtained IQ scores around or more than 1 SD below normal. The discrepancy might be due to the small sample size, which may also have resulted in a potential selection bias.[18] However, despite our, on average, good test results, it has to be noted that participation of CDH patients in special education (12%) was more frequent than in the general Dutch population (4%),[19 20] compatible with the lower HUI single attribute score on cognition, suggesting that CDH patients learn and/or remember school work more slowly than classmates and sometimes require special education.

It has been suggested that neurological abnormalities in CDH patients might (also) be due to CDH repair, since surgery induces a significant inflammatory response, which may provoke cerebral white matter injury. White matter injury, which has been described in infants asphyxiated at term[35] as well as in CDH patients,[17 36] might result in cognitive impairment.[37] In addition, children who underwent surgery in the neonatal period because of oesophageal atresia, imperforate anus or abdominal wall defects, had more learning, emotional and behavioural problems,[38–40] implying that surgery in the neonatal period might play a role.

In this study approximately one fifth of the mothers and the teachers of CDH survivors reported significant emotional and behavioural problems, especially in the internalising broad-band grouping. Sub-analysis showed that according to their mothers, most children had a deviant score on the item somatic complaints without a physical cause. A possible explanation is that parenting a child with a potentially life-threatening congenital anomaly is stressful, since follow-up studies of children with other serious congenital anomalies (eg, oesophageal atresia, abdominal wall defects) also have also found increased levels of emotional and behavioural problems.[39 40] However, this does not explain the relatively high incidence of

Table 3 Results of the CBCL

CBCL score	Mother (CBCL) (n = 28)		Teacher (TRF) (n = 24)	
	n (%) T score ≥63	95% CI difference (SD)	n (%) T score ≥63	95% CI difference (SD)
Total problem score	6 (21%)	−3.6 (6.0)	3 (13%)	−2.4 (8.6)
Internalising problem score	6 (21%)	−3.1 (6.5)	5 (21%)	−2.2 (9.4)
Externalising problem score	3 (11%)	−5.6 (2.9)	2 (8%)	−3.6 (7.8)

CBCL, Child Behavior Checklist; TRF, Teacher Report Form.
95% Confidence intervals (CI) of the difference with norm scores of the mother and teacher (both 50 (SD 10)) were calculated. No significant differences were found when compared to the norm score.

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Table 4 Results of the CHQ-PF50 and the CHQ-CF87 compared to reference populations

CHQ-PF50	CDH patients (n = 33)	Reference population* (n = 353)	p Value	Effect size
Physical functioning	93.4 (15.3)	99.1 (4.3)	<0.001	0.37
Role functioning: emotional/behaviour	98.6 (4.7)	97.9 (7.2)	0.58	0.10
Role functioning: physical	99.5 (3.0)	95.8 (15.6)	0.18	0.24
Bodily pain	90.6 (14.4)	85.7 (17.2)	0.11	0.29
General behavior	80.7 (12.6)	78.5 (13.1)	0.35	0.17
Mental health	79.5 (15.4)	81.4 (12.1)	0.41	0.12
Self esteem	77.7 (11.4)	79.2 (11.0)	0.47	0.13
General health perceptions	66.4 (19.0)	82.9 (13.4)	<0.001	0.87
Parental impact: emotional	77.3 (24.1)	86.3 (15.2)	0.002	0.37
Parental impact: time	93.1 (18.5)	94.0 (13.0)	0.70	0.05
Family activities	89.1 (17.1)	91.5 (11.9)	0.28	0.14
Family cohesion	72.5 (18.6)	72.2 (19.4)	0.93	0.02
Physical summary score	53.3 (6.7)	56.4 (5.7)	0.003	0.46
Psychosocial summary score	52.8 (7.2)	53.2 (6.4)	0.73	0.06

CHQ-CF87	CDH patients (n = 16)	Reference population (n = 475)†	p Value	Effect size
Physical functioning	92.8 (8.6)	96.0 (6.9)	0.07	0.37
Role social limitations: emotional/behavior	91.3 (15.0)	89.4 (17.2)	0.66	0.11
Role functioning: physical	91.7 (14.9)	95.0 (12.9)	0.31	0.22
Bodily pain	80.0 (16.7)	73.5 (22.7)	0.06	0.29
General behavior	79.7 (7.4)	80.9 (10.6)	0.66	0.11
Mental health	80.6 (7.4)	76.5 (15.4)	0.29	0.26
Self esteem	80.5 (12.0)	74.7 (12.2)	0.06	0.47
General health perceptions	63.7 (18.5)	73.5 (16.5)	0.02	0.53
Family activities	87.5 (13.7)	80.0 (17.7)	0.09	0.42
Family cohesion	78.4 (21.0)	70.6 (23.5)	0.19	0.33

CDH, congenital diaphragmatic hernia; CHQ, Child Health Questionnaire.
Values are mean (SD). Effect sizes (d) were calculated as follows: [mean (a)−mean (b)]/largest standard deviation. According to Cohen, effect sizes between 0.2 and 0.5 indicate a small effect, an effect size between 0.5 and 0.8 indicates a moderate effect, and effect sizes of 0.8 or larger are considered to be a large effect.[31]
*Reference population from Raat et al[29]; †reference population from Raat et al.[30]

Figure 2 Effect sizes of all item scales of the CHQ-CF87 and the CHQ-PF50. BP, bodily pain; FA, family activities; FC, family cohesion; GB, general behavior; GH, general health perceptions; MH, mental health; PF, physical functioning; PhSS, physical summary score; PIE, parental impact: emotional; PIT, parental impact; PsSS, psychosocial summary score; REB, role functioning emotional/behavior; RFP, role functioning physical; SE, self esteem.
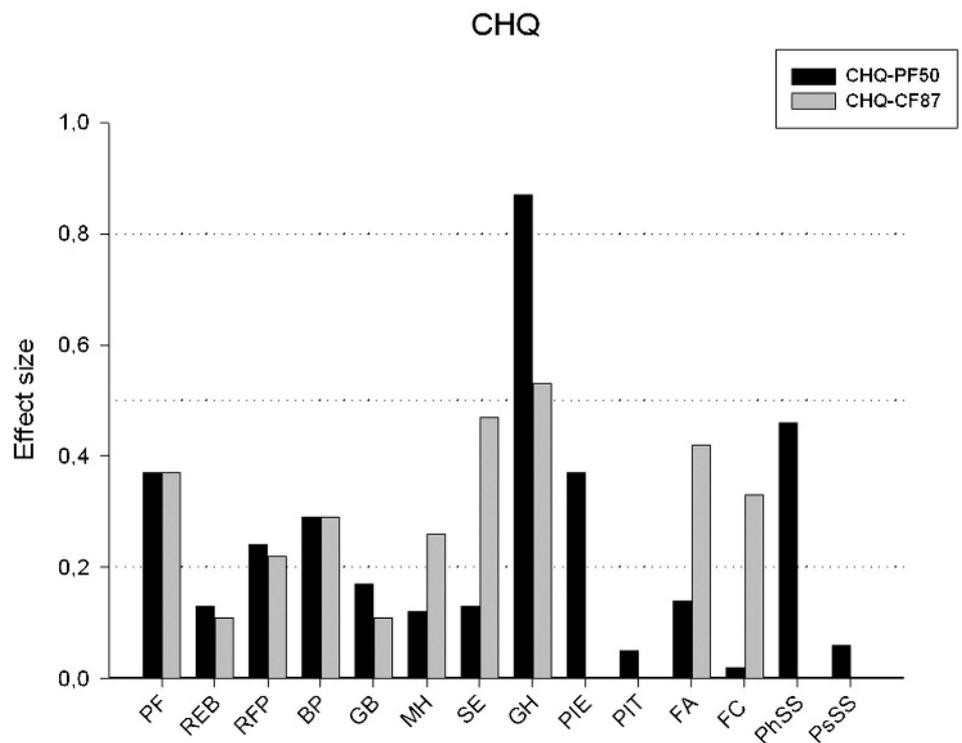
Table 5 Results of the HUI-3

| Attribute | Single attribute utility scores, mean (SD) | | |
	CDH patients, n = 33	Reference population, n = 1435*	p Value
Vision	0.981 (0.050)	0.994 (0.038)	0.05
Hearing	1.000 (0.000)	0.996 (0.037)	0.58
Speech	0.964 (0.092)	0.971 (0.082)	0.58
Ambulation	1.000 (0.000)	0.998 (0.036)	0.70
Dexterity	0.995 (0.031)	0.999 (0.022)	0.36
Emotion	0.984 (0.035)	0.977 (0.067)	0.57
Cognition	0.938 (0.112)	0.970 (0.090)	0.04
Pain	0.986 (0.045)	0.976 (0.076)	0.43
	Multi attribute utility score, mean (SD)		
	CDH patients	Reference population	p Value
	0.906 (0.133)	0.929 (0.124)	0.29

CDH, congenital diaphragmatic hernia.
The HUI-3 multi-attribute utility score (u) is calculated according to the following formula: u = 1.371
$(b1 \times b2 \times b3 \times b4 \times b5 \times b6 \times b7 \times b8) - 0.371$. The letter b represents the single attribute utility score for a specific attribute at a specific functional level.[41]
*Reference population from Raat et al.[42]

problems in the internalising broad-band grouping reported by teachers.

We found that health related quality of life was lower than in other studies.[19][20] CDH patients gave themselves a higher CHQ score than their parents. Whereas CDH survivors only rated the domain general health perceptions significantly lower than the general population, parents of CDH patients also documented a lower physical functioning, general health and physical summary score for their child, but with rather small effect sizes. An explanation could be that CDH patients tend to underestimate their physical complaints and might not fully comprehend their limitations. Another possibility may be that the way CDH patients experience themselves reflects a self-defensive adaptation style. Except for two CHQ domains (general health perceptions and physical functioning) and length of hospital stay, we did not find a correlation between test results and estimation of severity of CDH. This could be due to the relative small sample size. Furthermore, we defined a selected group of variables with most relevant clinical information to be included in the univariate and multivariate analysis. We may have missed associations of perinatal variables that could not be established unequivocally, such as using the best oxygenation index on day 1 to represent hypoxaemia rather than Apgar scores.

Our cohort had similar neonatal characteristics compared to those survivors who did not participate. We therefore infer that the results from our cohort are generalisable to the group of CDH patients that present with early respiratory symptoms (ie, high risk CDH patients).

We recognise that, despite comparing our data with norm scores based on a healthy reference population, a control group is preferable. Another limitation is the broad age range of the studied patients and, as stated above, the relatively small sample size (although larger than in most other reports), which is almost inevitable due to the relatively low incidence of CDH and the high mortality. Furthermore, we are aware that assessment of health related quality of life in children can be difficult, especially for the younger children who might have problems with abstract concepts and language.

In summary, our study demonstrated that, 6–16 years after repair, the perception of the general health of CDH survivors is reduced when compared to the reference population, indicating that parents as well as CDH survivors themselves believe their health is poor and likely to get worse. CDH patients may be at risk for behavioural problems, which is not related to estimation of severity of CDH. This may contribute to school failure and the need for special educational services. In contrast with other studies, we did not find evidence of severe cognitive deficits. This underscores the fact that a long-term prospective cross-sectional follow-up study, with a standardised test battery particularly of cognitive functioning, is mandatory in all CDH patients.

Competing interests: None.

Ethics approval: Ethics approval for the study was granted by the local ethics committee.

Patient consent: Obtained.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Treatment for cryopyrin-associated periodic syndrome

The term cryopyrin-associated periodic syndrome (CAPS) embraces several rare, inherited, inflammatory disorders including the familial cold autoinflammatory syndrome, the Muckle-Wells syndrome and neonatal-onset multisystem inflammatory disorder (otherwise known as the chronic infantile neurologic, cutaneous and articular syndrome). Common features include onset in infancy, severe fatigue, fever, myalgia, anaemia, and inflammation of skin, eyes, bones, joints and meninges. Sensorineural deafness and intellectual impairment may occur and systemic AA amyloidosis develops in about a quarter of all patients. CAPS is caused by mutations in the cryopyrin gene, *NLRP3*, causing overproduction of interleukin-1β. Now (Helen J Lachmann and colleagues. *New England Journal of Medicine* 2009;**360**:2416–25; see also Editorial, ibid: 2467–70) a human anti-interleukin-1β monoclonal antibody (canakinumab) has been shown to be a highly effective treatment for CAPS. Thirty four of 35 patients (four aged 4–16 years) responded completely to a single dose of canakinumab. Of the responders, 31 were then randomised to canakinumab or placebo every 8 weeks for up to 24 weeks. Patients continuing canakinumab remained in remission but disease flares occurred in 13/16 in the placebo group. Concentrations of C-reactive protein and serum amyloid A protein returned to normal on treatment with canakinumab. The incidence of suspected infections was greater with canakinumab and two serious adverse events occurred during treatment, one of urological sepsis and one of vertigo.

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