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Article type : Regular Article

Quality of life was similar in children with congenital diaphragmatic hernia and oesophageal atresia and related to respiratory morbidity

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Short title: Quality of life and thoracic congenital malformations

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/APA.15426

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Key words: congenital diaphragmatic hernia, oesophageal atresia, lung function tests, quality of life, respiratory morbidity.

Abbreviations

QoL, quality of life; CDH, congenital diaphragmatic hernia; OA: oesophageal atresia; FRC, functional residual capacity; FEV1, forced expiratory volume in one second; VC, vital capacity; FEF25-75, forced mid expiratory flow between 25% and 75% of forced vital capacity; TLC, total lung capacity; IQR, interquartile range; VACTERL: Vertebral defects, Anal atresia, Cardiac defects, Tracheo-Esophageal fistula, Renal anomalies, and Limb abnormalities.

ABSTRACT

Aim: To assess quality of life (QoL) in children with congenital diaphragmatic hernia (CDH) and to compare it with oesophageal atresia (OA).

Methods: A cross-sectional study in CDH children (≥ 7 years) was conducted in Lille University Hospital, France, from January 2013 to April 2014. History, lung function (rest, exercise), Pediatric Quality of Life Inventory questionnaires (PedsQoL 4.0) were collected. Data of OA children were previously published.

Results: Fifty-four CDH patients (male: 53%, median age: 11 years, IQR 9-14) were compared to 54 OA patients (male: 61%, median age: 13 years, IQR: 11-15). CDH children had significantly more frequent history of pneumonia (30% versus 11%), exercise limitation (54% versus 35%), and chest deformity (39% versus 11%), 46% had an obstructive pattern and 66% an abnormal cardiopulmonary exercise test. The median PedsQoL total score in children was 81 (IQR 73-90) in CDH and 81 (IQR 72-91) in OA (p=0.8). In CDH, duration of neonatal oxygen therapy, hospitalisation for respiratory disease, exercise limitation, inhaled corticosteroids treatment, chest deformity, abnormal cardiopulmonary exercise test and lower forced expiratory volume in one second were significantly associated with lower QoL scores.

Conclusion: PedsQoL scores remained satisfactory in CDH children with CDH, with no difference compared to OA. Patients with respiratory morbidity and lung function impairment, who displayed lower scores, should be identified in order to optimize their management in reference centres.

Key notes

In congenital thoracic malformations, improving knowledge on respiratory morbidity and its consequences on quality of life remains an important issue.

Whereas quality of life of children with congenital diaphragmatic hernia was close to that described in oesophageal atresia, patients with higher respiratory morbidity and lung function impairment at rest and exercise displayed lower scores.

This population should be identified early and followed in reference centres.

INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a rare congenital intra-thoracic malformation, with an incidence rate of one out of 2,200-3,000 births (1). This malformation is defined as a partial or complete defect of the diaphragm affecting lung development and potentially resulting in pulmonary hypoplasia, pulmonary arterial hypertension and chronic lung disease. CDH is currently diagnosed before birth in most cases (1). Following advances in neonatal intensive care, survival rate has significantly improved, reaching as high as 70% at first hospital discharge (2). However, as a consequence, increased long-term respiratory, digestive and neurocognitive morbidity in survivors has been reported (2–5). Previous studies in children with CDH have shown conflicting results and highlighted the impact of the disease severity, neonatal history, and comorbidities on QoL (6–15). Oesophageal atresia (OA) is another rare congenital disease in which improvement in surgery and neonatal care has also led to a considerable increase in survival rate, currently reaching more than 90% of cases. Substantial long-term morbidity remains, with consequences on QoL (2,16). These two rare malformations share respiratory and digestive long-term consequences, and it is important to identify patients at higher risk and to assess factors impacting their QoL. Reference centres have been created in France for CDH and OA (Reference Centre for Diaphragmatic Hernia and Reference Centre for Chronic and Malformative Conditions of the Oesophagus) and are part of the FIMATHO network (Abdominal-thoracic rare disease Network). Their main objectives are to improve patients' care and follow up, to develop research program and to create a national registry.

The aim of this study was to assess QoL in children with CDH followed at Lille University Hospital Reference Centre, France and to compare it with the previously published results of children with OA followed in the same centre (16). We also investigated the impact of neonatal history, respiratory and digestive outcomes on QoL of patients with CDH.

METHODS

We conducted a cross-sectional follow-up study, approved by the Institutional Review Board of the Société de Pneumologie de Langue Française (French-speaking Pulmonology Society). Written informed consent was obtained from parents or caregivers.

Population

We included all children born between 1995 and 2006, aged seven to 18 years old, with a history of neonatal CDH repair. Data were collected during a scheduled visit with a paediatrician (LD, FdL), occurring between January 2013 and April 2014. We excluded children with a gestational age of less than 32 weeks and those with history of complex congenital heart disease. Patients with congenital or acquired neurological disorders, who were unable to perform lung function tests and to fill in QoL questionnaires, were also excluded.

Children's characteristics

We collected the following data from the medical records: gender, weight and gestational age at birth, including intrauterine growth restriction defined by birth weight below the 10th percentile for gestational age. Regarding CDH, we recorded: side, type of repair (patch or not), history of extracorporeal membrane oxygenation support, duration of neonatal mechanical ventilation and oxygen therapy and pulmonary hypertension requiring medical treatment beyond first hospital discharge. We also collected history of respiratory events up to age four: diagnosis of pneumonia, and hospitalisation for any acute lower respiratory tract infection. Other recorded data were: history of hernia recurrence, gastrostomy tube, and persistent gastro-oesophageal reflux disease defined by prolonged proton pomp inhibitor treatment or surgery.

At the scheduled visit we collected the body mass index, chest wall deformity, static spinal disorder, self-reported exercise limitation, wheezing episodes and maintenance treatment with inhaled corticosteroids during the previous year. Undernutrition was defined by a body mass index Z-score of lower than -2, and overweight by a body mass index Z-score of more than 1.2.

Lung function tests

Lung function tests were performed at scheduled visit, according to the European Respiratory Society guidelines, before and after administration of beta2 agonists (17). We recorded: total lung capacity (TLC), functional residual capacity (FRC), forced expiratory volume in one second (FEV1), vital capacity (VC), FEV1/VC ratio, forced mid expiratory flow between 25% and 75% of forced vital capacity (FEF25-75). All results were expressed as percentages of predictive values for height and weight, except for FEV1/VC ratio (18). An obstructive pattern was defined by a reduction in the FEV1/FVC less than 0.80. A positive response to beta2 agonists was defined as an increase in FEV1 of at least 12%. A restrictive pattern was defined as a reduction in TLC to less

than 80% of predictive value, and a lung hyperinflation as an increase in FRC to more than 120% of predictive value.

The cardiopulmonary exercise test was carried out by bicycle or treadmill according to a standardized protocol (19). Normal testing was retained in case of cardio-circulatory, pulmonary ventilation and gas exchange adaptations within normal ranges. The test was defined as abnormal in case of: hyperventilation (breathing rate > 45 cycles per minute); alteration of breathing reserve (< 15% of predictive value at the end of exercise); hypoxemia (partial pressure of oxygen < - 2 standard deviations); and hypercapnia (partial pressure of carbon dioxide > + 2 standard deviations).

Quality of life

Quality of life was measured with the validated Pediatric Quality of Life Inventory 4.0 questionnaire (PedsQoL) (20,21), consisting of 23 items, evaluating physical, emotional, social and school functioning, and ranked on a reverse 0-100 scale, where a higher number is indicative of a better QoL perception. Questionnaires are adapted to age-range, *i.e.* young children (aged 5-7), children (aged 8-12), and teens (aged13-18). Parents were instructed to complete the questionnaire separately from their child and questions were read out loud to the child by the paediatrician for children under 13 years of age, whereas teens were handed the questionnaire and filled it on their own. For children and teens, response choices in the questionnaire ranged as followed: never (100 points), almost never (75), sometimes (50), almost always (25), always (0). For young children, response choices were presented as faces for the children to circle while the questions were read to them: happy face (never = 100 points), neutral face (sometimes = 50), sad face (always = 0).

Comparison with previously described children with OA

We compared our population to a cohort of children aged 6 years and older with a history of OA repair and followed in the same centre, all of whom had an associated tracheoesophageal fistula, thus corresponding to type III or IV of Ladd classification. We excluded three children with a history of birth before a gestational age of 32 weeks. In this cohort, QoL had been previously assessed with the same questionnaire and published (16). **Statistical analysis**

Categorical variables were reported as numbers and percentages and continuous variables as medians [interquartile range (IQR)]. Normality was assessed graphically and using the Shapiro-Wilk test. Comparisons of CDH and OA children were conducted using chi-square tests or

Fisher's exact test for categorical variables and using Mann-Whitney U tests for continuous variables. In children with CDH, factors associated with QoL (total scores and subscores) were assessed in bivariate analyses using Mann-Whitney U tests for categorical factors and Spearman's correlation for continuous factors. All statistical tests were performed at the two-tailed alpha level of 0.05 using SAS software, release 9.4 (SAS Institute, Cary, North Carolina, USA).

RESULTS

Children's characteristics

Of the 141 children born with CDH in the reference centre, 54 children were included in the present study, 61 had died, 26 were lost to follow up, and those did not display significantly different neonatal characteristics from children included (Table S1). Thus, the mortality rate in our CDH population from 1995 to 2006 was 43%. The main characteristics of the population are reported in Table 1. Hernias were left-sided in 83%, median duration of neonatal oxygen therapy was 10.5 (IQR, 4-27) days, and thirteen (24%) children required oxygen therapy beyond 28 days of life. Nine (16.7%) patients were born prematurely and 12 (22.2%) had a history of intrauterine growth restriction. Two (4%) children had associated congenital anomalies: one child with a Golabi-Rosen syndrome, one with an association of 47XXY and 1q31-3 deletion. In OA, mortality rate was of 6%, and the characteristics of the 54 OA children included in the study are also reported in Table 1 (16). Only two patients had a long-gap defect justifying Livatidis'circular myotomy. Fifteen patients (28%) were born prematurely and 16 (30%) had a history of intrauterine growth restriction, 67% had at least one associated malformation, including congenital heart disease in 21%, and, or, VACTERL association [Vertebral defects, Anal atresia, Cardiac defects, Trachea-Esophageal fistula, Renal anomalies, Limb abnormalities] in 26%. None of them had a history of oxygen supplementation at 28 days of life.

At the time of QoL assessment, children with CDH were younger than those with OA (11 years versus. 13 years, $p<0.01$). History of pneumonia was more frequent in children with CDH (29.6% versus 13.0%, $p=0.03$), so were self-reported exercise symptoms (53.7% versus 35.2%, $p=0.05$) and chest wall deformity (38.9% versus 11.1%, $p<0.01$). Chronic cough was more frequent in children with OA (37.0% versus 16.7%, $p=0.02$) (Table 1).

Lung function tests were available for all children with CDH and 35 (64.8%) children with OA (Table 2). Children with CDH had significantly higher TLC and FRC, more obstructive pattern,

lower pre beta2 FEV1/VC ratio and lower pre and post beta2 FEF 25-75 than children with OA (Table 2). Fifty-three children with CDH performed a complete cardiopulmonary incremental exercise test (bicycle in 36 and treadmill in 17), all of them had normal oxygen saturation at rest, and one third performed a normal exercise test. The main abnormalities observed were: high breathing frequency (n=36, 67.9%), low breathing reserve (n=31, 58.5%) and hypoxemia at peak of exercise (n=9, 18.4%) (Table 2).

Comparison of quality of life

Quality of life questionnaires were filled in by all the CDH patients. The median of PedsQoL total score was 81 (IQR 73-90) in children and 82 (IQR 68-89) in parents, with a strong correlation between total score results of children and their parents (r=0.69, p<0.01) (Table 3). The comparison of PedsQoL scores between CDH and OA children is shown in Figures 1A (children's scores) and 1B (parents' scores). In OA patients, the median of total score was 81 (IQR 72-91) in children and 79 (IQR 69-87) in parents, not different from CDH children (p=0.82 and p=0.37, respectively). In both groups, the highest scores were obtained in physical domain and the lowest in emotional domain.

Determinants of QoL in CDH patients

Table 4 shows the factors affecting QoL in CDH children. A higher duration of oxygen therapy in the neonatal period was associated with a significantly lower total QoL score in children (p=0.04), but not in parents (p=0.07). Furthermore, a duration of more than 27 days was associated to significant lower scores in children (<0.01) and parents (p<0.01). There was no significant difference in patients who underwent extracorporeal oxygenation support, whereas history of pulmonary hypertension requiring medical treatment beyond first hospital discharge was associated with a lower physical score (p=0.04 for both children's and parents' score) (Table S2). Persistent gastroesophageal reflux disease was correlated with lower total PedsQoL score in children (p=0.04) and parents (p=0.05) and so was history of hospitalisation for acute respiratory disease (p<0.01 for children's and parents' scores). History of wheezing episodes in the previous year (p=0.03 for children's scores and p=0.05 for parents' scores), current treatment with inhaled corticosteroids (p<0.01 for children's and parents' scores), chest wall deformity (p<0.01 for children's scores and p=0.02 for parents' scores), and self-reported exercise limitation (p<0.01 for children's score; p=0.02 for parents' score) were associated with significantly lower scores.

Children and parents' PedsQoL scores were correlated with FEV1 levels and children scores for all items were significantly higher in patients with a normal cardiopulmonary incremental exercise test (Table 4, S2 and S3). Finally, an age of less than 13 years at evaluation was associated with a lower physical score (p=0.03 for children's scores, p=0.01 for parents' scores) (Table S2).

DISCUSSION

To our knowledge, our study was the first to compare two populations of children with CDH and OA followed in the same tertiary care centre. In these congenital thoracic malformations, patients require a thoracic repair in the neonatal period and their follow-up is organized in France in designated reference centres, with surgical, medical and paramedical teams with experience in both diseases. Although mortality rates differ, these patients share similarities, especially regarding respiratory, digestive and feeding impairment, and they may have an impact on QoL. We reported that QoL in children with CDH repair, assessed with the PedsQoL generic questionnaire, was not different from a population of children with OA repair (mainly constituted of type III OA, without long gap). Respiratory morbidity assessed by a history of prolonged neonatal support, hospitalisations for acute respiratory disease, chest wall deformity, wheezing episodes, current therapy with inhaled corticosteroids and abnormal lung function at rest and at exercise was associated with lower QoL scores in this population. Identifying the patients at risk for long-term respiratory disease impacting QoL would allow to optimize their management through multidisciplinary approach in a reference centre.

Collectively, total QoL scores were high, with a median total score of 81 in both populations, and similar to those of healthy children as described in previous studies. Varni, *et al* reported a mean total score of 83 in 401 healthy children, 78.7 in 148 children with acute disease sand 77.19 in 367 children with chronic diseases (20). In previous studies of children with CDH repair, conflicting results were described, with some studies showing an overall perception of health QoL significantly lower to that observed in healthy controls (7–9), and other more recent studies showing similar QoL scores in CDH and age-matched healthy controls (10–14). In the present study, children with CDH reported lower QoL scores in the emotional domain. Comparable results were reported by Poley *et al* with Taiqol questionnaire (7) and Michel *et al* with Kidscreen-27 questionnaire (9). Bouman *et al* also described more learning disability, emotional and behavioural problems in 11 CDH children aged eight to 12 years, compared to children from the general population (22).

We confirmed the burden of long-term respiratory morbidity in children with CDH, and especially its impact on QoL (21–23). Interestingly, we observed twice as many pneumonias in early childhood, more self-reported exercise limitation and chest wall deformity in children with CDH than in those with OA. When performing lung function tests, more than half of the children with CDH displayed an obstructive pattern, and one third had pulmonary hyperinflation, whereas only fourteen per cent of children with OA displayed an obstructive pattern, two had a restrictive pattern, and two a pulmonary hyperinflation. Those results are consistent with the description of abnormal lung function parameters after CDH repair, which may worsen over time, showing that this affection is a complex developmental lung disease (1,4,24). On the other hand, children with OA usually have a history of barky cough and a lung function profile of central airway obstruction (low peak expiratory flow; high ratio FEV1/peak flow) or restrictive pattern, with less frequent typical obstructive pattern (low FEV1/FVC) (25,26), especially for children with tracheobronchial fistula (27).

As previously observed in children with AO (16), we confirmed a negative impact of respiratory morbidity parameters on the QoL scores in patients with CDH. These risk factors should be identified early in the course of childhood, with a follow-up of these patients in multidisciplinary reference centres. In CDH, lower QoL scores were associated with increased duration of oxygen therapy in the neonatal period, higher occurrence of hospitalisations for acute respiratory disease, current wheezing episodes, and maintenance treatment with inhaled corticosteroids. Moreover, the overall QoL score in children with CDH was positively correlated with levels of FEV1 and cardiopulmonary incremental exercise test performances. This examination, which can be performed in school-age children and teenagers, provides complementary information on long-term functional respiratory consequences of CDH repair (24). In children with OA, persistent respiratory symptoms, especially barky cough and self-reported dyspnoea at exercise were also associated with poor QoL scores, and so was persistent gastroesophageal reflux disease (16). Although more than a quarter of this population had a VACTERL association, there was no impact of other associated malformations on QoL score (16).

Previous studies have shown the impact of high neonatal respiratory morbidity on the QoL scores of children with CDH (8,9,13). As in our study, Sheikh, *et al* also observed lower scores in parents of children with a history of oxygen therapy need at 30 days of life (10). The impact of extracorporeal membrane oxygenation support has also been studied. In our study, QoL scores

were not significantly different in children who underwent this treatment strategy in the neonatal period, whereas other studies have suggested a trend toward lower QoL scores in children and parents (11,12,14). Interestingly, we also found an inverse correlation between the physical score of QoL and history of persistent pulmonary hypertension after neonatal discharge, which is a known marker of disease severity (1). Finally, we observed that the youngest children in our population, aged less than 13 years, had lower physical scores. This may reflect an increased risk of mid and long-term morbidity due to improved neonatal care management and higher survival rate of newborns presenting with severe forms of CDH.

Our study had several strengths. First, we compared two populations followed in the same tertiary centre, and managed according to the French national guidelines for CDH and OA, specific to each disease with shared similarities. Second, almost all the perinatal characteristics were available for patients with CDH, who were assessed during a scheduled visit, including a specialised medical exam and the completion of the QoL questionnaire in the presence of a paediatrician. In previous descriptions, study populations were smaller, and QoL data were mostly collected using mail and/or phone surveys, without a concomitant clinical evaluation (9-15). One of the main limitations of our study was the absence of a control group with children from the general French population. Thus, we compared our results with published data collected in healthy patients using the same QoL questionnaire (20), but those might be different from children in our geographical area. Nonetheless, our primary aim was to describe QoL scores in children with CDH and to compare them with those of children with another thoracic congenital malformation, followed in the same tertiary centre. In addition, some antenatal data were lacking, preventing us from stratifying our population based on CDH severity before birth. However, we observed that patients requiring oxygen therapy beyond day 28, which is a described marker of chronic lung disease and has been associated with a more severe presentation, had lower QoL scores. Another limitation could be the difference in study periods between patients with CDH and those with OA, possibly entailing a chronological discrepancy. Children with OA repair were indeed born 6 to 13 years earlier than those with CDH repair, and were slightly older at the time of assessment (median age of 13 years versus 11 years, $p<0.01$). Finally, the PedsQoL score that we used remains a generic questionnaire, possibly foreclosing some particularities of CDH and OA. Consistent with this point, Dellenmark-Blom M, *et al* previously highlighted the contribution of a specific health-related QoL questionnaire in patients with OA (28).

CONCLUSION

Our study did not show any difference in overall QoL between children with CDH repair and children with OA repair. However, patients with a more severe disease and higher respiratory morbidity displayed lower QoL scores. This specific at-risk population should be identified early, and managed in reference centres with multidisciplinary approaches, throughout the course of childhood. The cardiopulmonary incremental exercise test appears as an efficient tool to assess respiratory morbidity associated with QOL impairment. Finally, the development of disease-specific QoL questionnaires could improve the assessment of CDH repair impact on QOL (29).

Acknowledgements

We are grateful to Mrs Sophie Charbonnel for her assistance with reviewing the manuscript in English.

Finance

This study did not receive any specific funding.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Table 1: Anamnestic and clinical characteristics of the patients

	Congenital diaphragmatic hernia (n=54)	**Oesophageal atresia (n=54)**	**P**
Female	23 (42.6)	21 (38.9)	0.70
Prematurity	9 (16.7)	12 (22.2)	0.47
Gestational age (weeks)	39 (37- 40)	38 (37- 40)	0.54
Birth weight (g)	3010 (2520-3450)	2675 (2200-2970)	**<0.01**
Intrauterine growth restriction	12 (22.2)	16 (30)	0,4
Left hernia	45 (83.3)		
Age at repair (days)	6 (4-9)		
Mechanical ventilation (days)	7 (3-14)		
Extracorporeal membrane oxygenation	7 (13)		
Patch	24 (44)		
Oxygen duration (days)	10.5 (4-27)		
Oxygen need at 28 days of life	13 (24.1)		
Early childhood (< 4 years)			
Gastro oesophageal reflux disease*	22 (40.7)	20 (37)	0.69
Gastrostomy tube	13 (24.1)	9 (16.7)	0.34
Hospitalisations for acute Respiratory diseases			0.47
• None	34 (63)	28 (53.8)	
• 1 episode	9 (16.7)	8 (15.4)	
• ≥ 2 episodes	11 (20.3)	16 (30.8)	
Pneumonia	16 (29.6)	7 (13)	**0.03**
At visit			
Age (years)	11 (9- 14)	13 (11-15)	**<0.01**
BMI (Z-score)	-0.25 (-1.3-0.7)	-0.5 (-1.4 -1.4)	0.75
Size (Z-score)	0.1 (-0.6-1.0)	0.0 (-1.0 -0.7)	0.31
Undernutrition	6 (11.1)	7 (13)	0.77
Chronic cough	9 (16.7)	20 (37)	**0.02**
Barking cough	NA	13 (24.1)	-
Exercise limitation	29 (53.7)	19 (35.2)	0.05
Wheezing episodes in previous year	9 (16.7)	8 (14.8)	0.79

Current Daily inhaled corticosteroid	12 (22.2)	7 (13)	0.21
Chest wall deformity	21 (38.9)	6 (11.1)	<**0.01**
Static spinal disorder	21 (38.9)	25 (46.3)	0.44

Values are expressed as median (interquartile range 25-75) or frequency (percentage),

Abbreviations: BMI: body mass index, SD: standard deviation; NA: not available

*: GERD defined by prolonged proton pomp inhibitor treatment or surgery (N=5)

Table 2: Lung function tests

	Congenital diaphragmatic hernia (n=54)	**Oesophageal atresia (n=35)**	**P**
TLC	100 (96-111)	92.5 (86- 99)	**<0.01**
FVC	93 (80-104)	85 (81-91)	0.10
FRC pre β2	116 (104-131)	89 (84-97)	**<0.01**
FRC post β2	109 (99-123)	87 (79-97)	**<0.01**
RV/TLC pre β2	118 (108-144)	119 (107-145)	0.76
RV/TLC post β2	111 (95-145)	124 (105-143)	0.54
FEV1 pre β2	87 (72-103)	88 (84-96)	0.71
FEV1 post β2	95 (79-111)	92 (80-98)	0.25
FEV1/VC pre β2	81 (72-87)	85 (83-91)	**<0.01**
FEV1/VC post β2	84 (77-91)	88 (82-92)	0.09
FEF 25-75 pre β2	65 (50-92)	83 (64-98)	**0.04**
FEF 25-75 post β2	83 (60-108)	88 (75-99)	0.56
Hyper-inflation	20 (37)	2 (5.6)	**<0.01**
Obstructive pattern	25 (46.3)	5 (14)	**<0.01**
Normal exercise test	18 (34)		
High breathing frequency	36 (67.9)		
Low breathing reserve	31 (58.5)		
Hypoxemia at peak	9 (18.4)		

Values are expressed as median (interquartile range 25-75) or frequency (percentage). Abbreviations: CDH: congenital diaphragmatic hernia; EA: oesophageal atresia, FVC, forced vital capacity; FEV1: forced expiratory volume in 1 second; FEF 25-75: forced expiratory flow between 25% and 75% of forced vital capacity; TLC: total lung capacity; FRC: functional residual capacity, RV: residual volume.

Table 3: Correlation between PedsQoL scores in CDH children and their parents

	Children	Parents	R	P
Total PedsQoL Score	81 (73-90)	82 (68-89)	0.69	<0.01
Physical health summary score	88 (75-94)	88 (75-94)	0.61	<0.01
Psychosocial health summary score	80 (65-88)	80 (63-90)	0.62	<0.01
- **Emotional score**	70 (55-85)	68 (50-85)	0.60	<0.01
- **Social score**	90 (75-100)	93 (70-100)	0.54	<0.01
- **School score**	80 (70-90)	80 (65-95)	0.73	<0.01

Values are expressed as median (interquartile range 25-75).

R indicates the Spearman correlation's coefficient.

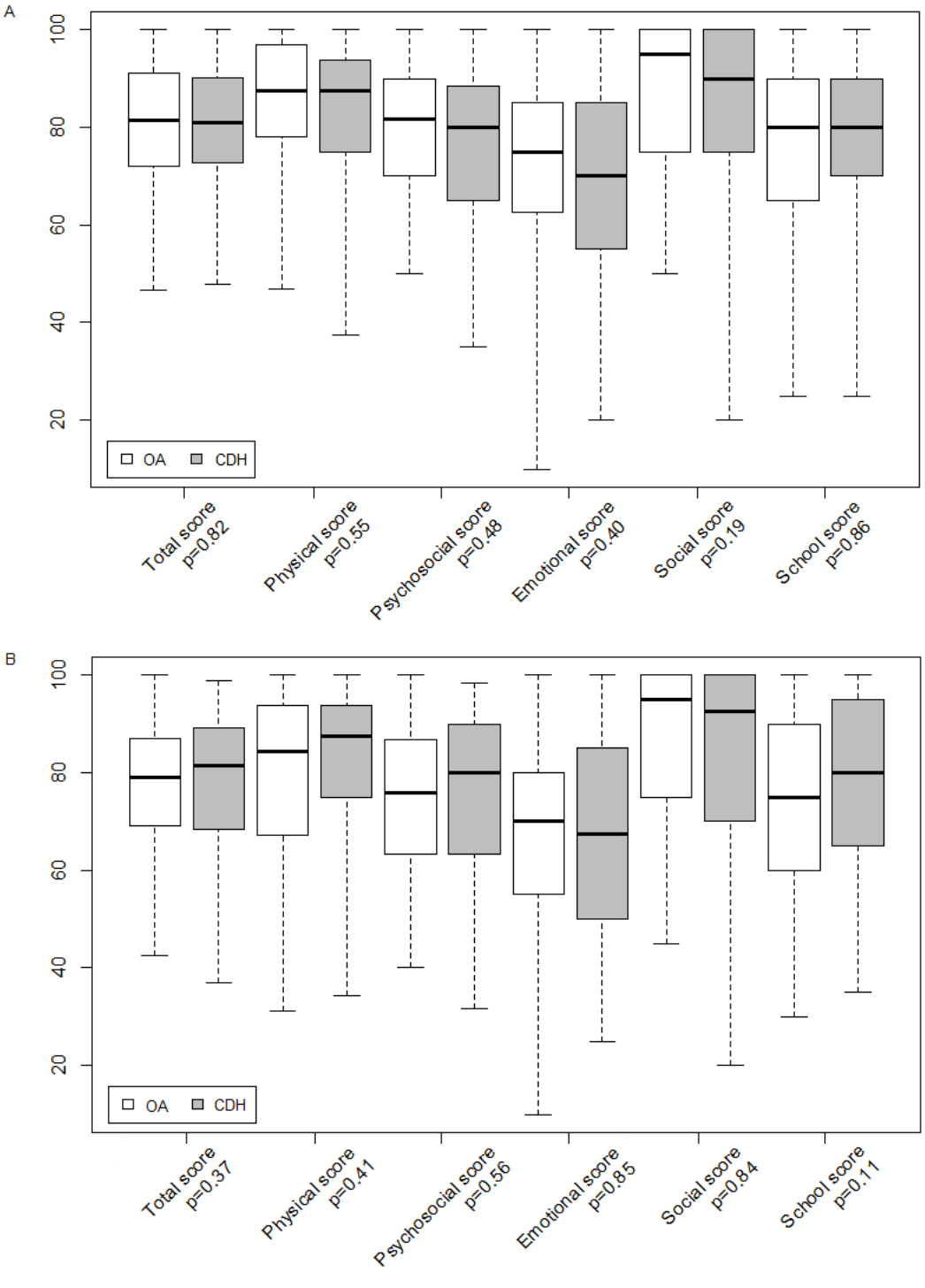
Abbreviations: QoL: Quality of life.

Table 4: Factors associated with total QoL scores in CDH patients (bivariate analysis)

	Children		Parents	
Factors	**Value**	**P**	**Value**	**P**
Patch		0.43		0.59
Yes	80 (74-87)		80 (68-87)	
No	84 (67-92)		84 (67-91)	
Oxygen therapy duration	-0.27	**0.04**	-0.25	0.07
Oxygen therapy duration		**<0.01**		**<0.01**
≤ 27 days	85 (78-91)		85 (76-91)	
> 27 days	69 (52-77)		69 (64-76)	
ECMO		0.14		0.14
Yes	69 (51-88)		69 (64-80)	
No	82 (75-90)		84 (69-90)	
Persistent pulmonary hypertension		0.18		0.25
Yes	78 (64-88)		76 (65-88)	
No	85 (77-90)		84 (76-89)	
History of gastro-oesophageal reflux disease		**0.04**		
Yes	76 (57-87)		76 (67-83)	0.05
No	84 (78-92)		86 (72-91)	
Feeding disorders		0.25		0.12
Yes	77 (68-88)		76 (69-83)	
No	85 (75-90)		85 (71-90)	
Wheezing episodes		**0.03**		0.05
Yes	77 (66-87)		78 (66 -87)	
No	85 (80-92)		87 (76-93)	
Hospitalisation for a respiratory disease before the age of 4 years		**<0.01**		**<0.01**
Never	85 (80-94)		86 (76-93)	
More than once	75 (60-81)		71 (64-82)	
Current daily inhaled corticosteroids		**<0.01**		**<0.01**
Yes	71 (55-78)		69 (63-76)	
No	85 (76-91)		85 (75-91)	
Exercise limitation		**<0.01**		**0.02**
Yes	77 (67-85)		76 (67-85)	
No	86 (80-93)		88 (75-93)	
Chest wall deformity		**<0.01**		**0.02**
Yes	76 (54-85)		74 (64-84)	
No	85 (78-91)		87 (76-90)	

Scoliosis		0.53		0.20
Yes	79 (74-89)		80 (65-87)	
No	84 (71-90)		85 (69-91)	
FEV1	0.33	**0.01**	0.3	**0.03**
Normal cardiopulmonary exercise test		**< 0.01**		**0.04**
Yes				
No	90 (84-94)		88 (77-96)	
	78 (68-86)		80 (67-87)	
Age ≥ 13 years at assessment		0.20		0.18
Yes	86 (75-92)		85 (80-90)	
No	80 (71-87)		77 (67-88)	

Values are median (interquartile range 25-75) or the Spearman's correlation coefficient - FEV1: forced expiratory volume in one second



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