Session 7: Transition to Adulthood and Long term care
Chairs: Hanneke Ijsselstijn & Jonathan Coutts

29th April 09.00 – 11.15

22 High Altitude Simulation Testing in Patients with Congenital Diaphragmatic Hernia

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59 Self-Reported Respiratory and Gastrointestinal Outcomes in Children Managed at Fetal Treatment Centers with Isolated Congenital Diaphragmatic Hernia

Dr Patrice Eastwood[1,7,8], Dr Lennart Van der Veeken[1], Dr Luc Joyeux[1], Dr Laura Salazar[2], Dr Juan Otano[2], Dr Rashmi d'Souza[3], Dr Martin Sidler[4], Dr Francesca Maria Russo[1], Dr Jordi Prat[5], Professor Paolo de Coppi[3], Professor Eduard Gratacós[2], Professor Jan Deprest[6]
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88 Neuropsychological outcome at five years of age in survivors of congenital diaphragmatic hernia

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High Altitude Simulation Testing in Patients with Congenital Diaphragmatic Hernia

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Background: Congenital diaphragmatic hernia (CDH) is a life-threatening malformation, associated with lung hypoplasia, V/Q mismatch, abnormal lung function, and pulmonary hypertension. Many patients receive care in specialty centers at birth and may require air travel to return home after initial hospitalization, and for subsequent follow-up care. Premature infants have been reported to have significant hypoxemia during airflight and may require supplemental oxygen. Noting the potential risk of hypoxemia in the CDH population, patients are offered screening prior to air travel in our center. This study describes our center's experience with altitude testing among CDH patients.

Methods: A single center retrospective cohort study was performed, analyzing CDH patients who underwent High Altitude Simulation Test (HAST) from 1991-2019. Patients were tested when flight was anticipated. HAST simulates increased altitude by reducing oxygen tension to an FIO2 of .15. The patients that required supplementation were challenged on their baseline oxygen requirement. We assessed safety to fly based on maintaining an oxygen saturation above 90% and 94% if pulmonary hypertension was present. Supplemental oxygen was added or increased to maintain the goal.

Results: Twenty patients were included in the study (See Table). Only 30% passed on their first attempt. 50% eventually passed, after an average of 3.2 additional attempts over 1.8 years. No patients passed initially who had a history of ECMO support, diaphragmatic agenesis, or elevations of right ventricular pressure on echocardiogram. All patients achieved a safe spO2 with supplemental oxygen.

Conclusions: Patients with CDH are at high risk of significant hypoxia when exposed to the hypobaric nature of air travel and may require oxygen supplementation. Factors predicting failure seem to correlate with disease severity. This study suggests that CDH patients should be screened and counseled regarding the risk of flying and need for supplemental oxygen to ensure safe air travel.

Images

High Altitude Simulation Test (HAST)	**Total Population (20)**	**Initial Pass- 30% (6)**	**Eventual Pass -50% (10)**
Sex	13 (65%) male 7 (35%) female	5 (83%) male 1 (17%) female	6 (60%) male, 4 (40%) female
Birth Weight (kg), Gestational age (weeks)	2.96, 37.8	2.68, 36.6	2.95, 37.6
Elevated Right Ventricular Pressure on Echo Within Month of HAST	1 (5%)	0	0
Side of Defect (n=20)	15 (75%) Left 5 (25%) Right	10 (50%) Left 10 (50%) Right	7 (70%) Left 3 (30%) Right
Size of Defect (n=18)	3 (16.7%) A 5 (27.8%) B 7 (38.9%) C 3(16.7%) D	1 (16.7%) A 3 (50.0%) B 2 (33.3%) C 0% D	1 (10%) A 3 (30%) B 4 (40%) C 2 (20%) D
History of ECMO	9 (45%)	0	3 (30%)
Oxygen supplementation at 30 days of age	16 (80%)	3 (50%)	6 (60%)
Oxygen requirement at time of test	6 (30%)	1 (16.7%)	3 (30%)
Age at first HAST, age at passing HAST (months)	33.4	5.8	5.6, 14.67

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Self-Reported Respiratory and Gastrointestinal Outcomes in Children Managed at Fetal Treatment Centers with Isolated Congenital Diaphragmatic Hernia

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Background: Medium term outcomes in CDH patients managed at fetal treatment centers are under reported. We evaluated our population through age-specific self-reported respiratory and gastro-intestinal outcomes correlating these with perinatal variables.

Methods: This multi-centric prospective study surveyed families with isolated left-sided CDH children surviving >1 year of age. Families received age-specific validated questionnaires for gastro-intestinal and respiratory outcomes. Perinatal data included lung size (O/E LHR %), fetal intervention, gestational age (GA) at delivery, birth weight, pulmonary hypertension, ventilator days, O2 >28 days, patch use and time to full feed. Respiratory scores were classified categorically or as continuous data; gastro-intestinal scores as continuous data. Univariate analysis was used to look for predicting factors with O/E LHR% correlated to self-reported scores. For sensitivity, participants and non-participants were compared.

Results: Three-hundred and forty-two families were surveyed of whom 152 (44%) responded. Participating mothers were older ($P<0.05$) but had similar time lapse from the index pregnancy, rates of fetal intervention, numbers of inborn babies and gestational age of delivery. One hundred and thirty-nine patients completed the survey, the majority being <8 years old (89%). Respiratory score was age group dependent, children under 5 years having higher scores than older children. O/E LHR was less likely to predict for higher respiratory scores with increasing age. No predictors were identified for higher gastro-intestinal scores.

Conclusion: Medium self-reported respiratory and gastro-intestinal outcomes in CDH patients managed at a fetal surgery center are similar regardless of the degree of pulmonary hypoplasia in utero. Furthermore, ageing appears to be associated with less respiratory symptoms.

Images

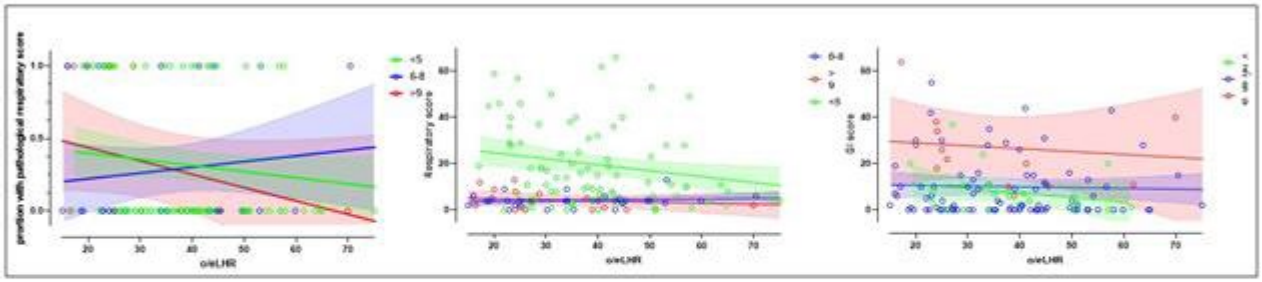

Figure showing correlation between *a) children with a pathological respiratory score b) absolute respiratory score c) GI score and* O/E LHR

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Cardio-pulmonary Exercise Testing in Scottish children and adolescents with repaired congenital diaphragmatic hernia

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Background:
Children and adolescents with congenital Diaphragmatic Hernia (CDH) can present with exercise intolerance which could be secondary to impaired pulmonary development. Cardio-Pulmonary Exercise Testing (CPET) measures aerobic capacity and the cardiovascular, ventilatory and gas exchange responses to incremental maximal exercise. By doing so, It can help identify the physiological or pathophysiological cause of exercise intolerance.
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Methods
Children attending our CDH clinic had CPET testing routinely. An incremental ramp protocol using a cycle ergometer was performed. The ramp chosen was based on the predicted peak power output to achieve a test time of between 8-12 minutes. Descriptive statistics were analysed.

Results
24 patients performed a technically adequate CPET. Mean age was 14.1 ± 2.2. Summary statistics are shown in table 1. The majority (16 patients; 67%) had a reduced aerobic capacity defined as a VO2peak < 85% of predicted. 7 of these and another 3 who had a normal aerobic capacity, had evidence of ventilatory limitation consistent with abnormal lung growth and development. 7 patients had a reduced aerobic capacity despite normal physiological responses to exercise which is most likely due to deconditioning. Only 2 of the patients who had ventilatory limitation also showed impaired gas exchange as shown by an oxygen desaturation to <94% at peak exercise.

Conclusion
Impaired lung development and growth in CDH caused ventilatory limitation on CPET testing in less than half the children attending our clinic. Deconditioning was shown to contribute to exercise intolerance in some children. Patients with or without ventilatory limitation can improve aerobic performance with participation in physical exercise and increasing cardiovascular function, thereby alleviating symptoms of breathlessness. Formal assessment with CPET and targeted advice is likely to improve long term quality of life in young people with CDH.

Images

Parameter	Mean	SD
VO_{2peak} (% predicted)	81	17
Ventilatory Threshold (% of pred VO_{2peak})	45	9
Peak Heart Rate (bpm)	189	10
Respiratory Exchange Ratio	1.21	0.10
End test S_pO_2 (%)	97	2
Ventilatory Efficiency slope (V_E/VCO_2)	29.9	3.6

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Longitudinal evaluation of health status and quality of life in school-aged children with congenital diaphragmatic hernia

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Background
To evaluate disease burden in children with congenital diaphragmatic hernia (CDH), long-term follow-up should include routine assessment of self-perceived health status (HS) and quality of life (QoL). We aimed to longitudinally evaluate self-reported HS and QoL in 8- and 12-year-old survivors of CDH.

Methods
We included 133 children born between 1999 and 2013 who joined our standardized follow-up program. Self-reported HS and QoL at the ages of 8 and 12 were routinely assessed using the internationally validated Pediatric Quality of Life Inventory (PedsQL) and the Dutch-Child-AZL-TNO-Quality-of-Life (DUX-25), respectively. Longitudinal evaluation of total scores was performed using linear mixed model analyses. In addition, we compared these scores to sex- and age-specific normative data.

Results
See Table 1 for patient demographics. Between ages 8 and 12, boys experienced a significant decline in HS (mean difference (md) -7.15, $p < 0.001$). Self-reported QoL tended to improve in both boys and girls. Compared to healthy peers, girls with CDH reported significantly lower HS at 8 (mean (M) = 77.94, standard deviation (SD) = 10.25, $p = 0.012$) and 12 years of age (M = 74.30, SD = 11.94, $p < 0.001$), whereas boys only reported significantly lower HS at 12 years of age (M = 71.63, SD = 13.98, $p < 0.001$). Self-reported QoL was significantly lower in girls at 8 (M = 77.03, SD = 9.36, $p = 0.003$) and 12 years of age (M = 78.73, SD = 9.77, $p = 0.015$) compared to healthy peers.

Conclusions
Children born with CDH experienced a decline in HS over time, whereas QoL tended to improve. At both 8 and 12 years of age, self-reported HS and QoL were below normal. Routine measurement of both outcomes may contribute to a better understanding of disease burden.

Images

	Participants (n=133)
Male	82 (61.7)
Gestational age in weeks	38.7 (38.0-39.6)
Birth weight in grams	3000 (2800-3470)
Preterm birth	16 (12.0)
Small for gestational age [A]	29 (21.8)
ECMO	33 (24.8)
Side of hernia	
Left	115 (86.5)
Right	18 (13.5)
Bilateral	0
Type of repair	
Primary	44 (33.1)
Patch	88 (66.2)
Unknown	1 (0.8)[B]
Length of ICU stay in days	21 (12-44)
Duration of anesthetic exposure ≤24 months in minutes	271 (181-423)
Maternal educational level	
Low (ISCED 0–2)	8 (6.0)
Middle (ISCED 3–4)	46 (34.6)
High (ISCED 5–8)	57 (42.9)
Unknown	22 (16.5)

Table 1. Demographic variables of participating children with congenital diaphragmatic hernia (CDH). Data are presented as n (%) or median (IQR). ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit, ISCED = International Classification of Education (as a proxy for socio-economic status). [A] Birth weight <10th percentile. [B] Surgery elsewhere.

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Neuropsychological outcome at five years of age in survivors of congenital diaphragmatic hernia

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Background

Neurocognitive deficits in eight-year-old children with congenital diaphragmatic hernia (CDH) may contribute to school problems (Schiller, 2018). Yet, timing and onset of these problems is currently unknown. We therefore aimed to evaluate intelligence, inhibition, and memory together with possible determinants in preschool children with CDH.

Methods

All eligible five-year-old children born with CDH (2010-2015), who participated in our structural prospective longitudinal follow-up program, were included. We used the Wechsler Preschool and Primary Scale of Intelligence-III (WPPSI-III, normative mean (SD) 100 (15)) to assess intelligence, two subtests of the Kaufman Assessment Battery for Children (K-ABC) for verbal and visuospatial memory, and NEPSY-II to assess inhibition (mean 10 (3)). In univariate analyses, the following determinants were tested: being inborn (yes/no), birthweight, duration of PICU stay, maximal vasoactive inotropic score, laparotomy (yes/no), primary repair (yes/no), and sociodemographic background (maternal education level).

Results

We included 63 children, who were assessed with at least one test. Intelligence was normal in our study population (n=51): total IQ=103.4 (15.7) (p=0.13, compared to norm). Score for verbal memory was within normal ranges (n=61): 10.2 (2.8) (p=0.61), and significantly higher for visuospatial memory=11.4 (2.6) (p<0.01). As for NEPSY-inhibition (n=52), the score was 10.5 (2.2), (p = 0.10). The determinants studied revealed no significant association with neurocognitive outcomes, except for educational level of the mother, which was associated with total IQ (B=5.72, CI 3.23 – 8.20, p < 0.01).

Conclusions

At five years of age, neuropsychological outcome was on average normal in CDH patients. The selected determinants appeared not to be predictive of neurocognitive functioning. Other, more neurodevelopmentally specific determinants, for instance obtained by brain imaging, may be more appropriate at this age. Future research should look for more sensitive assessments in a structured follow up program, in order to predict and possibly prevent neurocognitive problems in later childhood.

Images

Table 1. Baseline characteristics	n=63	
Boys	38	(60.3)
Birthweight, grams	3000[d]	(1900 - 3900)
Gestational age, weeks	38.3[a]	(34.9 - 42.0)
Inborn	47	(74.6)
Left sided defect	56	(88.9)
O/E LHR %	47.9*	(24-89.1)
Age at surgery, days	3	(1-14)
Primarily closed	23	(36.5)
Thoracoscopic repair	36	(57.1)
Initial ventilation, days	8	(1-258)
Initial PICU stay, days	16	(1-274)
Anesth. procedures < 24 months	2	(1-13)
Sepsis	13	(20.6)
Cardiac malformations	7	(11.1)
Inhaled nitric oxide treatment	21	(33.3)
Maximum VIS	10.3	(0-67.9)
Veno-arterial ECMO	6	(9.5)
Time on ECMO, hours	183	(85-561)
Abnormal cranial ultrasound	7[d]	(11)
Dutch ethnicity	50	(79)
Maternal education level		
Low (ISCED 0-2)	3	(4.8)
Middle (ISCED 3-4)	16	(25.4)
High (ISCED 5-7)	29[e]	(46)
Not available	15	(23.8)

Data presented as median (range), or n (%). Inborn: born in our hospital or another CDH center, O/E LHR: observed to expected lung to head ratio, PICU: pediatric intensive care unit, VIS: vasoactive inotropic score, ECMO: extracorporeal membrane oxygenation

[a] 1 missing data, [b] 2 missing data, [c] 3 missing data, [d] 5 missing data , [e] 15 missing data,

*measured only in 42 out of 47 inborn patients